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NOVELTIES IN CARDIAC RESYNCHRONISATION THERAPY

4856 | BEDSIDE
Transseptal endocardial left ventricular lead implantation after failed CRT implantation- long term results

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Introduction: CRT implantation is a well estabilished therapy in chronic heart failure patients. Transvenous left ventricular (LV) lead positioning might be challenging or in some cases impossible.
Objectives: The aim of this study was to investigate the effectiveness and safety of transseptal endocardial left ventricular lead implantation (TELVLI) in severe heart failure patients, and evaluate the long term follow-ups of the patients.
Methods: TELVLI was performed in 35 patients (30 men, 64±6 years, NYHA III-IV stage). Transseptal (TS) puncture was performed via the femoral vein. Intracardiac ulrasound was used to guide the puncture in 25 pts. The site of the puncture was dilated with a 6mm (3 pts), later with an 8 mm balloon (32 pts). After the puncture of the left subclavian vein, an electrophysiological deflectable CS catheter was introduced into the CS sheath. The CS catheter was used to reach the left atrium and the left ventricle through the dilated transseptal puncture hole. At the latest LV activation site 65 cm active fixation bipolar lead was screwed into the LV wall, at the site of the latest activation.
Results: The lead was fixed in the left ventricle in all cases with good pacing threshold (0,84±0,4 V;0,4 ms). Puncture complication, pericardial effusion was not observed. Because of intraoperatively started anticoagulation, pocket haematoma was observed in three (9%) and needed evacuation in one case (3%). Follow-up was longer than one month in 34 patients [38 (22–49) months]. Significant improvement of NYHA was observed in all but one case (97%), at the first month control LV EF was 30±9% vs 38±6%. Early lead dislocation was noticed in two cases (6%), reposition was performed using the original puncture site in one, and transvenous implantation was succesfully carried out in the other case. Explantation of the system was necessary because of pocket infection in four cases (11%), in two of these cases TELVLI was carried out succesfully 3 months later, in one patient 22 months later. All patients were maintained on anticoagulation therapy with INR between 2–3. No thromboembolic complication was noticed during the follow up. 13 patients were lost, one of them died five years after the implantation in renal failure, the other patient died in malignant tumor 4 years after the implantation, 11 patients died due to the progression of the heart failure in average 16 months after the implantation.
Conclusion: TELVLI approach might be a very promising alternative technique of the surgical epicardial procedure when transvenous implantation could not be applied.

4857 | BEDSIDE
Cardiac resynchronization therapy improves left ventricular volumes in patients with ejection fraction between 36 and 50% with left bundle branch block: MIRACLE EF study

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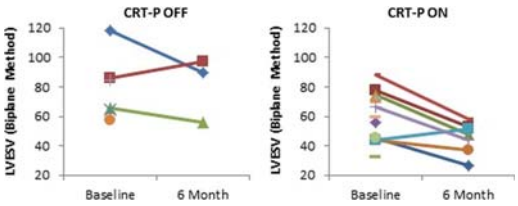
Background: Cardiac resynchronization therapy (CRT) improves clinical status as well as left ventricular (LV) volumes in patients with QRS >120ms and left ventricular ejection fraction (LVEF) <35%. However, preliminary data suggest similar benefits might be realized in heart failure patients with EF >35% and increased QRS duration. The MIRACLE EF trial was designed to test this hypothesis. However, the study was stopped prematurely due to slow enrollment. Here we present LV volume data on those who qualified.
Methods: Major inclusion criteria were LVEF >35% and <50%, QRS >130 ms, and left bundle branch morphology. Patients were randomized 2:1 to treatment with CRT-P vs. Control (implanted, LV lead turned OFF). In addition to clinical assessments, echocardiograms were obtained at baseline and at 6 months.
Results: Twenty-six patients were successfully implanted with a CRT pacemaker and randomized (19 CRT, 7 Control). Of these patients, 10 (7 CRT, 3 Control) completed the 6-month visit with paired echocardiographic data. The median LVEF at baseline was 45% in CRT and 46% in Control. No significant increases in LVEF over time were observed. The CRT patients, however, showed reductions in median LVESV (28% decrease) and LVESVi (25% decrease). (Figure) In contrast, the Control patients showed no changes in LVESV (4% increase) or LVESVi (8% decrease). Similar data are seen with average values. The change in LVESV over time was significantly different between groups (p=0.05) but the change in LVESVi was not (p=0.11).
Conclusions: In a small sample of patients with HF symptoms, LBBB and LVEF between 36 and 50%, CRT-P appeared to reduce LV volumes compared with control. The hypothesis that CRT can benefit selected HF patients with LVEF >35% should be tested.



Cardiac volumes

4858 | BEDSIDE
Cardiac resynchronization therapy in the elderly - is there an indication for a defibrillator?

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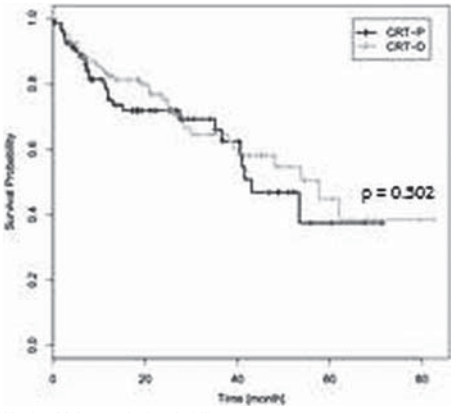
Introduction: Cardiac resynchronization therapy (CRT) is an effective treatment option for heart failure in elderly patients, but the additional benefit of an implantable defibrillator (ICD) in these patients is not evidenced.
Purpose: To evaluate the impact of an ICD on all-cause mortality in elderly patients undergoing a CRT device implantation.
Methods: Patients at the age of ≥75 years who underwent implantation of either a CRT-pacemaker (CRT-P) or CRT-defibrillator (CRT-D) were identified out of hospital records. Only patients with a Class I or IIa indication for CRT and the primary prophylactic implantation of an ICD due to a severe impairment of the left ventricular ejection fraction (LV-EF) were included in the analysis. Patient characteristics, procedural data and all-cause mortality were compared between the two groups.
Results: Between January 2008 and August 2014 two-hundred forty-five seniors were implanted with a CRT device in our centre, whereof 80 patients with CRT-P and 97 patients with CRT-D represent the two study groups. Patients in the CRT-P group were more often females (44 vs. 25%; p<0.001), older (82.6±4.5 vs. 77.8±1.9 years, p<0.001), had a better LV-EF (29,6±5,9 vs. 27,4±6,0%; p=0.015) and narrower QRS-complexes (150±19 vs. 158±18ms; p=0.025). During a mean follow-up of 25.0±19.3 months 62 (35%) of the 177 study patients died, 28 (35%) in the CRT-P and 34 (35.1%) in the CRT-D group, respectively. The Kaplan-Meier analysis of survival probability showed no significant difference (p=0.502) between the groups (Figure). Inadequate ICD interventions were recorded in 4 patients (4.1%) and 5 patients (5.2%) received adequate therapies in the CRT-D group.



Kaplan-Meier survival probability

Conclusion: An additional ICD has no impact on survival in elderly patients implanted with a CRT device.

4859 | BEDSIDE
Relationship between indices of left ventricular lead electrical position in spontaneous rhythm and right ventricular pacing: implications for optimization of cardiac resynchronization therapy

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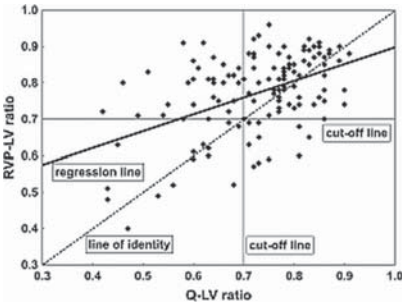
Purpose: Left ventricular (LV) electrical delay measured from the beginning of the QRS complex to the local LV lead electrogram (EGM), normalized by QRS duration (Q-LV ratio), was found to be a strong and independent predictor of short-term response to cardiac resynchronization therapy (CRT), heart failure events and mortality. We investigated relationship between Q-LV ratio and similar index obtained during right ventricular pacing (RVP-LV ratio).

Methods: We prospectively collected ECGs and EGMs in 133 consecutive patients (aged 66±10 years; 72% males; 56% nonischemic cardiomyopathy; LVEF 26±5%, 81% true-LBBB) with native non-RBBB QRS morphology undergoing CRT implant. Recordings of spontaneous rhythm and RV midseptum paced rhythm were edited, signal-averaged and measured by electronic calipers.
Results: The LV lead position was characterized by the Q-LV ratio of 0.73±0.11 and RVP-LV ratio of 0.77±0.11. Native QRS width (180±21 ms) was shortened by 14±28 ms during biventricular pacing. There was significant but weak correlation between Q-LV and RVP-LV ratios (r^2=0.23, p<0.0001, Figure). With a cut-off value for both Q-LV and RVP-LV ratios >0.70, defining adequate electrical LV lead positioning, 67% of patients with suboptimal Q-LV ratio had optimal RVP-LV ratio and 13% of patients with optimal Q-LV ratio had suboptimal RVP-LV ratio.



Q-LV versus RVP-LV ratios correlation

Conclusions: While observational studies found association between Q-LV ratio and CRT outcome, this measure may not be optimal for LV lead positioning because intrinsic atrioventricular conduction is not maintained during biventricular pacing. Therefore, RVP-LV ratio may better reflect the interlead electrical distance and deserves further evaluation.

4860 | BEDSIDE
Prognostic role of right ventricular function in patients with heart failure undergoing cardiac resynchronization therapy

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Introduction: Since 20–40% of patients undergoing CRT do not respond to therapy, the identification of potential factors predicting response to CRT is a relevant research topic. Recent evidence suggests a possible association between right ventricular function and response to CRT.
Methods: We analyzed data from the CRT MORE registry, about patients who received CRT according to current guidelines (NYHA class II-IV, optimal medical drug therapy, Left ventricular ejection fraction (LVEF) ≤35% and a QRS duration ≥120ms) from April 2013 to December 2013. Response to therapy was defined as an absolute improvement in LVEF ≥10% and as a decrease of at least 15% in left ventricular end-systolic volume (LVESV) on echocardiography at 6 months.
Results: A total of 163 patients with a baseline estimation of tricuspid annular plane systolic excursion (TAPSE) and echocardiographic examination at 6 months follow up were considered for this analysis (age 70±10 years, male gender 71%, ischemic etiology 37%, history of atrial fibrillation 27%, NYHA class II in 46% of patients, spontaneous QRS duration 160±25ms, left bundle branch block 85%). Baseline echocardiographic parameters were: LVEF 28±6%, Mitral regurgitation grade ≥3 in 31% of patients, TAPSE 18.8±5mm, LVESV132±48 ml. On the basis of receiver operating characteristic curve analysis of TAPSE, the cutoff that best predicted improvement in LVEF (sensitivity 60%, specificity 61%) and LVESV (sensitivity 69%, specificity 52%) was 17mm. Stratifying patients according to the TAPSE, LVEF improved ≥10% in 49% of patients with TAPSE ≤17mm (versus 30% in patients with TAPSE >17mm, p=0.019) and LVESV decreased ≥15% in 79% of patients with TAPSE ≤17mm (versus 59%, p=0.008). At multivariate analysis, TAPSE ≤17mm was independently associated with LVESV improvement (OR 2.26, 95% CI 1.1 to 4.6, p=0.024), together with ischemic etiology (OR 0.44, 95% CI 0.22 to 0.89, p=0.022). TAPSE ≤17mm was the only predictor of improvement in LVEF (OR 2.08, 95% CI 1.1 to 3.9; p=0.024).
Conclusions: Baseline signs of right ventricular dysfunction suggest possible remodeling after CRT. A TAPSE value of 17mm was identified as a good cutoff for predicting improvement in both LVESV and LVEF.

4861 | BEDSIDE
Different long-term outcome depending on cardiac rhythm in heart failure patients undergoing cardiac resynchronization therapy

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Purpose: The aim of the study was to assess the prognostic impact of heart rhythm (sinus rhythm – SR/ atrial fibrillation – AF) with and without low biventricular pacing percentage (CRT%) in heart failure (HF) patients undergoing cardiac resynchronization therapy (CRT).
Methods: A single centre cohort of 304 consecutive patients implanted with CRT-D and subsequently monitored via remote monitoring was divided into four groups depending on rhythm type (SR – sinus rhythm vs AF – atrial fibrillation) and the mean CRT%:
– Group 1 – SR and CRT%≥95% (n=132; 43.4%)
– Group 2 – SR and CRT%<95% (n=12; 3.9%)
– Group 3 – AF and CRT%≥95% (n=95; 31.3%)
– Group 4 – AF and CRT%<95% (n=61; 20.1%)
Results: The mean CRT% in Group 1–4 was 98.6%, 88.8%, 97.5%, 85.5%, respectively. Patients with SR and low CRT% had higher mortality than AF subjects with high CRT% (33.3% vs 8.4%, P=0.01). Within subgroups of patients with high or low CRT% mortality rates were similar in SR and AF subjects (9.1% for Group 1 vs 8.4% for Group 3, P=NS; 33.3% for Group 2 vs 26.2% for Group 4, P=NS). Mortality rates for both group of patients with low CRT% were higher than subjects with high CRT% (Group 2 vs Group 1: P=0.01; Group 4 vs Group 3: P=0.002). The main cause of CRT% lost in SR group were premature ventricular contractions (81.8%).
Conclusion: Irrespectively from underlying rhythm (SR, AF), high CRT% seems to be crucial to improve the prognosis in HF patients undergoing CRT. Long-term survival of patients in SR and low CRT% is worse than those with AF and high CRT%.

4862 | BEDSIDE
Effect of apical and non-apical right ventricular lead position on cardiac resynchronization therapy outcome

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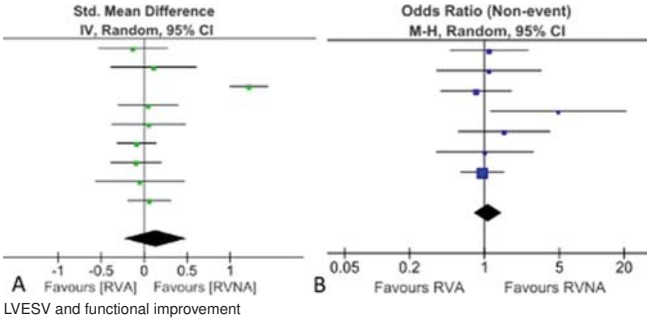
Introduction: Cardiac resynchronization therapy (CRT) has been shown to improve outcomes in patients with heart failure (HF). The optimal site of right ventricular (RV) stimulation in CRT has not been established. We aimed to conduct a meta-analysis of randomized controlled trials and observational studies comparing the mid- and long-term effects of RV apical (RVA) and non-apical (RVNA) pacing on CRT outcome.
Methods: We systematically searched the Cochrane library, EMBASE, and MEDLINE databases for studies assessing RVA versus RVNA pacing in CRT with regards to left ventricular end-systolic volume (LVESV) reduction and functional status improvement (defined as ≥1 New York Heart Association class improvement). Effect estimates [standardized mean difference (SMD) and odds ratio (OR) with 95% confidence intervals (CI)] were pooled using random-effects models.
Results: Twelve studies comprising 2,670 patients (1655 with an apical and 1015 with a non-apical RV lead position) were included. In meta-analyses, LVESV reduction and functional status improvement were similar in patients with RVA and RVNA pacing (SMD 0.13, 95% CI: −0.24 to 0.50, p=0.48; OR 1.08, 95% CI: 0.81 to 1.45, p=0.60, respectively).



LVESV and functional improvement

Conclusion: Our meta-analysis suggests that the beneficial effect of CRT on LV remodeling and functional status is similar irrespective of RV lead location

4863 | BEDSIDE
Targeting the LV pacing site by means of electrical delay and LVdP/dtmax may predict the long term clinical outcome in CRT patients

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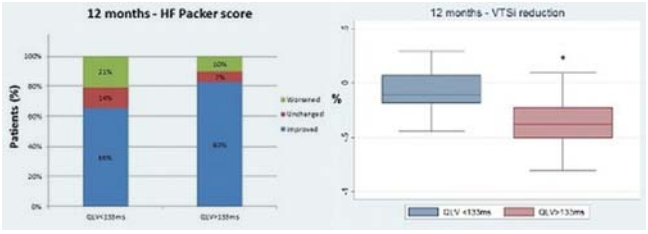
Background: Targeting the optimal LV pacing site is decisive for CRT effectiveness.

Purpose: The aim of the study is to assess the 12 months clinical response of CRT patients whose LV lead was positioned, after the systematical screening of all the available pacing sites, according to the criterion of the maximum electrical delay (Q-LV) and the highest response in LV dP/dtmax.
Methods: 58 patients (43 male, 35 with ICM, 34 with LBBB) underwent to CRT implantation. All available tributary veins of the coronary sinus were tested, on average 3.2±0.7 different veins and 7.2±1.8 pacing sites. The Q-LV interval and the hemodynamic effects by invasive measurement of LV dP/dtmax at baseline and during pacing were evaluated at each site. In 57/58 (98%) patients the highest LV dP/dtmax coincided with the maximum Q-LV interval and the corresponding pacing site was selected as the target site.
Results: At 12 months follow up, the HF clinical composite score (Packer) was evaluated in 57 patients. 42/57 (78%) patients improved their clinical status, 6/57 (11%) unchanged, 9/57 (16%) worsened (4 died, 5 were hospitalized because of worsening of HF). Mean LV EF was 30±6% at baseline, and 40±11% at follow up ($p<0.001$). Mean ESVi was 73±29 mL/m^2 and 59±28 mL/m^2, at baseline and at follow up respectively ($p<0.001$). The patients whose target site was associate with a higher Q-LV (median value 133 ms) reported better 12 months clinical response (figure).



Conclusions: In our experience, with advanced NYHA class patients, the acute optimization of LV lead target site, by means of a systematical screening of local electrical delay and LV dP/dtmax, resulted in 74% of patients who responded clinically to CRT. A subanalysis in patients with higher QLV reported 83% of responders.

4864 | BEDSIDE
Impact of collagen turnover markers on echocardiographic response and mortality after CRT-D implantation in TRUST-CRT study population

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Introduction: Cardiac resynchronization therapy (CRT) was showed to effectively reduce mortality and provide the symptomatic relieve for subpopulation of heart failure patients with LBBB and wide QRS. However despite of continuous efforts CRT is still burdened with a relatively high proportion of unresponsiveness. The aim of present study is to assess the impact of serum level of collagen turnover biomarkers (PINP and PIIINP), NT-proBNP, CRP and metalloproteinases (MMP-2, MMP-9) on echocardiographic response and clinical outcomes in population of patient of TRUST-CRT study.
Materials and methods: Study population consisted of patients enrolled into the Triple Site Versus Standard Cardiac Resynchronization (TRUST-CRT) trial. TRUST-CRT was a single-center, single-blind, parallel, randomized, clinical trial to test the hypothesis that triple-site (double-left single-right) pacing with defibrillator is superior over conventional CRT with defibrillator. Echocardiographic evaluation was performed at baseline, and after 6 months. The echocardiographic response was defined as an increase of left ventricle ejection fraction for more than 10%. Serum and plasma samples for PINP, PIIINP, MMP-2 and MMP-9 measurements were obtained on admission before CRT-D implantation and stored in –80 ℃ until analysis. Concentrations of PIIINP, PINP MMP-2 and MMP-9 ware determined by commercially available ELISA kits. Concentrations of hsCRP and NT-proBNP were determined with standard way in hospital laboratory.
Results: Between 2008 and 2010, 100 consecutive patients were enrolled to the TRUST CRT study. Blood samples for further analysis were collected from 74 of 100 patients before CRT-D implantation. Three years follow-up data were available for 97 of the 100 patients. PINP and PIIINP level was significantly lower in echocardiographic responders. Results of multivariate logistic regression demonstrated that among analyzed parameters only low level of PIIINP is associated with favorable echocardiographic response (P=0.011). Univariate and multivariate logistic regression showed that higher all-cause mortality is associated with higher baseline PIIINP (P=0.01) and NT-proBNP (P=0.02) concentrations. Survival analysis with cutoff value 9,315 ng/ml, identified on the basis of ROC analysis (sensitivity –50%, specificity-90%). revealed significant survival benefit associated with low baseline PIIINP (HR-4.58; 95% CI 2.05–10.24; P=0.0002) level.
Conclusion: Results of our study indicate that low baseline level PIIINP is associated with favorable echocardiographic response and longtime survival in CRT recipients.

4865 | BEDSIDE
Ventricular antitachycardia pacing therapy in heart failure patients with cardiac resynchronization therapy defibrillator: efficacy, safety and impact on heart failure hospitalizations and mortality

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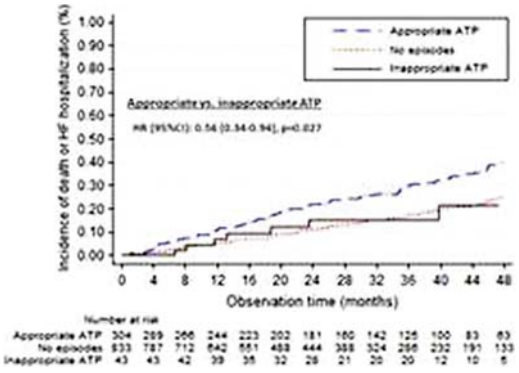
Background: Cardiac resynchronization therapy defibrillator (CRT-D) can terminate slow ventricular tachycardia (VT) and fast VT (FVT) via antitachycardia pacing (ATP).
Purpose: We evaluated efficacy and safety of ATP, and whether ATP may be associated with mortality and heart failure (HF) hospitalizations.
Methods: 1404 ICD patients (286 female,67±10 years) were prospectively followed in a multicenter observational research. Mortality and hospitalization rates were estimated in patient' sub-groups in order to uncouple the trigger (VT/FVT or other rhythms causing inappropriate detections) from the ATP therapy.
Results: Over a median follow-up of 31 months, 2938 VT/FVT were treated with ATP in 361 patients. The adjusted ATP success rate was 63% (95% CI: 57–69%) on FVTs and 68% (CI: 62–74%) on VTs. Acceleration occurred in 55 (1.87%) and syncope in 4 (0.14%) of all ATP-treated VT/FVT episodes. The rate of death, per 100 patient-years, was 5.6 (CI: 4.3–7.5) in patients with ATP on true VT/FVT, 3.3 (CI: 2.6–4.2) in patients with no episodes and 1.5 (CI: 0.4–6.1) in patients with inappropriate ATP (p=0.045 vs. appropriate ATP patients and p=ns vs. patients with no episodes after adjusting for baseline differences between patients' groups). The attached figure shows freedom from endpoint composed by death or HF hospitalizations for the sub-groups of 304 patients with ATP only on true VT/FVT, 833 patients with no episodes/therapies and 43 patients with only inappropriate ATP.



Conclusions: ATP was highly effective in terminating VT/FVT episodes and displayed a good safety profile. Patients with inappropriate ATP had a better prognosis than those with ATP on true VT/FVT suggesting that an adverse prognosis is related to the arrhythmia itself – a marker of disease progression – rather than to an adverse effect of ATP.

HAEMODYNAMICS IN HYPERTENSION

4866 | BENCH
The VKORC1 (-1639) G>A promoter polymorphism is associated with elevated systemic arterial blood pressure

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Background: Genetic variations in the vitamin K epoxide reductase complex subunit 1 (VKORC1) have been found to affect warfarin dose response. VKORC1 haplotypes may represent novel genetic markers for cardiovascular disease and aortic calcification. We hypothesized that genetic polymorphisms in the VKORC1 gene effect arterial blood pressure either directly or via vascular calcification thus contributing to cardiovascular diseases.
Methods and results: We focused on two frequent VKORC1 single nucleotide polymorphisms (SNPs), (3730) G>A polymorphism in the 3'-region and the (–1639) G>A promoter polymorphism. 1164 consecutive patients who were admitted for assessment of coronary artery disease were tested by allele specific

multiplex PCR. Individuals carrying the VKORC1(–1639) A variant showed significantly elevated invasively measured systolic, diastolic and mean arterial blood pressures compared with carriers of the G allele. The (3730) SNP showed only a borderline significance for the diastolic blood pressure. No association with vascular calcification could be observed.
Conclusions: The VKORC1 (–1639) A allele is associated with elevated systemic arterial blood pressure. This suggests a novel concept of blood pressure regulation through pathways involving vitamin K epoxide reductase and calcium binding proteins.

4867 | BEDSIDE
Lack of regression of left ventricular hypertrophy is accompanied by increased incidence of stroke and combined cardiovascular disease in essential hypertensives

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Purpose: Blood pressure (BP) reduction produces regression of left ventricular hypertrophy (LVH) which is considered to be associated with improved prognosis. We sought to investigate the prognostic role of left ventricular hypertrophy (LVH) regression regarding incidence of cardiovascular disease in essential hypertension.
Methods: We prospectively followed up for a median period of 3.8 years 1226 essential hypertensives (mean age 57.8 years, baseline office BP = 143.6/89.3mmHg). All subjects visited periodically the outpatient hypertensive unit of our institution and office BP at follow up was calculated based on the measurements of the last 3 visits. Echocardiographic evaluation and determination of the metabolic profile and creatinine levels was performed at entry and at follow up. LVH was defined as LV mass index $\geq$116g/m^2 in men and LV mass index $\geq$96g/m^2 in women. Endpoint of interest was the incidence of stroke, coronary artery disease and their composite.
Results: At the end of follow up the incidence of the composite end-point was 4.0% (17 patients with stroke, 34 with CAD, 2 with both). According to the presence of LVH at baseline (20.2%) and at the end of follow-up (15.9%) patients were divided in two groups: with normal LV mass index at both examinations or with LVH at baseline and regression of hypertrophy (n=1031, 84.1%, group 1) and with LVH at baseline and at follow-up and with normal LV mass index at baseline and LVH at follow-up (n=195, group 2). Hypertensives of group 2 compared to those of group 1 were older (by 6.3 years, p<0.001), more frequently females (by 19%, p<0.001) and had at baseline greater duration of hypertension (by 2.6 years, p<0.001), increased number of antihypertensive drugs (by 0.6, p<0.001) office pulse pressure levels (by 5mmHg, p<0.001), increased body mass index (by 0.8kg/m^2, p=0.024), glucose (by 7.4 mg/dl, p<0.001) and decreased creatinine clearance (by 10.5 ml/min/, p<0.001). Survival analysis revealed that hypertensives without LVH regression (group 2) compared to those of group 1 exhibited significantly higher rates of stroke (5.1% vs. 0.7%, log rank p<0.001) and the composite end-point (7.7% vs. 3.3%, log rank p=0.020).
Conclusions: Lack of regression of LVH is accompanied by increased incidence of stroke and combined cardiovascular disease in essential hypertensives.

4868 | BEDSIDE
Prognostic implications of left ventricular strain and strain risk score in patients with hypertensive heart disease

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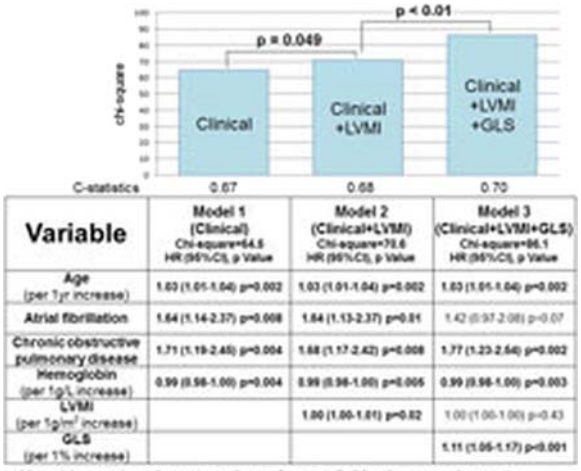
Background: Major adverse cardiovascular events (MACE) in pts with hypertensive heart disease (HHD) are associated with LV geometry, but their association with LV function is unclear.
Purpose: We sought to investigate the associations of LV strain and its serial change with MACE in HHD, independent of and incremental to clinical and LV geometric parameters, and to develop a risk score for predicting MACE.
Methods: We studied 697 non-ischemic patients with hypertension who had abnormal LV geometry at baseline echo examination from 2005–2014. Global longitudinal and circumferential strain (GLS, GCS) were measured using speckle tracking. Echocardiographic follow-up was performed after 3 years and pts were followed for MACE (death and admission due to heart failure, myocardial infarction, and stroke) over 3.9 years. A Cox proportional hazards model was used to examine the association of baseline parameters with MACE.
Results: MACE (n=147, 21%) were associated with increased LV mass index (LVMI) and impaired GLS and GCS (all, p<0.01). The association of GLS with MACE was independent of and incremental to clinical parameters and LVMI (Figure). In pts undergoing a 2nd echo (24% of whom had MACE), a deterioration in GLS was also independently associated with MACE. After pts were randomly divided into 2 groups, a risk score was developed using age>75, AF, COPD, anaemia, abnormal LVMI, and baseline GLS>-15% from the derivation cohort (c-statistic = 0.74). A validation cohort showed it to have good discrimination for MACE (c-statistic = 0.73).
Conclusion: GLS and its deterioration are independently associated with MACE in HHD. Strain risk score was useful for predicting risk of MACE.



Variable	Model 1 (Clinical) Chi-square=64.5 HR (95%CI), p Value	Model 2 (Clinical+LVMI) Chi-square=70.6 HR (95%CI), p Value	Model 3 (Clinical+LVMI+GLS) Chi-square=86.1 HR (95%CI), p Value
Age (per 1yr increase)	1.03 (1.01-1.04) p=0.002	1.03 (1.01-1.04) p=0.002	1.03 (1.01-1.04) p=0.002
Atrial fibrillation	1.64 (1.14-2.37) p=0.008	1.64 (1.13-2.37) p=0.01	1.42 (0.97-2.08) p=0.07
Chronic obstructive pulmonary disease	1.71 (1.19-2.45) p=0.004	1.68 (1.17-2.42) p=0.008	1.77 (1.23-2.54) p=0.002
Hemoglobin (per 1g/L increase)	0.99 (0.98-1.00) p=0.004	0.99 (0.98-1.00) p=0.005	0.99 (0.98-1.00) p=0.003
LVMI (per 1g/m^2 increase)		1.00 (1.00-1.01) p=0.02	1.00 (1.00-1.00) p=0.43
GLS (per 1% increase)			1.11 (1.05-1.17) p<0.001

*All models were also adjusted by **male gender, systolic blood pressure, heart rate, diabetes, and blood urea nitrogen**, but they were not significant in the final model.

Abstract 4868 – Figure 1. Sequential model

4869 | BEDSIDE
Predictive role of hypertension related organ damage and blood pressure control patterns for the incidence of new-onset atrial fibrillation in essential hypertensives

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Purpose: Hypertension is one of the key factors in the pathogenesis of atrial fibrillation (AF) with further implications in both hypertension and AF management. The aim of our study was to compare the predictive role ofhypertension related organ damage and blood pressure control patterns for the incidence of new-onset AF.
Methods: We studied 2.280 hypertensive patients (aged 57.7±11 years, 50% males) without history of AF episodes for a median period of 3.3 years (IQR 2.3–5 years). All subjects had at least one visit annually and at entry underwent complete echocardiographic study and additional workup for exclusion of secondary causes of resistant hypertension (RH). Four groups were identified depending on presence or absence of RH (office-based uncontrolled hypertension under at least 3 drugs including a diuretic or controlled hypertension under 4 or more drugs) at baseline and follow-up: 1.494 patients (65.7%) never having RH, 185 (8.1%) with resolved RH, 230 (10.1%) with incident RH and 365 (16.1%) with persistent RH. Endpoint of interest was new-onset AF.
Results: The incidence rate of new-onset AF over the whole follow-up period was 7.06/1000 persons-years. In the univariate analysis age (HR=1.08, p<0.001), office pulse pressure (HR=1.02, p=0.003), duration of hypertension (HR=1.03, p=0.011), left ventricular mass index (HR=1.02, p<0.001), left atrium diameter (HR=3.27, p<0.001), E/Em (HR=1.09, p<0.001), creatinine clearance (HR=0.98, p=0.002),resolved RH (HR=2.65, p=0.009) and persistent RH (HR=1.97, p=0.036)were predictors of new-onset AF. Multivariate Cox regression analysis revealed that age (HR 1.07, p<0.001) and LAD (HR 2.67, p=0.001) turned out to be the only independent predictors of new-onset AF while resolved RH just lost statistical significance (HR 2.00, p=0.09). Based on ROC analysis LAD>39 mm predicted new-onset AF with sensitivity 76.5% and specificity 56.7%.
Conclusions: Hypertensives with new-onset AF are characterized by a greater prevalence of cardiorenal adaptations and a longer and unfavorable patent of hypertension control.However, only older age and enlarged LA sizeturned out to predict new-onset AF in the setting of essential hypertension.

4870 | BEDSIDE
Hypertensive left ventricular geometry and myocardial mechano-energetic efficiency: refining cardiovascular risk profile in arterial hypertension

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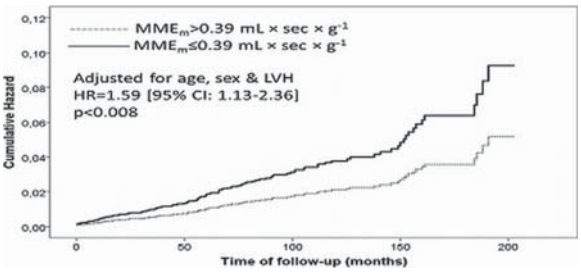
Background: Myocardial mechanical efficiency (MME) can be approximated by the ratio of stroke work (i.e. systolic blood pressure [SBP] times stroke volume [SV]) to a rough estimate of energy consumption, the "double product" (SBP times heart rate [HR]), which can be simplified as SV/HR).
Purpose: We characterized MME in relation to LV geometry and evaluated its prognostic value.
Methods: Hypertensive participants of the Campania Salute Network (n=12,104) without prevalent coronary or cerebrovascular disease and with ejection fraction (EF) >50% were analysed cross-sectionally and longitudinally over a follow-

up of 38±50 months. MME was estimated by echocardiographic SV (z-derived)/(HR×0.6). Left ventricular (LV) mass (LVM) and relative wall thickness were also computed.
Results: MME was greater in women (0.35±0.08 mL×sec) than in men (0.33±0.07 mL×sec, $p<0.0001$) and was closely related to LVM ($p<0.0001$). MME was normalized for LVM (MMEm) and divided in quartiles. In logistic analysis, the lowest quartile of MMEm was associated with older age, male gender, obesity, diabetes, LV hypertrophy (LVH), concentric geometry, more use of diuretics and CCB, less use of β-blockers and higher blood pressure (all $p<0.002$). During follow-up, age and sex-independent risk of composite fatal and non-fatal myocardial infarction and stroke was higher in the lowest quartiles of MMEm than in the three higher quartiles (HR=1.79 [1.29–2.49], $p<0.001$), and was only attenuated by addition of LVH (HR=1.59, $p<0.008$) in the model (figure).



Conclusions: A simple estimate of low MME, expressing the amount of ejected volume per second per gram of LVM is associated with altered metabolic profile, LVH, especially if concentric, and less use of β-blockers, and predicts hard CV end-points, independently of age, sex and LVH.

4871 | BEDSIDE
Aortic stiffness and essential hypertension phenotypes

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Purpose: Despite that recently normative and reference values have been published for Carotid-femoral Pulse Wave Velocity (cf-PWV), they did not take into account all phenotypic expressions of hypertension (HTN), such as isolated office (white coat) and masked HTN.
Methods: We studied 1163 consecutive subjects (383 normotensive, 780 newly HTN), free of diabetes and overt cardiovascular disease. Cf-PWV was evaluated by Sphygmocor device using intersecting tangent algorithm and substructed path length method. According to age and office, home and ambulatory blood pressure monitoring participants were categorized in 8 blood pressure (BP) categories and 6 age groups.
Results: The prevalence of optimal, normal, high normal, white coat, masked, HTN stage I, stage II and stage III was 3.1%, 6.5%, 12.3%, 11.2%, 3.9%, 36.9%, 18.7% and 7.4%, respectively. Cf-PWV increased with age and BP category, it was significantly higher in HTN compared to normotensive subjects (8.3 vs. 7.5 m/sec, $p<0.001$) and there were not any gender differences (8.09 in males vs. 8.06 in females, p=0.771). Importantly, normal BP category exhibited significantly higher values of PWV compared to optimal BP group (7.4 vs. 6.3, p=0.001). Moreover, white coat category had significantly higher cf-PWV compared to masked and high normal groups (8.1 vs. 7.2 vs. 7.5, p=0.004 and p=0.001, respectively) and significantly lower compared to HTN stage II and stage III (8.1 vs. 8.6 vs. 9.2, p=0.035 and $p<0.001$, respectively), while they did not differ regarding HTN stage I (8.11 vs. 8.15, p=0.833). In contrary, masked category had significantly higher cf-PWV compared to optimal group (7.23 vs. 6.32, p=0.008), and significantly lower compared to HTN I, II and III (7.23 vs. 8.15 vs. 8.55 vs. 9.24, $p<0.001$ for all, respectively), while they did not differ regarding normal and high normal groups (7.23 vs. 7.35 vs. 7.47, $p>0.3$ for all, respectively).
Conclusion: In a large population of normotensive and essential hypertensive newly diagnosed never treated patients, even normal levels of BP are characterized by increased cf-PWV compared to optimal levels. Contrary to widely held beliefs, white coat phenotype presents a worse aortic stiffness profile compared to masked HTN.

4872 | BEDSIDE
An increase in left ventricular wall thickness augments ejection fraction in hypertensive heart disease through changes in absolute wall thickening: a cardiac magnetic resonance imaging study

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Background: Hypertensive heart disease is often associated with the paradox of impaired longitudinal strain but preserved left ventricular ejection fraction (LVEF). We explored the impact of absolute wall thickening (AWT) on LVEF in hypertensive heart disease using cardiac magnetic resonance (CMR).
Methods: CMR studies from 55 hypertensive patients (mean age: 52±12.8, 58% male) performed at 1.5T were analysed. Ventricular volumes and LVEF were calculated. LV thickness was measured at end-diastole (EDWT) and end-systole (ESWT) in basal and mid myocardial segments from long axis cines. AWT was defined as ESWT minus EDWT. Longitudinal fractional shortening (LAS) was estimated using a modified 6-point mean mitral annular plane systolic excursion and expressed as a percentage of end-diastolic LV length. Radial strain was defined by AWT as a percentage of EDWT. Midwall fractional shortening (mFS) was estimated using an established equation. Multivariate linear regression analysis was performed to investigate the independent influence of EDWT, LAS and mFS on LVEF.
Results: Increasing EDWT correlated with significantly reduced LAS (R=–0.62, $p<0.001$), radial strain (R=–0.48, $p<0.001$) and mFS (R=–0.68, $p<0.001$). However as EDWT increased, and myocardial shortening decreased, AWT was maintained. On multivariate analysis (Table 1), increasing EDWT by 1mm independently resulted in an absolute increase in LVEF of 3.43 percentage points (3.43 [2.60–4.26], $p<0.0001$), which compensates for the independent negative effects of LAS and mFS on LVEF with increasing EDWT.

Multivariate linear regression analysis

Variable	Crude β coefficient (95% CI)	p-value	Adjusted β coefficient (95% CI)	p-value
EDWT	0.91 (–0.01–1.82)	0.051	3.34 (2.60–4.26)	<0.0001
LAS	0.86 (0.06–1.66)	0.035	2.01 (1.29–2.74)	<0.0001
mFS	0.91 (0.23–1.59)	<0.01	1.05 (0.26–1.84)	<0.01

CI, confidence interval.

Conclusion: We show how hypertensive patients can maintain normal LVEF despite significantly impaired longitudinal, radial and circumferential myocardial shortening. We propose that an increase in EDWT augments LVEF as a consequence of a preserved AWT. LVEF and systolic function are not synonymous. LVEF should not be used in hypertensive heart disease, without correction for the degree of EDWT. Our findings have wider implications for understanding the pathophysiology of heart failure with preserved ejection fraction.

4873 | BEDSIDE
Associations of hemodynamic load with impaired myocardial flow reserve: role of sex and hypertension

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Background: Heart failure with preserved ejection fraction (HFpEF) predominantly affects hypertensive women, with coronary microvascular dysfunction and rarefaction recently described as novel arterial abnormalities. To determine alterations in ventricular-arterial interactions that may predispose to HFpEF, we evaluated sex-specific associations of hemodynamic load with microvascular coronary artery function in subjects without heart failure.
Methods: Subjects with a cardiac 82Rb positron-emission tomography between 2010 and 2013, ejection fraction ≥50%, no heart failure, dyspnea, coronary artery disease or regional perfusion defects were eligible. Left ventricular microvascular reactivity was assessed by myocardial flow reserve (MFR = peak hyperemic stress/rest myocardial blood flow). “Low MFR” was defined as the lowest sex-specific quartile. Steady and pulsatile components of load were estimated by systemic vascular resistance index [SVRi = (80*mean arterial pressure/ cardiac output)*BSA] and indexed aortic compliance [AoCi =(stroke volume/pulse pressure)/BSA], respectively. Multivariable linear and logistic regression evaluated associations of SVRi and AoCi with MFR and “low MFR”, adjusting for age, heart rate, hypertension, diabetes, dyslipidemia, smoking, use of aspirin, statins and anti-hypertensives. Interaction terms for sex and hypertension with load measures were included.
Results: 297 subjects (61% women, age: 61.3±11.0 yrs) were eligible. Risk factors, medications and MFR did not differ, but SVRi was higher [5348±1676 vs. 4616±1514 (dyn·s/cm^5) m^2] and AoCi was lower [0.40±0.16 vs. 0.52±0.28 (mL/mmHg)/m^2] in women ($P<0.0001$), confirming greater arterial load in women. Interaction analyses showed that associations of SVRi and AoCi with MFR were only present in hypertensive women (β±SE: 0.24±0.09,P=0.008 and 0.21±0.08, P=0.01, respectively). Findings persisted after adjusting for rest flow. Each 1SD decrease in SVRi and AoC was associated with 2.24 (95% CI: 1.12–4.98,P=0.02) and 1.95 (1.06–4.70, P=0.03) greater odds of having “low MFR”, respectively, in hypertensive women. SVRi and AoCi interacted in the prediction of MFR (P=0.01).
Conclusions: In subjects at highest risk for HFpEF (hypertensive women), but not in men or normotensive women, lower steady and higher pulsatile arterial load were associated with worse MFR. Since coronary perfusion is related directly to diastolic and inversely to systolic aortic pressure, a combination of lower SVR and higher aortic stiffness (lower AoCi) in hypertensive women may adversely affect the coronary microvasculature, a mechanism that could predispose to HFpEF.

4874 | BEDSIDE

Left ventricular mass versus pulse wave velocity as predictors of coronary artery disease in patients with essential hypertension: data from a Greek 6-year-follow-up study

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Background and introduction: Although arterial stiffening is related to atherosclerosis progression, its prognostic role in hypertension is not fully elucidated, while augmented left ventricular mass index (LVMI) is linked to adverse outcome.
Purpose: The aim of the present study was to compare the predictive role of arterial stiffness and LVMI for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients.
Methods: We followed up 1033 essential hypertensives (mean age 55.6 years, 538 males, office blood pressure (BP)=145/92 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and at baseline underwent complete echocardiographic study for estimation of LVMI and blood sampling for assessment of metabolic profile. Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior SP) and the distribution of PWV was split by the median (8.1 m/sec) and accordingly subjects were classified into those with high (n=520) and low values (n=513). Moreover, LV hypertrophy (LVH) was defined as LVMI $\geq$125 g/m^2 in males and LVMI $\geq$110 g/m^2 in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.
Results: The incidence of CAD over the follow-up period was 2.8%. Hypertensives who developed CAD (n=29) compared to those without CAD at follow-up (n=1004) had at baseline higher waist circumference (101.8±11.1 vs 97.2±11.9 cm, p=0.033), LVMI (123.7±22.9 vs 107±24.2 g/m^2, p=0.014), prevalence of LVH (46% vs 25%, p=0.027) and prevalence of high PWV levels (69% vs 48%, p=0.019). No difference was observed between hypertensives with CAD and those without CAD with respect to baseline office BP, serum creatinine and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that baseline PWV levels predicted CAD (hazard ratio=1.218, p=0.025). However, in multivariate Cox regression model baseline glomerular filtration rate (hazard ratio=1.020, p=0.026) and LVMI (hazard ratio=1.021, p<0.0001) but not baseline PWV turned out to be independent predictors of CAD.
Conclusions: In essential hypertensive patients LVMI predicts future development of CAD, whereas high baseline PWV exhibits no independent prognostic value. These findings support that LVMI constitutes a superior prognosticator of events than PWV and its estimation is essential in order to improve overall risk stratification in hypertension.

4875 | BEDSIDE

Electrocardiographic detection of hypertensive left ventricular hypertrophy in the presence of obesity and left ventricular remodeling: re-calibration against cardiac magnetic resonance

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Background: ECG criteria for left ventricular hypertrophy (LVH) have traditionally been validated against echocardiography. Cardiac magnetic resonance (CMR) is the non-invasive gold-standard for assessing left ventricular mass (LVM). We re-calibrated 6 ECG criteria for LVH against CMR-defined LVM. We also investigated the impact of obesity and LV remodeling on the diagnostic performance of the ECG at detecting LVH.
Methods: Consecutive referrals for CMR (1.5T) from a tertiary hypertension clinic were reviewed. Patients with cardiac pathology that may confound the hypertrophic response were excluded. LVM was measured (including papillary muscles and trabeculations) from CMR, blinded to ECG data. From a 12-lead ECG, the Sokolow-Lyon voltage and product, Cornell voltage and product, Gubner-Ungerleidger voltage and Romhilt-Estes score were evaluated, blinded to CMR data. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Area under the receiver operator curve analysis was performed.
Results: 150 patients were reviewed, 22 were excluded due to concomitant cardiac pathology, resulting in a sample size of 128 (age: 51.0±15.2 years, 48% male). LVH by CMR was present in 37% (n=47) and obesity in 51% (n=65).
Lower sensitivity than specificity was demonstrated for all ECG criteria, with further significant inferior sensitivities for obese patients. In patients with LVH, the mean ECG values for Cornell voltage (22.2±5.7 vs 26.4±9.4 mm, P<0.05), Cornell product (2540±942 vs 3023±1185 mm.ms, P<0.05) and for Gubner-Ungerleider voltage (18.2±7.1 vs 23.3±1.2 mm, P<0.05) were significantly lower for obese compared to non-obese patients. However, in those without LVH, there was no significant difference for obese versus non-obese patients. In those without LVH, the prevalence of LV remodeling (normal LVM but increased mass:volume ratio) was significantly higher in obese subjects (36% vs 16%, P<0.05), and higher mean ECG values were found in the presence of LV remodeling.
At fixed 95% specificity, new obesity-specific partition values were generated; the Cornell voltage had the highest sensitivty in non-obese patients and Sokolow-Lyon product in obese patients (56% and 24% respectively).
Conclusions: Obesity significantly lowers the ECG sensitivity for detecting LVH, by attenuating ECG LVH values. We also show for the first time that LV remodeling, in the absence of LVH, influences ECG LVH criteria. Our obesity-specific partition values could improve the diagnostic performance of the ECG in this important subgroup of hypertensive patients.

REDUCING CARDIOVASCULAR RISK IN DIABETES: ONE SIZE DOES NOT FIT ALL

4885 | BEDSIDE

Improved cardiovascular risk factors control associated with a large-scale risk reduction program among diabetes population

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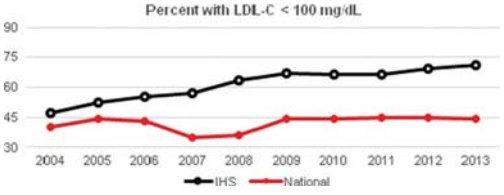
Background: Risk factors control in the diabetes population in clinical practice remains a challenge. We describe a large-scale cardiovascular risk reduction program in a large integrated health care delivery system (IHS) in Northern California and compare rates of hemoglobin A1C (HbA1C), LDL-C and blood pressure (BP) control in that program with national estimates.
Methods: In 2004 the IHS implemented PHASE (Preventing Heart Attacks and Strokes Everyday) program, which utilized a multifaceted approach to risk factors control including a comprehensive diabetes registry and performance metrics sharing. Diabetes patients from performance years 2004–2013 (N range = 104,075 to 122,383) with reported National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS) commercial rates of risk factors control were included. The comparison group comprised of reported national mean NCQA HEDIS rates. We conducted a Joinpoint regression analyses and calculated average annual percentage change (AAPC), to evaluate changes in trends.
Results: The rates of percent HbA1C >9% levels declined from 28.3% to 18.2% for IHS (AAPC, p<0.05) versus national rates (30.7% to 33.6%; AAPC, p=0.8). The rates of percent LDL-C <100 mg/dL increased (figure) for IHS (AAPC, p<0.05) versus national rates (AAPC, p=0.2). The HEDIS rates for percent BP <140/90 mmHg were only reported for performance years 2007–2013. Although AAPCs were not statistically significant, the IHS control rates remained much higher (77% to 82%) versus national (57% to 62%).



Conclusions: Among diabetes population, implementation of a large-scale cardiovascular risk reduction program in this IHS was associated with continued improvement in risk factors control rates when compared with national rates.
Acknowledgement/Funding: Community Benefits Grant, Kaiser Permanente Northern California

4886 | BEDSIDE

Resting heart rate and measures of effort related cardiac autonomic dysfunction predicts cardiovascular events in asymptomatic type 2 diabetics

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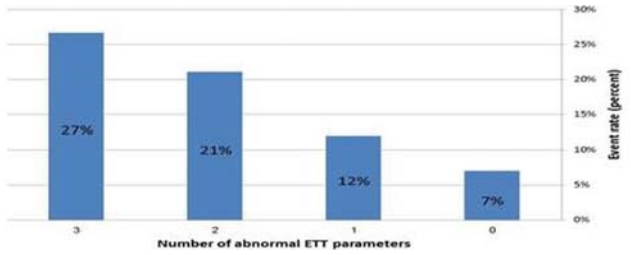
Background: Autonomic control of the cardiovascular (CV) system can be impaired in diabetes and is associated with increased morbidity and mortality. Parameters obtained during stress testing may identify early stages of cardiac autonomic dysfunction and provide prognostic information in asymptomatic diabetics.
Methods: We performed maximal exercise treadmill testing in 594 type 2 diabetics without known coronary heart disease. Prognostic significance of parameters associated with autonomic dysfunction were assessed, including chronotropic incompetence (<80% heart rate reserve), abnormal heart rate recovery at 1 min (HRR1)<18 beats, and resting tachycardia >100 beats/min. Cox proportional hazards analysis was used to determine the association of exercise parameters with a composite event of all-cause mortality, myocardial infarction or stroke.
Results: Resting heart rate>100/min was observed in 18% of patients, chronotropic incompetence in 30% and HRR1<18 beats in 35%. During mean

follow-up of 79±16 months, there were 72 (12%) events. Each of the 3 abnormalities was significantly associated with event risk in an adjusted multivariate analysis: chronotropic incompetence [HR 1.89, 95% CI 1.18–3.01; p=0.008], resting heart rate≥100 beats/min (HR 1.97, CI 1.19–3.26; p=0.008) and HRR1<18 beats (HR 1.77, CI 1.12–2.81; p=0.015). A progressive relationship between the number of abnormal parameters and event risk was observed (P<0.001).



Conclusions: Chronotropic incompetence, resting tachycardia and reduced heart rate recovery are independently and additively associated with long-term mortality, myocardial infarction or stroke in type 2 diabetics without known CV disease. Exercise testing may identify early stages of cardiac autonomic dysfunction with considerable long-term prognostic significance.

4887 | BEDSIDE

Impact of stress testing for coronary artery disease screening in asymptomatic patients with diabetes mellitus: a community-based study

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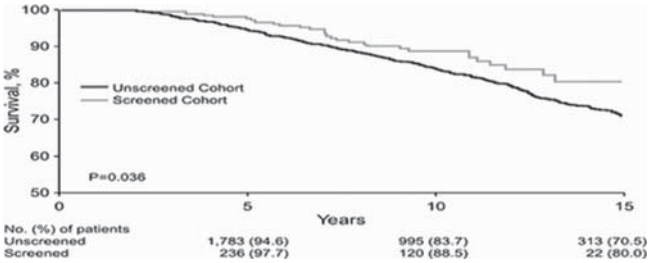
Purpose: Asymptomatic patients with diabetes mellitus (DM) are at increased risk for cardiovascular events. We evaluated the impact of screening stress testing for coronary artery disease (CAD) in asymptomatic diabetic patients in a community-based cohort.
Methods: Using Rochester Epidemiology Project resources, we studied 3,146 adult patients with a new diagnosis of DM from 1992–2008 without prior history of CAD. Weighted Cox proportional hazards regression was performed with screening stress testing within 2 years of diagnosis of diabetes as a time-dependent covariate. In a landmark analysis, subjects were classified into a screened cohort and an unscreened cohort based on their experience during the 2 years following DM diagnosis. Kaplan Meier methods were used to compare event rates. The primary outcome was all-cause mortality or myocardial infarction (MI).
Results: The age at diagnosis of diabetes was 55±13.8 years. Participants were 53% men and 97% had type 2 DM. The time-dependent variable of having a screening stress test within 2 years of DM diagnosis was associated with improved MI-free survival (HR=0.67, p=0.02), independent of other risk factors. In the landmark analysis, 294 patients received stress testing within 2 years (screened cohort) and 2246 remained at risk without stress testing (unscreened cohort). Median follow-up was 9 years (IQR: 4.1, 8.7) for the screened cohort and 9.8 years (IQR: 4.5, 9.6) in the unscreened cohort. Death or MI occurred in 455 patients [33 patients in the screened cohort and 422 in the unscreened cohort (5 year rates 2.3% and 5.3%, respectively)] (Figure).



Kaplan-Meier of Unscreened vs Screened

Conclusion: Screening cardiac stress testing in asymptomatic diabetic patients in a community-based cohort was associated with improvement in long-term event-free survival.

LEFT VENTRICULAR HYPERTROPHY

4898 | BEDSIDE

Urinary albumin predicts future hypertension and increases in blood pressure in the general population

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Background: Primary prevention of hypertension is an important public health aim. An intensive targeted strategy focused on identified individuals at highest risk of developing hypertension is an attractive approach for primary prevention of hypertension. The kidney plays a central role in regulating blood pressure. Indeed, glomerular filtration rate has been reported to be a novel predictor of the onset of hypertension in the general population.
Purpose: The present study sought to investigate whether increased excretion of urinary albumin within the low-grade levels (<300 mg/g creatinine) is associated with increased risk of hypertension and future elevations of blood pressure in the general population.
Methods: Normotensive subjects who visited our hospital for a physical checkup (53.4±11.4 years old, n=6,205) were enrolled in this study. A single-void, morning urine sample was used to measure urinary excretion of albumin. Urinary albumin concentrations were expressed as the ratio of concentrations of urinary albumin to urinary creatinine (mg/g Cr). After the baseline examination, subjects were followed up with the endpoint being the development of hypertension.
Results: The actual follow-up period was 17,025 person-years and the median follow-up period was 1,089 days. Urinary albumin was in the normal range (<30 mg/g Cr) in most subjects (97.5%). During the follow-up, hypertension developed in 1,184 subjects (19.1%, 69.5 per 1,000 person-years). Kaplan-Meier analysis revealed that the incidence of hypertension was increased across the quartiles of urinary albumin (log-rank, P<0.0001). The hazard ratio (lowest quartile [median urinary albumin, 1.14 mg/g Cr] as reference) was 1.39 (95% confidence intervals, 1.18–1.64) in the highest quartile (median urinary albumin, 8.87 mg/g Cr). Furthermore, multivariate Cox hazard analysis where urinary albumin was taken as a continuous variable identified urinary albumin as a significant predictor of hypertension (hazard ratio; 1.24, 95% CI; 1.09–1.41). Urinary albumin was also an independent predictor of future increases in systolic blood pressure (P<0.01).
Conclusions: Urinary albumin is a novel predictor of future hypertension and increases in blood pressure in the general population. The risk of developing hypertension increases even with levels of urinary albumin near the threshold defined for microalbuminuria. Thus, minor alterations in kidney function could be an important sign for managing blood pressure with the view to preventing hypertension onset.

4899 | BEDSIDE

The hypertrophic microRNAs miR-208b, miR-499 and miR-21 are related to left ventricular hypertrophy in patients with essential hypertension

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Purpose: To determine whether cardiac hypertrophy related microRNAs were differentially expressed in peripheral blood mononuclear cells of hypertensive patients in relation to left ventricular hypertrophy. Left ventricular hypertrophy is an initial compensatory mechanism in response to cardiac stress that can degenerate into heart failure and sudden cardiac death. It is one of the most recognized features of hypertensive heart disease, a marker of subclinical organ damage related to hypertension and an established risk factor and strong predictor for adverse cardiovascular outcomes in hypertension. MicroRNAs (miRs) modulate cardiovascular development and disease and thus they represent potential biomarkers and promising therapeutic targets in cardiovascular disease. Recent studies have shown that microRNAs regulate several aspects of physiological and pathological cardiac hypertrophy. The myomiRs miR-208b and miR-499 as well as the fibrosis related miR-21 have been shown to be agonists of the hypertrophic response in animal models. We evaluated whether miR-208b, miR-499 and miR-21 were differentially expressed in peripheral blood mononuclear cells of hypertensive patients in relation to left ventricular hypertrophy.
Methods: We assessed the expression levels of the microRNAs miR-208b, miR-499 and miR-21 in 102 patients with essential hypertension (50 men, mean age 62.51±9.7 years) and 30 healthy individuals (14 men, mean age 58.8±8.3 years). All patients underwent two-dimensional echocardiography. MicroRNA expression levels in peripheral blood mononuclear cells were quantified by real-time reverse transcription polymerase chain reaction.
Results: Hypertensive patients showed significantly higher miR-208b (22.29± 2.96 versus 8.73±1.59, p=0.016), miR-499 (10.06±1.05 versus 5.70±0.91, p=0.033) and miR-21 (2.75±0.15 versus 1.82±0.20, p=0.002) expression levels compared with healthy controls. In hypertensive patients, we observed significant positive correlations of miR-208b (r=0.426, p<0.001), miR-499 (r=0.433, p<0.001) and miR-21 (r=0.498, p<0.001) expression levels with left ventricular mass index.
Conclusions: Our data reveal that the myomiRs miR-208b and miR-499 as well as the fibrosis related miR-21 are upregulated in hypertensive patients relative to healthy individuals and they show strong positive correlations with left ventricular mass index in hypertensive patients. Thus, they may be implicated in the pathogenesis of left ventricular hypertrophy in hypertensive patients and possibly they are candidate therapeutic targets in hypertensive heart disease.

4900 | BEDSIDE

Probability of echocardiographic left ventricular hypertrophy regression during antihypertensive treatment in a real-word context: The Campania Salute Network

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Background: Regression of hypertensive left ventricular (LV) hypertrophy (LVH) is a successful goal in clinical trials, but less in known of LVH regression in a real-world context.
Methods: We identified 2234 hypertensive patients (mean age 57±10 years, 48% women) free of prevalent cardiovascular (CV) disease, with baseline LVH (LV mass index (LVMi) ≥47 g/m$^{2.7}$ in women and ≥50 g/m$^{2.7}$ in men) and at least 24 months follow-up (80±49 months) from the Campania Salute Registry. The characteristics associated with LVH regression was assessed, also considering number and type of antihypertensive medications.
Results: 299 patients (13%) exhibited regression of LVH during follow-up (reduction in LVMi was 13±8% vs. 2±10% in patients with stable LVH, p<0.001). Patients with LVH regression were younger, more likely to be males, less likely to have diabetes or obesity and with a shorter history of hypertension (all p≤0.001). Average systolic and diastolic blood pressure (BP) during follow-up, baseline BMI, carotid IMT and LVMi were lower (all p<0.01), while lipid profile, renal function and type of antihypertensive medication did not differ. In multivariate analysis, significant independent predictors of LVH regression were: younger age, male gender, lower systolic BP during follow-up and lower baseline LVMi and BMI (all p≤0.004) (Table), after adjustment for duration of hypertension, diastolic BP during follow-up, fasting plasma glucose, renal function, carotid IMT, number of antihypertensive drugs and follow-up time (all p>0.1).

Table 1. Significant predictors of LVH regression in treated hypertensive subjects

Variables	OR	95%CI	p-value
Age (years)	0.97	0.96–0.99	0.001
Male gender	2.79	2.08–3.75	<0.001
Average systolic BP during follow-up (mmHg)	0.98	0.97–0.99	0.004
LVMi (g/m$^{2.7}$)	0.85	0.82–0.88	<0.001
BMI (kg/m^2)	0.91	0.88–0.95	<0.001

Conclusion: In a real-world context, LVH regression occurs in 13% of treated hypertensive patients, and is more likely in younger and male subjects, with better BP control during follow-up and more favorable CV risk profile. In particularly, obesity and more severe LVH at baseline reduce the chance of hypertensive LVH regression independent of BP control.

NEW ERA IN MYOCARDIAL PERFUSION IMAGING

4911 | BEDSIDE

Myocardial perfusion imaging predicts mortality in patients evaluated for kidney transplantation

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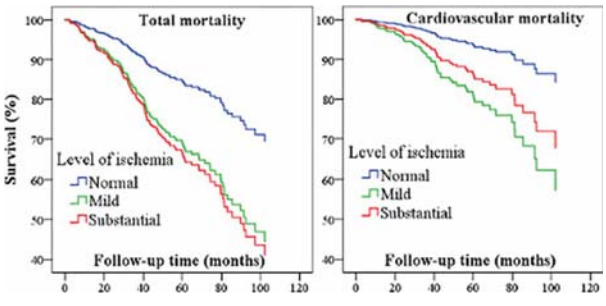
Background: Value of myocardial perfusion imaging (MPI) in patients with severe renal disease is controversial.
Purpose: To assess the prognostics of MPI in a large evaluation population for kidney transplantation.
Methods: The local MPI data was collected in 2004–2013 and linked with the national kidney registry. All the 564 patients evaluated for transplantation were also MPI scanned. Cox regression as well as integrated discrimination and net reclassification improvement were used.
Results: During the median follow-up of 43.5 months (IQR 21.7–68.5 months), 122 patients (21.6%) died, 54 of cardiovascular (CV) causes (9.6%). In comparison to those without myocardial ischemia, MPI with mild ischemia (5–10%) had an adjusted Cox hazard ratio (HR) 2.27 (95% CI 1.35–3.68, p=0.002) for all-cause mortality, while substantial ischemia (>10%) demonstrated HR 2.44 (95% CI 1.54–3.87, p<0.001). MPI offered incremental prognostic impact with both reclassification methods. Mildly abnormal MPI was linked with a higher risk for CV death, HR 3.24 (IQR 1.59–6.60, p=0.001), than substantial ischemia, HR 2.26 (IQR 1.10–4.62, p=0.026), when compared to those without ischemia. Revascularization was performed clearly more often to patients with severe than mildly abnormal or normal MPI (35.8%, 1.2% and 1.3%, respectively, p<0.001). Patients with no or mild ischemia received a kidney transplant more often than patients with severe ischemia (49.7%, 41.2% and 27.2%, respectively, p=0.001).
Conclusion: Myocardial ischemia in MPI is clearly linked with high mortality in patients screened for kidney transplantation. Interestingly, patients with substantial ischemia had lower risk for CV death than patients with mild ischemia, probably because of essentially more frequent revascularizations.
Acknowledgement/Funding: Helsinki University Central Hospital competitive research fund



4912 | BEDSIDE

Incremental Prognostic Value of Noninvasive Coronary Flow Reserve

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Background: Impaired coronary flow reserve is considered an early manifestation of coronary artery disease, even in vessels free of angiographic stenosis. The aim of this analysis is to determine whether noninvasive CFR in patients with suspected or known coronary artery disease adds incremental prognostic significance over clinical variables.
Methods: We included 2,645 consecutive patients with known or suspected coronary artery disease (mean age 61±11 years, 42% females) who underwent rubidium-82 rest/stress positron emission tomography for clinical indications. The scans were interpreted for the presence of perfusion defects. Rest and stress myocardial blood flows were calculated with factor analysis and a 2-compartment kinetic model and were used to compute coronary flow reserve (CFR). Patients were followed up for a median duration of 1.4 years (interquartile range, 0.5–1.8 years) for the incidence of cardiac death or myocardial infarction. (CD/MI)
Results: A total of 34% patients had evidence of perfusion defects while 42% had CFR <2. The overall rate of CD/MI was 4.7%. In univariate analysis, the lowest tertile of coronary flow reserve (<1.8) was associated with a 3.7-fold increase in the risk of CD/MI (95% confidence interval, 2.2–6.6 P<0.0001) compared with the highest tertile. This remained significant after adjusting for clinical variables, perfusion defect and resting ejection fraction (Hazard ratio 2.0, 95% confidence interval, 1.18–3.45; P=0.10)
Conclusion: Noninvasively measured CFR with positron emission tomography is an independent predictor of cardiac death or myocardial infarction in patients with known or suspected coronary artery disease.

4913 | BEDSIDE

Comparison of coronary flow reserve detected by positron emission tomography (PET) in patients with hypertrophic cardiomyopathy and hypertrophic cardiomyopathy with hypertension

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Background: Hypertrophic cardiomyopathy (HCM) is a common genetic cardiomyopathy and microvascular dysfunction is the major factor for clinical deterioration and cardiovascular disease–related death in HCM. Hypertension (HTN) may also lead to microvascular dysfunction which can be detectable by inadequately increased myocardial flow during pharmacologic stress infusion in PET.
Methods: We studied 38 patients with HCM (mean age 51±12,6 years) and 38 patients with HCM with HTN (mean age 53±15,4 years). Hypertension was defined by blood pressure value was >140/90 mmHg or those who were on antihypertensive medication. All patients underwent rest and stress 13N-ammonia studies following administration of dipyridamole or regadenoson. All data was obtained using the same PET/CT scanner in list mode, with CT attenuation maps. List-mode data was resampled to create static, electrocardiographically-gated and 36-frame-dynamic images. Coronary flow reserve (CFR) was determined as the ratio of the peak myocardial blood flow to rest myocardial blood flow.
Results: The patients were comparable, there was no differences in systolic function of the patients; ejection fraction (58,5±6,7 in HCM vs 57,1±7,3 in HCM with HTN) in both groups. End-diastolic and end-systolic total LV volumes were similar in the 2 groups in echocardiographic analyses. Patients in both groups had similar septal wall thickness (1,9±0,47 in HCM vs 1,99±0,39 cm in HCM with HTN). Patients with HCM with HTN had decreased CFR (2,3±0,62), whereas CFR in patients with HCM was 2,8±0,98 (p<0.01).
Conclusion: In patients with both HCM and HTN, decreased CFR was detected compared to that in HCM patients using PET.

STATE OF THE ART IN INVASIVE IMAGING AND FUNCTIONAL ASSESSMENT

4930 | BEDSIDE
Wave intensity analysis reflects microcirculatory capillary density: a combined histological and intracoronary physiology study

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Background: Assessment of coronary microcirculation is hampered by the availability of adequate techniques. Wave intensity analysis (WIA) is a novel method to analyse intracoronary pressure and flow with the potential to outline specific causes of microcirculatory dysfunction. Theoretically, the magnitude of the backward decompression wave in WIA is assumed conceptually to be related to the increase in diastolic capacitance of the capillary bed, but this has never been directly verified.
Purpose: We investigated this concept in vivo using histological samples in a population of cardiac transplant patients with variable degree of capillary rarefaction resulting from allograph vasculopathy.
Methods: 15 cardiac transplant patients with unobstructed epicardial vessels underwent combined pressure (from catheter tip) and flow (from a mid-LAD Doppler guidewire) during rest and hyperaemia. Offline wave intensity analysis was performed using bespoke Matlab software. Ventricular biopsies were simultaneously obtained using a 7F biopsy forceps. Capillaries were identified with specific antibodies against endothelium. Quantitative morphometric analysis of the histological sections was performed in dedicated workstation and the density of capillaries (capillaries per 1 mm^2) was assessed.
Results: Mean age was 49 (11 male) with the majority of transplantations having been undertaken for dilated cardiomyopathy (60%). Capillary density was 623±278 capillaries/mm^2 (range 259–1005). Resting mean coronary velocity was 17.0±8.3 and rose to 38.4±16.6 cm/s with adenosine (CFR 2.28±0.6). Mean systolic pressure was 127 and diastolic pressure 83mmHg. Resting microvascular resistance was 7.6±6.0 mmHg/cm/s and hyperaemic microvascular resistance 3.4±3.3 mmHg/cm/s. Coronary flow reserve was not correlated with capillary density ($r=0.41$, $p=0.1$). A good correlation was demonstrated between capillary density and both cumulative ($r=-0.65$, $p<0.01$) and peak ($r=-0.53$, $p=0.04$) backward decompression wave. Of the other waves a second correlation was noted was with the peak ($r=-0.76$, $p<0.01$) and cumulative ($r=-0.72$, $p<0.01$) late backward compression wave (of systolic microcirculatory compression). No other correlations were noted with the wave intensity profile.
Conclusions: This study supports coronary wave intensity analysis as a potential tool in the diagnosis of myocardial capillary rarefaction in cardiac diseases associated with microcirculatory remodeling. It also provides clinical evidence supporting the theoretical explanation of the documented coronary waves of WIA.

4931 | BEDSIDE
Performance of two novel invasive indices of coronary microvascular resistance using invasive and non-invasive reference standards: superiority of Doppler derived hyperaemic microvascular resistance

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Purpose: Coronary microvascular resistance (CMVR) is increasingly measured after myocardial infarction, both as a prognostic marker and to compare treatments. There is currently no gold-standard invasive measurement of CMVR. We compared two novel invasive measurements of CMVR measured in the cardiac catheter laboratory: a Doppler-derived hyperaemic microvascular resistance (hMR) and a thermodilution-derived index of microvascular resistance (IMR), against myocardial perfusion reserve index (MPRI) using high-resolution cardiac magnetic resonance imaging (CMR).
Methods: 37-patients (61±10 yrs) were recruited, 63% following an ACS. Simultaneous intracoronary pressure, Doppler flow velocity and cold-bolus transit time were measured in 45 coronary arteries, using a Volcano Combowire and St Jude Pressure Wire, at rest and during intravenous adenosine hyperemia. Measurements were taken post PCI in patients with significant coronary artery stenoses (stable angina and ACS patients). When clinically feasible, a second set of measurements was taken in a normal reference vessel. We calculated, using standard definitions: mean coronary flow reserve (CFR) from thermodilution and Doppler, hMR and IMR. 3-tesla CMR perfusion scans were performed, as close as possible to invasive measurements, and MPRI calculated in the corresponding segments as previously described. In ACS patients, regional wall motion in corresponding segments and overall left ventricular ejection fraction (from cine CMR images), and infarct size (from contrast enhanced CMR images) were also calculated.
Results: hMR correlated with IMR ($r=0.67$, $p<0.001$). In ACS patients, both were univariate predictors of LVEF, infarct size and regional wall motion. However hMR was the only independent predictor of regional wall motion. Moreover, hMR had superior diagnostic accuracy over IMR to predict mean CFR (area under curve 0.79 versus 0.59, $p<0.01$) and separately to predict MPRI (area under curve 0.97 versus 0.84, $p=0.09$), using Delong receiver operating characteristic comparison analysis.
Conclusions: Accurate assessment of CMVR on the cardiac catheter laboratory table is feasible, safe and rapid. This study, for the first time, simultaneously assessed the diagnostic accuracy of two such measures of CMVR. We demonstrated Doppler-derived hMR had superior diagnostic accuracy over IMR at predicting established invasive and non-invasive reference standards of CMVR; in CFR and MPRI respectively.

4932 | BEDSIDE
Accounting for right atrial pressure in the calculation of fractional flow reserve (FFR) significantly increases the number of physiologically significant stenoses suitable for PCI

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Background: Right atrial pressure (RAP) was included in the original validated FFR equations, but is now omitted from clinical use with a presumed negligible consequence.
Purpose: In this real world cohort, we investigate the effects omission of right atrial pressure has on the revascularisation decisions made in everyday clinical practice.
Methods: 304 coronary stenoses underwent coronary angiography with FFR measurement. FFR was calculated using the simplified equation of distal coronary pressure/proximal aortic pressure (Pd/Pa), and also accounting for right atrial pressure (Pd–RAP/Pa-RAP) across a range of right atrial pressure values between 0–15 mmHg and the clinical implications assessed.
Results: Mean FFR (Pd/Pa) of the cohort was 0.83 (±0.09). The inclusion of RAP significantly decreased the FFR value. Mean FFR of the cohort decreased to 0.82 (±0.10), 0.81 (±0.11) and 0.79 (±0.11) at RAPs of 5mmHg, 10mmHg and 15mmHg respectively. The decrease reached statistical significance at RAP 7mmHg ($p<0.04$), this is within the published normal RAP range (<8mmHg). Decrease in FFR increased the proportion of stenoses meeting revascularisation criteria (FFR$\leq$0.80). Due to the clustering of data around FFR 0.80, small changes in FFR value led to big changes in classification. The additional stenoses fulfilling reclassification criteria were 4% (11/304), 9% (27/304) and 17% (51/304) at RAPs of 5mmHg, 10mmHg and 15mmHg respectively. These represented potentially missed cases for appropriate revascularisation. In this cohort, FFR 0.83 was the highest non-significant FFR where reclassification still occurred at normal RAP (<8mmHg). In patients with elevated RAP (15mmHg), this figure was FFR 0.85. These FFR values are well above the FFR$\leq$0.80 cut off for revascularisation. Lastly, when RAP was included, systolic aortic blood pressure (Pa) became an important determinant of the FFR value. RAP always lowered the FFR of a stenosis more in patients with low systolic blood pressure. Therefore, the inclusion of RAP is non-linear, and its effects on FFR calculation are critically dependent on the systolic blood pressure.
Conclusions: FFR in its current form (Pd/Pa) systematically underestimates true stenosis severity, oversimplifies the relationship with systolic blood pressure and FFR and potentially denies patients the opportunity for appropriate revascularization. Using a RAP of 0mmHg should be abandoned in favor of routine measurement of RAP. Where not feasible, a pragmatic consideration would be to use a physiological RAP (8 mmHg) in the automated console calculation of FFR.
Acknowledgement/Funding: National Institute of Health Research

SUDDEN CARDIAC DEATH IN THE CARDIOMYOPATHIES

4959 | BEDSIDE
Clinical profile and predictors of arrhythmia-related symptoms in scandinavian arrhythmogenic right ventricular cardiomyopathy patients

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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically heterogeneous disease with largely unpredictable course. Prediction of prognosis and risk stratification in regard to sudden cardiac death (SCD) in patients with ARVC remains a challenging task. We aimed to assess clinical predictors of arrhythmia-related symptoms in ARVC patients enrolled in the Nordic ARVC registry.
Methods: Patients with definite ARVC by 2010 Task Force (TF2010) criteria recruited at 8 sites in Denmark, Norway and Sweden were included in the cross-sectional analysis. Patients were defined as symptomatic based on the occur-

rence of syncope, documented ventricular tachycardia (VT/VF), appropriate implantable cardioverter-defibrillator (ICD) therapy or aborted cardiac arrest (ACA). Demographical data and clinical characteristics, reflected in the TF2010 ARVC diagnostic criteria, as well as gender, genotyping results and extended repolarization abnormality defined as T-wave inversion in inferior limb leads were assessed for prediction of symptoms using multivariable logistic regression analysis. Patients were followed-up for a median of 8 (IQR 4–12) years.
Results: The study population included 243 subjects from 181 families (age 48±17 years, 64% men). Genetic cascade screening was initiated in 130, and revealed disease-causing variant in 61% of probands and PKP2 was the most commonly affected gene (66%) followed by DSG2 (23%). No arrhythmia-related symptoms were observed in 66 patients while 22 survived cardiac arrest, 35 had syncope and 120 had documented VT/VF. Median age at first symptom was 38 (IQR 27–49) years. ICD was implanted in 170 patients, of whom 106 had appropriate ICD therapies for VT/VF. ACA was the first symptom in 11% of symptomatic patients. In the multivariate analysis, arrhythmia-related symptoms were associated with male gender (OR 3.6, 95% CI 1.56–8.24, p=0.003), the presence of disease-causing PKP2 variant (OR 2.46 95% CI 1.07–5.64, p=0.034), the presence of epsilon-wave (OR 8.26 95% CI 1.76–38.70, p=0.007) and T-wave inversion in lead aVF (OR 6.20 95% CI 2.07–18.49, p=0.001).
Conclusions: In the Scandinavian cohort of patients with ARVC, male gender, presence of PKP2 mutations and advanced depolarisation and repolarization abnormalities independently predicted arrhythmia-related symptoms. T-wave inversions in inferior limb leads are not covered by current risk stratification schemes in ARVC and should be considered as an additional arrhythmia marker.

4960 | BEDSIDE
Heterogeneous myocardial contraction is related to cardiac fibrosis and predict ventricular arrhythmias in patients with hypertrophic cardiomyopathy

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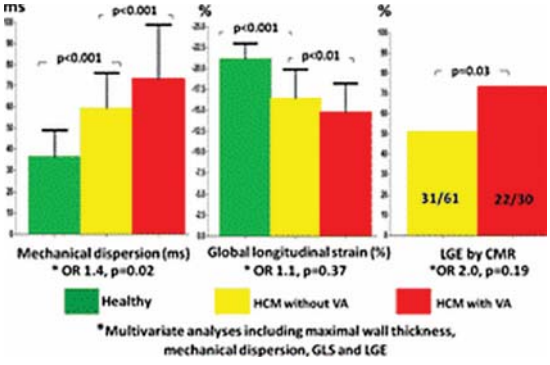
Background: Hypertrophic cardiomyopathy (HCM) patients are at risk of ventricular arrhythmias (VAs). Late gadolinium enhancement (LGE) by cardiac magnetic resonance (CMR) is a marker of fibrosis and is related to VAs.
Purpose: We aimed to explore if left ventricular (LV) systolic function by strain echocardiography is related to VAs and to the extent of LGE.
Methods: We included 150 HCM patients (54±14 years, 39% female) and 50 age and sex matched healthy individuals. VAs were defined as suspected arrhythmic syncope, ventricular tachycardia or aborted cardiac arrest. Global longitudinal strain (GLS) was assessed by speckle tracking echocardiography. Mechanical dispersion (MD), reflecting heterogeneous contraction, was calculated as standard deviation of time from Q on ECG to peak strain in 16 LV segments. In 85 (57%) patients, any LGE by CMR was defined as signal intensity 5 SD $\geq$ normal myocardium, and percentage LGE (%LGE) was determined.
Results: HCM patients had similar ejection fraction (61±5% vs.61±8%, p=0.77), but worse GLS (–15.7±3.6% vs. –21.1±1.9%, p<0.001) and more pronounced MD (64±22 ms vs. 36±13 ms, p<0.001) than healthy (Figure). Patients with VAs (n=54) had worse GLS (–14.7±3.5% vs. –16.4±3.5%, p<0.01) more pronounced MD (73±26 ms vs. 59±16 ms, p<0.001), and higher %LGE (4.3±6.9% vs. 0.5±1.0%, p<0.001) than patients without VAs (n=96). MD was correlated to %LGE (R=0.52, p<0.001), and was the only parameter that predicted VAs independently of maximal wall thickness, GLS and the presence of LGE (Figure).



Conclusion: HCM patients had reduced LV function by GLS, despite normal function by ejection fraction. MD was a strong and the only independent predictor of VAs and was related to fibrosis and may help risk stratification of VAs in HCM.

4961 | BEDSIDE
A validation study of the 2014 ESC sudden cardiac death risk prediction model in a population with hypertrophic cardiomyopathy

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Aims: Sudden cardiac death (SCD) is a common cause of death in hypertrophic cardiomyopathy (HCM). The objective of this study was to validate the power of the 2014 European Society of Cardiology (ESC) SCD risk prediction model in HCM (HCM risk-SCD), to identify low risk (LR) from intermediate risk (IR) and high risk (HR) patients who might be eligible for an implantable cardioverter defibrillator (ICD) for primary prevention of SCD in a population of South America.
Methods: This retrospective observational study included 502 consecutive HCM patients from one referral center in South America followed between 1993 and 2014 (we excluded patients treated with myectomy, alcohol septal ablation or heart transplant, <16 years old, metabolic diseases and syndromes, HCM treated with an ICD for secondary prevention, and patients lost to follow up). The primary endpoint was SCD or appropriate ICD shock (considered as equivalent to SCD). For the quantitative estimation of individual risk of SCD at 5 years, we used the HCM risk-SCD formula: Probability SCD at 5 years = [1–0.998exp (Prognostic index)] x 100, where Prognostic index = [0.15939858 x maximal wall thickness]-[0.00294271 x maximal wall thickness^2]+[0.0259082 x left atrial diameter]+[0.00446131 x maximal (rest/Valsalva) left ventricular outflow tract gradient]+[0.4583082 x family history SCD]+[0.82639195 x non-sustained ventricular tachycardia]+[0.71650361 x unexplained syncope]-[0.01799934 x age at clinical evaluation]. In our data base we also included the abnormal blood pressure response to exercise (ABPRE) as a risk marker. We analyzed the three categories of 5-year risk proposed by the 2014 ESC Guidelines on diagnosis and management of HCM (LR <4%; IR $\geq$4-<6% and HR $\geq$6%).
Results: 387 (77%) patients had LR; 39 (8%) IR, and 76 (15%) HR. During a mean follow-up period of 3.6 years, 14 patients (3%) died suddenly or had an appropriate ICD shock [in a LR category: 0%; IR: 2 of 39 (5%) and HR: 12 of 76 (16%)]. The Chi square analysis of contingency tables shows that the SCD was not independent from the HCM risk-SCD with p<0.00001. It should be underlined that two IR patients who received appropriate ICD shocks were young and had ABPRE.
Conclusions: The SCD risk prediction model in HCM proposed by the 2014 ESC Guidelines was validated in our population. It represents an evident improvement compared with the previous approach. However, the incorporation of additional predicting variables associated with SCD in published multivariable analysis such as ABPRE in young patients will probably improve the predictive value of the model.

FLASH NEWS ON ANTITHROMBOTICS

4971 | BEDSIDE
PER977 (ciraparantag) reverses edoxaban anticoagulation at steady state and has no effect on re-anticoagulation at the next scheduled dose

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Background: There is no approved reversal agent for non-vitamin K antagonist oral anticoagulants (NOACs), including edoxaban. Of the three reversal agents in clinical development, based on non-clinical data, PER977 is the only one that is a small molecule, and has the potential to reverse all approved NOACs and heparins with a single injection. To date, anticoagulation reversal with PER977 has been confirmed in edoxaban and enoxaparin clinical studies.
Methods: An ongoing Phase II single-blind, placebo-controlled clinical trial in healthy volunteers (n=50 completed) is evaluating escalating doses of PER977 in subjects administered 60 mg edoxaban daily to steady state. Reversal of anticoagulation measured by whole blood clotting time (WBCT) at 3 hours post dose was tested with single doses of 25, 50, 100, 300 and 600 mg of PER977 followed by re-anticoagulation with edoxaban at the next scheduled dose and a second reversal at the same PER977 dose to insure that re-anticoagulation was not compromised.
Results: Edoxaban increased mean WBCT by 30±2.2%. PER977 completely and statistically significantly reversed the increase in WBCT to pre-edoxaban levels within 60 minutes following administration of 100 mg PER977 (p<0.01) on Day 3 (Figure). Mean WBCT following re-anticoagulation with edoxaban was similar to that observed after the first anticoagulation and the impact of the second reversal with 100 mg PER977 on Day 4 was similar to Day 3. Reversal of anticoagulation was observed within 30 minutes at 300 mg PER977 (p<0.05) on Day 3. Electron micrographs of the clots showed restoration of normal fibrin structure indicating return to normal clotting following PER977after the anticoagulated state achieved with edoxaban. Prothrombin time remained elevated and does not appear to be a sensitive measure of reversal of anticoagulation by PER977. Adverse events, temperature sensations at the site of injection and flushing were mild and transient.
Conclusion: PER977, beginning at doses of 100 mg, completely reversed anticoagulation of steady state doses of edoxaban as demonstrated by decreased

mean WBCT to pre-edoxaban levels and return of clot formation to normal from its anticoagulated state. As noted in previous trials, a single injection of PER977 sustains reversal of edoxaban as measured by WBCT without the need for prolonged infusion and with no post-injection pro-coagulation signals.

4972 | BEDSIDE
Treatment pattern of dual antiplatelet therapy in 104,012 patients with acute coronary syndrome: a Swedish nationwide population-based cohort study

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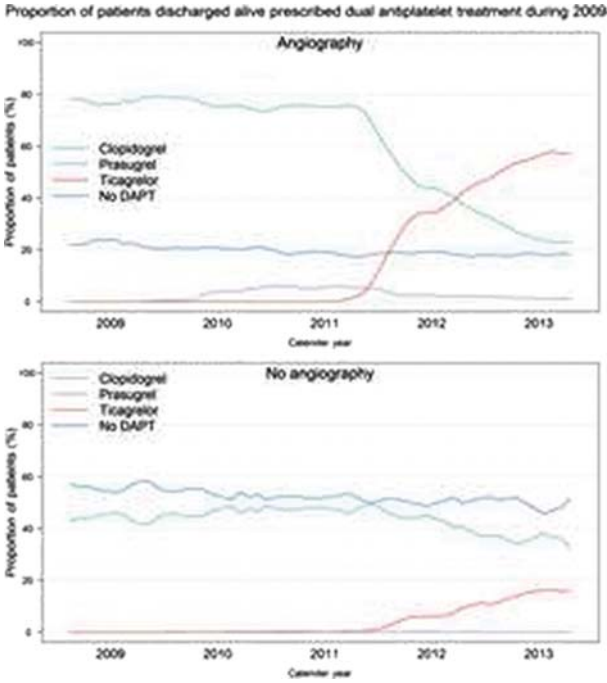
Introduction: Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has previously become a cornerstone in treatment of acute coronary syndrome (ACS). With the introduction of prasugrel and ticagrelor, new DAPT regimens are available. ESC guidelines recommend 12 months' DAPT after an ACS.
Purpose: To investigate DAPT patterns, changes in type and duration of DAPT, and patient characteristics associated with the various treatments in a nationwide population of all patients with ACS in Sweden over 5 years.
Methods: This observational, cohort study linked morbidity, mortality and medication data from national registries from all 104,012 patients alive after discharge from hospital with ACS during 2009–2013. Patients were categorized into two groups whether or not coronary angiography was performed.
Results: In patients investigated with angiography, treatment switch from DAPT/clopidogrel to DAPT/ticagrelor was observed in beginning of 2011. DAPT/clopidogrel remained the preferred DAPT treatment in patients not investigated with angiography. DAPT duration increased from 225 to 298 days in patients investigated with angiography, and from 155 to 208 days in patients not investigated with angiography. 10% of patients initiated on prasugrel or ticagrelor switched to clopidogrel within 1 year. Angiography increased 10%, PCI 11%, and patients prescribed DAPT 8% in 2013 vs 2009.



Conclusions: During the study period more patients underwent angiography and PCI. There was an increase in the proportion of ACS patients receiving DAPT, as well as longer duration of DAPT in line with ESC guidelines. Among DAPT treated patients, ticagrelor has emerged as the preferred P2Y12 antagonist in patients undergoing angiography, whereas clopidogrel tended to be prescribed to patients treated non-invasively
Acknowledgement/Funding: This work was supported by Astra Zeneca

4973 | BENCH
A new strategy to reverse the platelet inhibitory effect of ticagrelor

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Background: Platelets play a pivotal role in the pathogenesis of acute coronary syndromes (ACS). In contrast to Clopidogrel (Cl) and Prasugrel (Pr), Ticagrelor (Ti) has a different binding site from ADP with reversible blockage of the P2Y12-receptor. Like all the P2Y12-receptor antagonists Ti is bound to plasma proteins to a high extent.
In case of acute bleedings or emergent surgical procedures, the platelet inhibitory effect should be reversed rapidly. There are a few cases that report bleeding complications with the impossibility to reverse the effects of Ti.
In 2014 we presented the data of our ex vivo study, in which we could show a marked difference between the possibility to reverse the effect of Ti after administration of platelet-rich-plasma (PRP) or pooled-platelets (PP). Surprisingly there was a significant lower response to PP compared to PRP measured by the PRI-VASP. Aim of the continued work was to evaluate the mechanism of poor response of Ti to PP as well as to discover a new strategy to reverse successfully the platelet inhibitory effect of Ti ex vivo.
Methods: We collected blood samples from patients with ACS after intake of Ti. On one hand, the inhibition of the P2Y12-receptor was determined by measuring the Platelet Reactivity Index (PRI-VASP) ex vivo after addition of PRP-centrifugated platelets resuspended in PP-buffer solution. On the other hand we administrated pooled platelet concentrates (PP) in addition with human serum and human serum alone to take the high plasma protein binding into account.
Results: After addition of PP to Ti inhibited blood samples there was no significant increase in PRI-VASP values (Ti 11,7% ±10,9%->18,2%±9,6%,p=0,523). There was also no difference after addition of in buffer solution resuspended platelets received from centrifugated PRP (11,7±10,9%->12,8±9,4%,p=0,792). In contrast a significant increase in PRI-VASP index was observed after addition of PRP alone (14,8%±12,6%->36,7%±13,1%,p<0,001) or PP with human serum (11,7%±10,9%->61,3%±10,9%,p<0,006). These increase of the PRI-VASP was also obvious after administration of human serum alone (11,7%±10,9%->54,1%±2,7%,p<0,001).
Conclusion: The present study demonstrated a pioneer potential solution to reverse the platelet inhibitory effects of Ti ex vivo. We could show that administration of platelet rich plasma, pooled platelets with human serum and human serum alone are able to reverse the effects of ticagrelor ex vivo. This approach is unique and might be a possible solution to solve the problem of reversing the effects of ticagrelor in acute bleedings or urgent surgical procedures.

4975 | BEDSIDE
Balancing the risk of ischaemic and bleeding events in ACS

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Background: Evaluation of antithrombotic treatments for acute coronary syndromes (ACS) requires balancing ischaemic and bleeding risks to assess the net benefit. However, the impact on mortality of ischaemic events and bleeding complications may differ.
Purpose: Compare the impact and relative importance of different types of bleeding and ischaemic events on mortality.
Methods: Predicted probabilities of ischaemic (MI or stroke) and bleeding events at 1 yr following randomisation were estimated for all pts included in the PLATO trial using Cox proportional hazards regression. Time-dependent Cox models assessed the association of time-dependent bleeding and ischaemic events with subsequent mortality, adjusted for baseline characteristics.
Results: Only GUSTO severe bleeding had a similar impact on mortality compared to ischaemic events (Table 1).

Table 1Adjusted results – mortality endpoint

	≤30 days HR (95% CI)	p-value (vs MI/Stroke)	>30 days (95% CI)	p-value (vs MI/Stroke)
MI or Stroke	14.22 (11.54–17.53)		2.33 (1.66–3.26)	
PLATO Major	5.59 (4.48–6.97)	<0.001	1.25 (0.91–1.72)	0.014
TIMI Major	4.92 (3.81–6.36)	<0.001	0.87 (0.57–1.35)	<0.001
GUSTO Severe	11.73 (9.04–15.22)	0.201	2.29 (1.64–3.20)	0.485

MI, myocardial infarction.

Of 14,544 pts, 97.7% had a higher predicted ischaemic risk median (25th–75th) 6.3% (4.6%–9.2%) than the estimated risk of GUSTO severe bleeding 2.9% (2.0%–4.1%) (Figure 1).

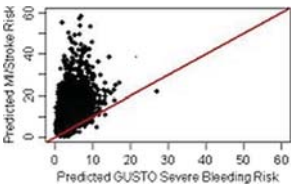

Figure 1

Conclusions: When comparing ischaemic to bleeding events of similar mortality, the higher predicted risk of ischaemic events emphasise the importance of potent antithrombotic therapy in ACS.
Acknowledgement/Funding: Astra Zeneca

4976 | BEDSIDE
Rivaroxaban and vitamin K antagonists are equally effective in preventing recurrent venous thromboembolism - a Danish nationwide study

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Background: In 2012, rivaroxaban was approved as an alternative to vitamin K antagonists (VKAs) for the treatment of venous thromboembolism (VTE).
Purpose: To investigate the risk of recurrent VTE in patients treated with either VKAs or rivaroxaban.
Methods: Through the Danish registries we identified all patients diagnosed with VTE from 6th of February 2012 through 31st of December 2012, and treated with either VKAs or rivaroxaban. Risk of recurrent VTE was estimated by cumulative incidence curves and multivariate Cox proportional-hazards model adjusted for sex, age, comorbidities and concomitant pharmacotherapy, both accounting for death as competing risk.
Results: A total of 3517 patients were included. Of these, 3259 (92.7%) were treated with VKAs (51.4% male; median age 67.8 years; IQR 54.0–78.2) and 258 (7.3%) were treated with rivaroxaban (50.8% male; median age 66.5 years; IQR 50.1–78.6). The two groups were similar with respect to comorbidities and concomitant pharmacotherapy. Recurrent VTE occurred in 248 (7.6%) of the patients in the VKA group and in 19 (7.3%) of the patients in the rivaroxaban group. No significant difference in the risk of recurrent VTE was found between the VKA group and the rivaroxaban group, with cumulative incidences after 180 days of 8.3% (95% CI: 0.07–0.09) and 10.9% (95% CI: 0.05–0.14) respectively (Figure 1), and an adjusted hazard ratio of 1.17 (95% CI: 0.73–1.87, P=0.51) associated with rivaroxaban treatment.

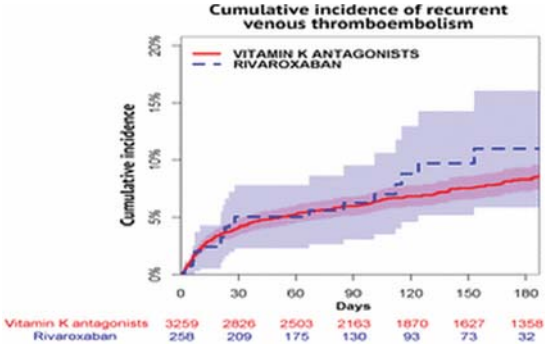

Figure 1. Cumulative incidence

Conclusion: In patients with VTE, rivaroxaban was equally effective as VKAs in preventing recurrent VTE.

4977 | BEDSIDE
Clinical outcome of patients with venous thromboembolism under oral anticoagulation in regular medical care versus a telemedicine-based anticoagulation clinic

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Background: Venous thromboembolism (VTE) is a life-threatening disease. Oral anticoagulation is an effective treatment to prevent thromboembolic recurrence.
Purpose: We aimed to compare the clinical outcome of VTE patients under oral anticoagulation therapy (OACT) in regular medical care (RMC) and in a telemedicine-based anticoagulation clinic (CC).
Methods: ThrombEVAL is a prospective, dual-armed, multi-center study to investigate oral anticoagulation treatment (NCT01809015). Data were assessed in clinical visits, computer-assisted personal interviews, self-reported data and laboratory measurements according to standard operating procedures with detailed quality control. Information on study endpoints was validated and adjudicated by a review committee. Study monitoring was carried out by an independent institution.
Results: The sample comprised 360 patients with history of VTE from RMC and 254 patients from CC, predominantly treated with phenprocoumon (97.4%). VTE patients in RMC were older (72.0 (IQR60.0/79.0) vs. 69.0 (IQR50.0/77.0), P=0.0020) and showed a higher Charlson-Index (5.67±2.56 vs. 4.42±2.71, P<0.0001) than those of CC. Median follow-up time in both cohorts were 12.0 (11.4/12.0) and 12.9 (6.3/19.4) months. The primary study endpoint, a composite of thromboembolic events, major and clinically-relevant non-major bleeding, and death as net clinical benefit outcome, differed significantly between both cohorts with 15.6 in RMC vs. 4.5 events per 100 patient-years (py) in CC (risk ratio (RR): 3.5, 95% CI 1.8/7.3; p<0.001). Rate of thromboembolic events (RR 4.84 [1.33–26.46], p=0.012), major bleedings (RR 5.58 [1.19–52.40], P=0.024) under OAC, hospitalisations (RR 2.08 [1.62–2.69], P<0.001) and mortality (RR 5.32 [2.21–15.47], P<0.001) were higher in RMC compared to the CC. In Cox regression analysis adjusted for age, sex, traditional cardiovascular risk factors and comorbidities, the net clinical benefit was substantially worse in RMC (HR 3.61 [1.42–9.14], P=0.0068). Mortality was still higher in RMC (HR 3.03 [1.22–7.52], P=0.017) and hospitalizations were also more frequent in RMC (HR 1.76 [1.19–2.58], P=0.0043).
Conclusions: The clinical outcome of VTE patients under treatment with VKA was distinctly better in a telemedicine-based CC than in RMC. Future studies should evaluate whether these findings can be translated into the treatment with new oral anticoagulants.
Acknowledgement/Funding: grants of state initiative health economy of ministries of health and economy, Rhineland-Palatinate Germany, federal ministry of education and resear

4978 | BENCH
Prothrombin complex concentrate or Idarucizumab in combination with fibrinogen plus tranexamic acid are equally effective in a dabigatran anticoagulation experimental polytrauma model

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Aim: Trauma-induced bleeding and coagulopathy may be complicated by the direct thrombin inhibitor dabigatan. To restore hemostasis and control bleeding a multimodal approach using hemostatic agents is essential.
Methods: This study assessed the effect of prothrombin complex concentrate (PCC) or the antibody fragment (Fab) idarucizumab in combination with tranexamic acid (TX) and fibrinogen (FG) in a porcine polytrauma model. After ethical approval dabigatran etexilate (n=6/group) was administered orally and infused prior to injury to achieve supratherapeutic plasma levels. A standardized polytrauma including bilateral femur fractures and a blunt liver injury was induced. Subsequently, animals received either placebo (control); TX (20 mg/kg)+FG (80 mg/kg, TF); PCC+TX+FG (PCC: 50 U/kg, TFP) or idarucizumab+TX+FG (Idarucizumab: 60 mg/kg, TFI) according to randomization. Coagulation was assessed by coagulation parameters and diluted TT. Blood loss (BL) was measured over 240 min.
Results: Dabigatran levels were 506±153 ng/mL prior to injury and remained significantly elevated in controls, TF and TFP animals over the 240 min. Dabigatran was not measurable in TFI-substituted animals. The degree of injury was similar with a BL of 798±56 mL prior to intervention. Control and TF animals had the highest BL (3583±507 mL) and 100% mortality (mean survival time 101 min). TFP (1234±215 mL) or TFI (987±168 mL) resulted in a significant reduction in BL and 100% survival. TAT levels and thrombin generation were significantly elevated in the TFP group.
Conclusion: This study shows that cessation of life-threatening bleeding necessitates either substitution with a thrombin-generating drug or the neutralization of the anticoagulant effects of dabigatran. This is supported by the lack of impact on BL following monotherapy with FG plus TX. However, therapy with the Fab may be favorable since there is no overcorrection of thrombin generation of coagulation.
Acknowledgement/Funding: Boehringer Ingelheim

4979 | BEDSIDE
Management and clinical consequences of major bleeding in high-risk patients following an acute coronary syndrome. Is aspirin the problem? Insights from the APPRAISE-2 trial

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Background: High-risk patients with a recent acute coronary syndrome (ACS) treated with antiplatelet and anticoagulant agents are at risk of bleeding. Recent

data indicate that aspirin may be associated with a higher risk of bleeding than other antithrombotics in select patient populations.
Purpose: The aim of this study is to explore antithrombotic therapy changes and clinical events following major bleeding.
Methods: APPRAISE-2 was a multinational clinical trial that included 7392 high-risk patients with a recent ACS randomized to apixaban (5 mg twice daily) or placebo in addition to antiplatelet therapy, most commonly aspirin and a P2Y12 inhibitor. Antithrombotic therapy changes and clinical events during a 30-day period after an ISTH major/clinically relevant non-major (CRNM) bleed were reported and analyzed in Cox proportional hazard models during a median follow-up of 241 days. The models were adjusted for baseline characteristics, comorbidities, prior diseases, and antithrombotic therapy at baseline.
Results: Of the 214 (2.9%) patients who experienced an ISTH major/CRNM bleed during follow-up, 42% continued, 35% interrupted, and 31% discontinued randomized study drug (apixaban or placebo). Patients with bleeding had a higher risk of subsequent myocardial infarction (MI) or ischemic stroke (HR 6.6, 95% CI 3.6–12.1, p-value <0.001) during a 30-day period following the bleeding event. Patients with ISTH major/CRNM bleeding had a higher risk of subsequent mortality, but the increase in risk differed across antithrombotic therapy status at randomization (interaction p-value = 0.021). The risk of subsequent mortality in the 30-day period after a bleeding event was higher in patients receiving aspirin alone (n=604; HR 70.6, 95% CI 9.5–527) or aspirin + apixaban (n=595; HR 64.7, 95% CI 26.9–156) compared with patients receiving a P2Y12 inhibitor alone (n=3334; HR 16.6, 95% CI 7.7–35.5) or a P2Y12 inhibitor + apixaban (n=2833; HR 12.7, 95% CI 6.2–26.4).
Conclusions: In this cohort of high-risk post-ACS patients, bleeding was associated with a higher rate of subsequent major ischemic events and mortality. Patients receiving aspirin, irrespective of concomitant anticoagulation, had a markedly higher risk of subsequent bleeding events compared with treatments not including aspirin. The data suggest that having a bleed post-ACS, regardless of the cause, is associated with a higher risk of subsequent ischemic events, which is at least in part likely related to aspirin treatment.
Acknowledgement/Funding: APPRAISE-2 was supported by Bristol-Myers Squibb and Pfizer

4980 | BEDSIDE
Clinical outcomes of atrial fibrillation patients receiving NSAIDs in the RE-LY trial

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as analgesics and antipyretics. A combination of NSAIDs and anticoagulants may increase the risk of bleeding.
Methods: The aim of this analysis was to compare clinical outcomes in patients who used NSAIDs at least once versus patients who had never used NSAIDs in the RE-LY trial and to compare outcomes of dabigatran etexilate (DE) at both doses (150 mg and 110 mg bid) vs. warfarin, using p-values for interaction for treatment-by-subgroup effect using Cox regression models.
Results: Of the 18,113 patients in RE-LY, 2,279 (12.6%) used NSAIDs at least once in the RE-LY trial in combination with either dabigatran or warfarin. Compared to patients who had never taken NSAIDs, patients who had used NSAIDs were more often females (39.0 vs. 36.1%; p=0.0074), more often had valvular heart disease (24.3 vs. 21.4%; p=0.0024), but slightly less frequently suffered from congestive heart failure (30.1 vs. 32.3%; p=0.037). Both patient groups were comparable in age, CHADS2 scores, frequency of coronary artery disease, diabetes and hypertension.
Whereas the rate of death (p=0.2109), ICH (p=0.3631) and myocardial infarction (p=0.6674) was comparable in NSAID-users and non-users, the risk of major bleeding (p<0.0001), specifically major GI bleeding (p=0.0004), life-threatening (p=0.0103) and any bleeding (p<0.0001), was higher in patients who used NSAIDs. Patients who used NSAIDs were hospitalized more often compared to patients who had never used NSAIDs (p<0.0001).
Irrespective of NSAID use, the relative benefits of DE compared to warfarin were similar regarding clinical outcomes including stroke and systemic embolism (DE 150 mg: HR 0.56 [95% CI 0.31, 1.01] with NSAID versus 0.67 [0.53, 0.84] without; DE 110 mg: HR 1.03 [0.63, 1.69] with NSAID versus 0.87 [0.70, 1.08] without), major bleed (DE 150 mg: HR 0.88 [95% CI 0.63, 1.22] with NSAID versus 0.96 [0.83, 1.11] without; DE 110 mg: HR 0.82 [0.59, 1.14] with NSAID versus 0.80 [0.68, 0.94] without), ischemic stroke, life-threatening or intracranial bleeds (all p-values for interaction were not significant). Lowest absolute numbers of any bleeds were found for DE 110 mg bid.
Conclusion: NSAID use in RE-LY was associated with a higher risk of bleeding and a higher rate of hospitalisations. Patients in the RE-LY trial who received NSAIDs derived similar relative benefits from DE compared to warfarin with lowest rates of bleeding with DE 110 mg bid. The combination of NSAIDs with any oral anticoagulant requires a careful benefit-risk assessment.
Acknowledgement/Funding: This study was funded by Boehringer Ingelheim

ANTITHROMBOTIC PROPHYLAXIS IN ATRIAL FIBRILLATION

P4981 | BEDSIDE
High burden of potentially avoidable stroke from discontinuation of warfarin therapy in non-valvular atrial fibrillation

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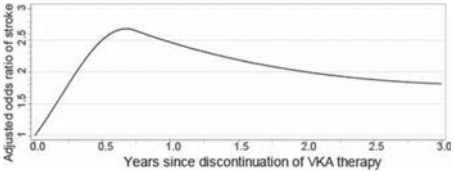
Background: Warfarin prevents stroke in non-valvular atrial fibrillation (AF) but high early discontinuation rates place patients at risk of stroke.
Purpose: To determine the actual increase in stroke risk and risk duration after stopping Vitamin K antagonist (VKA, principally warfarin) AF treatment.
Methods: The UK CPRD with linked Hospital Episode Statistics and medication data was used to identify a cohort with VKA-naive incident AF aged 45 - 89 years between 2001 and 2013. Within this cohort, patients with a new stroke were identified and up to 5 age- and gender matched AF controls without stroke randomly selected. The risk of VKA discontinuation was estimated using a conditional logistic regression model and presented as odds ratios (ORs), with current VKA treatment as the reference.
Results: Among 68,288 AF patients, 5,116 with subsequent stroke were matched to 25,540 controls. The OR (95% CI) for developing a stroke was 1.89 (1.53–2.34) in the 180 days after VKA discontinuation compared to patients on continuous VKA, 2.64 (1.84–3.78) 180–360 days after VKA discontinuation and 2.27 (1.81–2.85) between 1–3 years. Modelled stroke risk (Fig), shows a steep risk increase in the first 6 months, already apparent within 3 months, to a peak between 6–12 months, and a plateau between 2–3 years. In the first year after VKA cessation this equates to an absolute increase in stroke incidence rate of 2.2/100 patient years, and 2.7/100 patient years between 1–3 years. Restricting analysis to AF patients with CHA2DS2VASc scores ≥2 did not change results.



Modelled Stroke Risk (quadratic spline)

Conclusions: Stopping VKA in patients with AF more than doubles stroke risk. The high absolute risk persists for at least 3 years. Reducing the stroke burden from AF will require greater attention to issues surrounding anticoagulant discontinuation.

P4982 | BEDSIDE
Precipitated non valvular atrial fibrillation (NVAF): can we apply the CHA2DS2-VASc score in the determination of the risk of stroke and death?

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Purpose: Very few data are available on the risk of cardiovascular complications and also the pertinence of the validated risk scores in NVAF, including the CHA2DS2VASc score, in precipitated non valvular atrial fibrillation (pNVAF). We sought to investigate whether this score could also be useful to predict the risk of stroke and death in patients with pNVAF.
Methods: Between 1998 and 2011, among 1,212 consecutive NVAF patients, hospitalised for AF, 221 had a precipitating factor (sepsis, systemic disease, pericarditis, hyperthyroidism, pulmonary embolism, cancer or surgery). All patients were followed-up at least 6 months and cardiovascular events recorded. The endpoint was defined as the first occurrence of stroke or death. The Cox analysis was adjusted for year of inclusion, AF type and warfarin, antiplatelet and antiarrhythmic treatments at discharge.
Results: Mean age was 71±13 in pNVAF and 67.7±14.9 years in NVAF (p=0.0087). At baseline, in the pNVAF group CHA2DS2VASc score were =0 for 16 (7%) patients, = 1 for 27 (12%), ≥2 for 178 (81%). NVAF CHA2DS2VASc scores were = 0 for 159 (13%), =1 for 182 (15%), ≥2 for 871 (72%). The difference was statistically significant (p=0.016).

Cox regression at 1 year follow-up

	Event	Crude HR (95% CI); p	Adjusted HR (95% CI); p
NVAF & CHA2DS2VASc <2; n=341	5	ref	ref
pNVAF & CHA2DS2VASc <2; n=43	4	6.63 (1.78–24.69); 0.005	5.27 (1.41–19.71); 0.014
NVAF & CHA2DS2VASc ≥2; n=871	81	6.59 (2.67–16.27); <0.0001	5.46 (2.19–13.57); <0.0001
pNVAF & CHA2DS2VASc ≥2; n=178	40	17.75 (6.91–43.72); <0.0001	10.95 (4.29–27.95); <0.0001

During the first year of follow-up, the patients with pNVAF experienced 44 (20%) and the patients with NVAF experienced 86 (7%) stroke or death. The Kaplan-Meier curves (Log-rank p<0.0001) show that pNVAF patients with a CHA2DS2VASc score ≥2 were at higher risk of stroke or death but not pNVAF patients with a CHA2DS2VASc score <2. The adjusted Cox model showed that pNVAF and a CHA2DS2VASc score ≥2 (adjusted HR, 10.95, 95% CI 4.29–27.95, p<0.0001) were predictors of risk of stroke or death.
Conclusion: These results suggest that a CHA2DS2VASc score ≥2 is associated with a higher risk of stroke and death, at short-term follow-up in precipitated NVAF. The guidelines should be implemented to recommend the determination of CHA2DS2VASc stratification in all types of NVAF, including patients with a precipitating factor.

P4983 | BEDSIDE
Ablation of atrial fibrillation with uninterrupted NOAC treatment is not associated with severe peri- and postprocedural complications

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Catheter ablation of atrial fibrillation (AF) is a widely adopted therapy in patients with drug resistant AF. Pulmonary vein (PV) isolation is the cornerstone of that procedure. Since periprocedural thromboembolic complications represent one of the most worrisome complications of catheter ablation tailored periprocedural anticoagulation is of central importance. Accumulating evidence suggests that ablation performed without stopping vitamin K antagonists is associated with lower periprocedural complications as compared to discontinuation of vitamin K anatgonists and bridging with fractionated heparin. Whether the same holds true for uninterrupted treatment with the novel oral anticoagulants (NOAC) is a matter of intense debate.
During the observational period (Jan 2013–Oct. 2014) a total of 549 consecutive patients were scheduled for PVI because of drug refractory AF. All patients were ablated with support of 3 D mapping systems (CARTO 3, CARTO UNIVU or NAVx Ensite). The first group of these patients (n=233, mean age 67±8 years, 56.2% male, mean CHA2DS2 VASc score 2.6) was continuously anticoagulated with vitamin K antagonists (target INR 2–3). A second group of patients (n=316, mean age 64±11 years, 55.7% male, mean CHA2DS2-VASc score 2.3) were treated with uninterrupted NOAC therapy – i.e. no withholding of a single NOAC dose. A follow-up of three month was achieved for all patients. Baseline characteristics these two groups showed no relevant differences. Collectively, there were a total of three pericardial effusions requiring pericardiocentesis (VKA group: 1 PE, DOAK group: 2 PE, P=ns). Importantly, the two PE in the DOAK groups did not require a specialized treatment (like fresh frozen plasma etc.) Additionally, a total of 2 access complications were observed (VKA group: 1 pseudoaneurysm, DOAK group: 1 pseudoaneurysm, P=ns). Notably, no thromboembolic event occurred during the intervention or during the follow-up.
Our observational study demonstrates that catheter ablation without NOAK discontinuation is not associated with an increased periprocedural bleeding or thromboembolic complication rate.

P4984 | BEDSIDE
Warfarin therapy is associated with lower risk of dementia in patients with incident atrial fibrillation in a community based cohort

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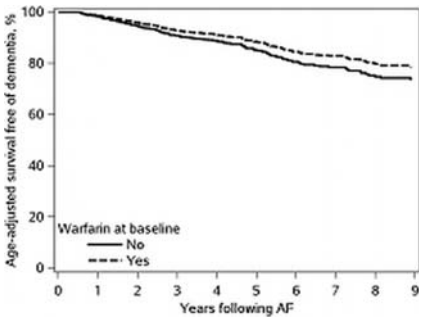
Background: Atrial fibrillation (AF) has been associated with dementia independent of clinical stroke. This risk may be modulated by clinically silent cerebral embolism, though influence of warfarin on risk of dementia in AF is not well understood.
Purpose: We hypothesized that warfarin may reduce incidence of dementia in AF by reducing cerebral thromboembolism.
Methods and results: 1860 cases of incident AF were identified in Olmsted County, MN between 2004–2010 [mean age 71 (±15) y, 54% males, median CHA2DS2-VASc score 3 (IQR 2–4)]. Warfarin was prescribed to 834 (45%) patients within the first 90 days after incident AF. Men and subjects with CHA2DS2-VASc score ≥2 were more likely to be prescribed warfarin. CHA2DS2-VASc score ≥2 was noted in 76% of patients not prescribed warfarin. Incident dementia identified using ICD codes occurred in 198 (11%) over mean follow-up of 4.3 y. Cox proportional hazards regression was used to identify significant predictors of dementia. After adjusting for age, patients prescribed warfarin were less likely to develop dementia (Fig). After adjustment for age and sex, warfarin therapy was protective [HR 0.75 (95% CI 0.57–0.99)]. In a fully adjusted model with pre-specified potential dementia risk factors, age [1.09 (1.07–1.10) p<0.0001], warfarin therapy at AF diagnosis [0.66 (0.47–0.91) p=0.01] and peripheral vascular disease [2.04 (1.26–3.31)] predicted dementia. Similar findings were noted when warfarin therapy was considered as a time dependent variable [HR 0.64 (0.45–0.91)].
Conclusion: Warfarin therapy is associated with 35% reduction in risk of dementia in a community based cohort of incident AF. Warfarin was underutilized however even in high risk patients. Further study is necessary to investigate the role of warfarin in reducing dementia in AF patients.



Age-adjusted survival free of dementia

P4985 | BEDSIDE
Prognosis in patients with atrial fibrillation and CHA2DS2-VASc score = 1 in a community based cohort study

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Objectives: Patients with atrial fibrillation (AF) and a CHA2DS2-VASc score = 1 may have an intermediate risk of stroke and are recommended to receive antithrombotic therapy but several recent guidelines propose slightly different management in such setting. It remains unclear whether individual components that constitute CHA2DS2-VASc score contribute equally to the ischemic stroke risk, particularly in patients with CHA2DS2-VASc score of 1. In addition, most recent trials with OAC did not include these patients at lower risk of stroke. Our objective was to describe and compare the risk of ischemic stroke of the six individual components constituting CHA2DS2-VASc and the impact of antithrombotic management in a community based cohort of unselected AF patients with a CHA2DS2-VASc score = 1.
Methods and results: All patients with AF seen in our institution between 2000 and 2010 were identified in a database. The adverse outcomes were investigated during follow-up. Among 8962 patients with AF, 1077 (12%) had a CHA2DS2-VASc score = 1 in whom an oral anticoagulant was prescribed in 49%, antiplatelet therapy alone in 21%, and no antithrombotic treatment in 26%. During a follow-up of 958±1146 days, 71 of these patients sustained events with 29 stroke/thromboembolism (yearly rate 1.0%) and 49 deaths (yearly rate 1.7%). The lowest yearly rate of these combined events was seen in female patients (0.8%) and was higher in patients with hypertension (1.8%), vascular disease (2%), age 65–75 (2.8%), heart failure (3.2%) and diabetes (4.4%) (overall p=0.004). Prescription of oral anticoagulation was not associated with a better prognosis for death/stroke/thromboembolism in female (HR=1.24, 95% CI 0.12–12.5, p=0.86 after adjustment on age and antiplatelet use) whilst it was independently associated with a better prognosis in all other patients with CHA2DS2-VASc score = 1 (adjusted HR=0.49, 95% CI 0.28–0.84, p=0.01). Antiplatelet therapy was not associated with a better prognosis in these patients.
Conclusion: In a real life cohort study, AF patients with CHA2DS2VASc score =1 had a risk of death/stroke/thromboembolism which was low in female patients and significantly higher in other patients. Oral anticoagulation was associated with a better prognosis in these patients except for females. This supports the current expert consensus in the European guidelines for oral anticoagulation in these not so "low risk" patients when they are not female patients.

P4986 | BEDSIDE
5-year real world experience using three LAA-closure devices

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Background: Left atrial appendage closure (LAAc) is a valuable option to prevent cardioembolic stroke in patients with atrial fibrillation. In clinical practice, LAAc is predominantly performed in patients with atrial fibrillation who are at a high thrombembolic risk but are not amendable for chronic oral anticoagulation due to relevant bleeding complications.
Methods and results: Between 2009 and 2014, 90 patients underwent interventional left atrial appendage closure at our institution. These patients were 76±8 years of age and male in the majority of cases (61.1%) and had a high thrombembolic (Chads2Vasc2 4.0±1.2) and bleeding risk (HasBled 3.8±0.5). LAAc was performed after relevant bleeding complications under OAC in 75% of patients. LAAc was successfully completed in 96.6% of patients (86/90) with implantation of the Watchman device in 52.3%, the Amplatzer Cardiac Plug in 34.9% and the Coherex Wavecrest device in 12.8% of cases. Procedural outcome was good, with one case of pericardial effusion and two cases of periprocedural device-embolisation. No differences in procedure duration or amount of constrast dye were observed between the three devices. After a mean follow up of 825±516 days, cardiovascular mortality was 4.6% including one case of suspected fatal stroke (1.2%) representing the overall thromboembolic events during FU. Of note,

the incidence of recurrent bleeding during FU including early anticoagulant therapy after LAAc was very low with only one patient suffering from major bleeding (1.2%).
Conclusion: In our real-word experience using all available occluder devices, LAAc in patients with high thromboembolic and bleeding risk proved to be safe and effective with low rates of stroke and bleeding during 2 years.

P4987 | SPOTLIGHT
Comparative cost-effectiveness of oral anticoagulants for stroke prevention in non-valvular atrial fibrillation patients in the UK

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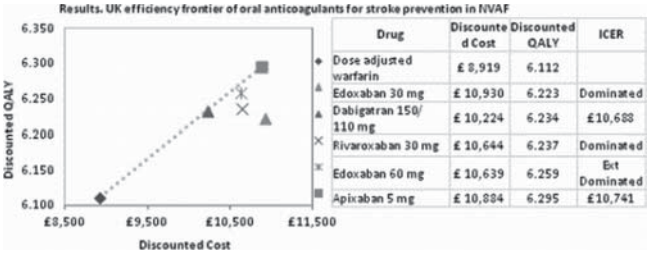
Background: Efficiency frontier analysis is increasingly used in many parts of Europe to aid in identification of the treatments that provide most clinical value for a given investment, considering the trade-offs between costs and benefits for each alternative in the context of other relevant interventions. Limited information is available about relative value of non vitamin K antagonist (VKA) oral anticoagulants (NOACs) versus warfarin in non-valvular atrial fibrillation (NVAF) patients.
Purpose: To assess cost-effectiveness dose-adjusted warfarin, apixaban 5mg BID, dabigatran 150mg BID followed by 110mg at the age of 80, rivaroxaban 20mg QD, edoxaban 30mg QD and edoxaban 60mg QD in the UK NVAF patients using efficiency frontier analysis.
Methods: A lifetime Markov model was developed to evaluate the health and economic impact of NOACs and warfarin from the UK NHS perspective. Clinical events comprised ischemic stroke, intracranial hemorrhage, other major bleed, clinically relevant non-major bleed, myocardial infarction, cardiovascular hospitalization and treatment discontinuations. Key input data sources were as follows: clinical and indirect treatment comparison data derived from ARISTOTLE, AVERROES, RELY, ROCKET-AF and ENGAGE-AF; UK life tables; published literature and NHS reference costs. Medical costs were estimated in 2012 GBP and discounted at 3.5% per year. Comparative cost-effectiveness of various anticoagulants was assessed by establishing efficiency frontier using total costs on horizontal axis and QALYs gained on vertical axis.



Drug	Discounted Cost	Discounted QALY	ICER
Dose adjusted warfarin	£ 8,919	6.112	
Edoxaban 30 mg	£ 10,930	6.223	Dominated
Dabigatran 150/ 110 mg	£ 10,224	6.234	£10,688
Rivaroxaban 30 mg	£ 10,644	6.237	Dominated
Edoxaban 60 mg	£ 10,639	6.259	Ext Dominated
Apixaban 5 mg	£ 10,884	6.295	£10,741

Conclusions: Warfarin, dabigatran and apixaban were the optimal treatment strategies with apixaban producing the highest QALY gain. Apixaban appears to be a more effective treatment alternative to other two drugs at an economically accepted cost.

ACUTE PHASE OF STEMI

P4988 | BEDSIDE
Impact of ESC guidelines system delays on myocardial salvage in STEMI

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Background: According to current ESC STEMI guidelines, primary PCI is accepted as the recommended reperfusion therapy if performed within 120 min of first medical contact (FMC). However, it is preferred to achieve shorter FMC to PCI delays, that is, a FMC to PCI delay ≤90 min and ≤60 min for patients initially presenting to a PCI-capable centre or patients within 120 min of symptoms onset.
Purpose: To quantify myocardial salvage provided by fulfillment of more restrictive preferred recommendations as compared to accepted system delays according to ESC 2012 guidelines.
Methods: The BARI score was adapted to quantify the angiographic myocardial area at risk in 333 patients (80% men, 46% anterior) with first STEMI admitted or referred to a tertiary hospital for primary PCI. A myocardial salvage index (MSI) was computed as the percentage of the area at risk that spared infarction by late gadolinium enhancement magnetic resonance. MSI was compared between subjects who fulfilled or not current ESC recommendations regarding FMC-to-PCI delays.
Results: MSI decreased with increasing ischemic time, but only up to 4 fours (Fig.1A). Achieving FMC-to-PCI ≤120 min (53% of cases) did not confer a significant increase in MSI (40±32% vs 35.3±28.7%, p=NS). However, MSI was higher among the 83 (25%) patients who met the more restricted and preferred FMC-to-PCI delays (43.9±33.0% vs 36.2±29.7%, p<0.05). This difference was mainly observed among patients with an initial TIMI flow 0–1 (Fig 1B).

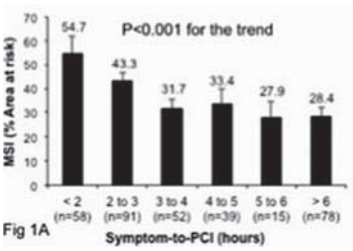

Fig 1A

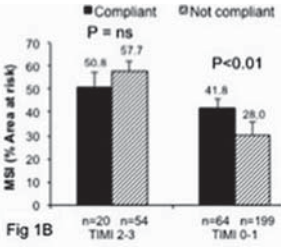

Fig 1B

Conclusion: Adherence to preferred shorter FMC-to-PCI delays (≤60 or ≤90 min) confers a benefit in myocardial salvage, compared to more relaxed and acceptable delays (≤120 min). The difference was mainly seen in subjects with an occluded artery and those reperfused within the first 4 hours from symptoms onset.

P4989 | BEDSIDE
High mortality in patients with ST elevations undergoing emergency coronary angiography not treated with primary PCI or CABG

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Background: Immediate coronary angiography is recommended in every patient presenting with acute chest pain and ST segment elevations suggestive for ST elevation myocardial infarction. Little is known about the fate of patients with ST elevations not treated with primary percutaneous coronary intervention (PCI).
Methods: We evaluated the diagnosis and in-hospital outcomes of patients undergoing emergency angiography for presumed STEMI within 24 hours after symptom onset in the ALKK-registry. We divided patients into groups
Results: Between 2009 and 2013 a total of 22429 patients underwent angiography for presumed STEMI <24 hours. Of these 20040 were treated with primary PCI, 635 underwent coroany artery bypass graft surgery and 1817 were treated conservatively.
The in-hospital mortality in patients with PCI was 7.1%, with CABG 6.3% and 6.8% in the conservative group. We than further subdivided the conservative group in patients with significant coronary artery disease (STEMI treated conservatively) (n=555), without significant coronary artery disease (n=877) and with other cardiac diseases (n=350; dilated cardiomyopathy 43%, hypertensive heart disease (12%), valve disease 3%, aortic aneurysm 0.5%, other 43%). The corresponding in-hospital mortality rates were 12.3%, 4.4% and 5.2%, respectively.
Conclusion: Patients undergoing angiography for STEMI having significant coronary artery disease but treated conservatively have a high mortality. Unexpectedly the mortality in patients with presumed STEMI without significant coronay artery disease or other cardiac dieases is around 5%. These patients deserve further research to improve outcome in this so far neglected patient group.

P4990 | BEDSIDE
Cerebral and renal impact in 5,040 patients with acute myocardial infarction wth cardiogenic shock combined coronary revascularization and intra-aortic balloon pump support: implications from populati

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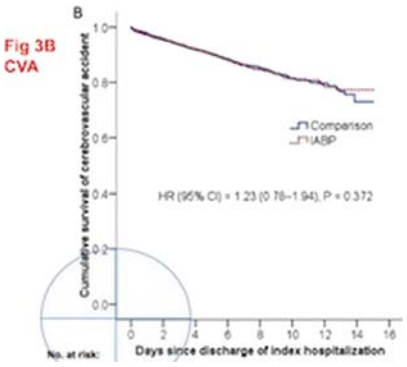
Objective: Prior studies have suggested intraaortic balloon pump (IABP) have a neutral effect on acute myocardial infarction (AMI) patients with cardiogenic shock (CS). However the effects of IABP on patients with profound CS remain unclear.
Purpose: We therefore investigated cerebral and renal outcomes between low-dose dopamine+IABP and high-dose dopamine in AMI patients with profound CS undergoing coronary revascularization.
Methods: The present study enrolled 5,040 adult patients with myocardial infarction (MI) and profound CS who underwent coronary revascularization and divided them into the IABP+low dose dopamine group (n=2520) and the high-dose dopamine group (n=2520) after propensity score matching to equalize confounding variables. Primary outcomes included MI, stroke or cardiovascular death. In-hospital events, including dialysis, pneumonia and sepsis, were secondary outcomes. We used propensity score matching to reduce selection bias and to balance baseline characteristics and clinical variables that could potentially affect outcomes.
Results: The MI recurrence rate was higher (HR=1.3, p=0.007) and cardiovascular death was much higher in the IABP+low dose dopamine group (HR=1.61, p<0.001). However, the incidence of stroke was similar between the two groups (HR=1.07, p=0.605). Interestingly, the IABP group had lower incidence of dialysis (HR=0.29, P<0.001), pneumonia (HR=0.43, P<0.001) and sepsis (HR=0.56, P<0.001) during hospitalization than the Nonuser group.
Conclusion: In AMI combined cardiogenic shock and PCI, IABP with low-dose



Cumulative survival of CVA

dopamine had worse cardiovascular outcome but it reduced incidence of acute renal failure and dialysis. They had neutral neuroprotective effects between two group.

P4991 | BEDSIDE

Gender differences in cardiogenic shock after acute myocardial infarction. The FAST-MI programme

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Rationale: Cardiogenic shock (CS) complicating acute myocardial infarction (AMI) occurs more frequently in women, but little is known about its potential specificities according to gender.
Methods: We analysed the incidence, management, and one-year mortality of CS according to gender in 4 nationwide French surveys carried out 5 years apart from 1995 to 2010, including consecutive STEMI and NSTEMI patients over one-month periods, and with one-year follow-up available.
Results: Among the 10,610 patients included in the surveys, the prevalence of CS was 4.8% in men and 8.2% in women (P<0.001). Absolute prevalence of CS decreased from 1995 to 2010 in both genders (5.4% to 3.0% in men, 10.5% to 6.5% in women). In men, the prevalence significantly decreased after adjusting for baseline characteristics (OR for 2010 vs 1995: 0.54, 0.39–0.75, P<0.001), but the decrease was not significant in women (OR 0.86, 0.58–1.29, P=0.47). In particular, in STEMI patients, the prevalence of CS decreased in men (OR 0.52, 0.35–0.77) but remained stable in women (OR 1.09, 0.69–1.71).
Mean age in patients with CS tended to decrease in men (from 72±12 to 69±13 years, P=0.09) and to increase in women (from 78±10 to 80±9 years, P=0.18). Use of PCI ≤3 days of admission increased for both men (from 24% to 68%, P<0.001) and women (from 11% to 56%, P<0.001). Occurrence of atrial fibrillation and ventricular fibrillation remained constant for both men and women. Atrioventricular block decreased in men (from 25% to 10%) and women (from 23% to 15%).
One-year mortality significantly decreased in men (from 70% in 1995 to 48% in 2010) and women (from 81% to 54%). By Cox multivariate analysis, female sex was not an independent correlate of one-year mortality (HR 0.98, 0.78–1.22). In men, only age, history of stroke, and study period (HR for 2010 vs 1995 0.41, 0.26–0.65) were associated with one-year death, while early use of PCI was associated with a non-significant trend only (HR 0.85, 0.61–1.19); in women, NSTEMI (HR 0.49, 0.32–0.75), early use of PCI (HR 0.55, 0.37–0.81) and study period (0.54, 0.33–0.89) were independent predictors of one-year death.
Conclusion: The prevalence of CS is higher in women. IN STEMI patients, the prevalence of CS has decreased in men, but not in women. One-year mortality, however, has significantly decreased for both men and women, and the role of early PCI as a potential mediator of decreased mortality seems greater in women than in men. Better understanding of the pathogenesis and specificities of cardiogenic shock in women is still needed.

P4992 | BEDSIDE

30 day clinical outcomes of bivalirudin vs heparin in the elderly patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention, a pooled analysis

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Background: Large randomized trials have demonstrated that bivalirudin administration in patients presenting with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) improved 30 day clinical outcomes (in particular less bleeding and thrombocytopenia) when compared with heparin with or without a glycoprotein inhibitor (GPI), although at the cost of greater stent thrombosis (ST). Since older age is a strong predictor of not only bleeding but also of thrombotic adverse events, understanding the effect of bivalirudin in the elderly is important.
Methods: We performed a patient level pooled analysis (n=5800) of two large randomized trials (EUROMAX and HORIZONS-AMI). A total of 2149 elderly patients (≥65 years of age) with STEMI were enrolled and randomly assigned to either bivalirudin or heparin with or without a GPI (control group) before pPCI. 30-day clinical outcomes were analyzed.
Results: Stroke (1.3% vs 0.4%, p<0.01), protocol-defined non-CABG major bleeding (8.8% vs 4.3%, p<0.001) and death (5.5% vs 1.1%, p<0.01) occurred significantly more often in elderly than in younger patients. Conversely, event rates of myocardial infarction (MI) and stent thrombosis (ST) were comparable in both age groups. In the elderly, bivalirudin significantly reduced 30-day non-CABG major bleeding (7.1% vs. 10.4%; relative risk [RR], 0.68; 95% confidence interval [CI], 0.51 to 0.90; p<0.01), subacute ST (0.4% vs. 1.5%; RR, 0.25; 95% CI, 0.08 to 0.73; p<0.01) and the composite endpoint of death, myocardial infarction, non-CABG major bleeding, stroke or ischemia-driven revascularization (IDR) (13.7% vs. 17.2% RR, 0.80; 95% CI, 0.65 to 0.98; p<0.03) with non-significantly different rates of acute ST (0.7% vs. 0.3% RR, 2.5; 95% CI, 0.65 to 9.56; p=0.17), MI (1.5% vs. 1.6% RR, 0.95; 95% CI, 0.49 to 0.1.84; p=0.87) and death (4.9% vs. 6.1% RR, 0.80; 95% CI, 0.56 to 1.14; p=0.21) when compared with heparin ± GPI.
Conclusion: In elderly patients enrolled in the EUROMAX and HORIZONS-AMI trials, bivalirudin significantly reduced 30 day non-CABG major bleeding and subacute ST with comparable rates of acute ST, MI and death, when compared with heparin with or without GPI.

P4993 | BEDSIDE

Revascularization strategies in patients with ST-segment elevation myocardial infarction and multivessel disease in a real world population

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Background: The ideal revascularization (Rv) strategy in patients (P) with ST-segment elevation myocardial infarction (STEMI) and multivessel coronary disease who undergo primary percutaneous coronary intervention (1ª PCI) is controversial.
Purpose: Identify in a real world population the factors that had been influencing our Rv strategies choices in P with STEMI and multivessel coronary disease. Determine the prognostic value of the different Rv strategies in these P.
Methods: Retrospective, unicentric study based on 1142 P admitted with STEMI over 5 years and during a minimal 6 months (6m) follow-up. P with multivessel coronary disease who undergone successful 1ª PCI were included (n=409). P were ineligible if they had: history of surgical myocardial revascularization (n=5); left main stem or ostial left anterior descending artery (LAD) disease (n=22); cardiogenic shock (n=21) or died during admission (n=30). The following Rv strategies were compared: 1) culprit artery 1ª PCI only (Rv1); 2) staged complete Rv (Rv2) and 3) ischemia guided Rv (Rv3). The primary endpoint studied was a composite of 6m mortality, nonfatal myocardial infarction and repeated revascularization.
Results: The most common Rv strategy performed was RV1 (59,8%) followed by Rv2 (29,3%). P managed with Rv1 were older (66±13 vs 60±12 vs 60±11y;p<0,001) and had more often chronic renal failure (3,9% vs 0% vs 2,1%; p=0,007). They had more often bifurcation (6% vs 5% vs 5,2%; p=0,07) and long (8,6% vs 5,2% vs 6,2%; p=0,07) coronary stenosis, in smaller branches (30,1% vs 8% vs 17,1%;p<0,001) and distal coronary segments (29,4% vs 15,6% vs 14,2%;p<0,001). P who undergone Rv2 had more often LAD non culprit lesions (31% vs 51% vs 40%;p=0,005) and more severe stenosis (76±11% vs 85±12% vs 83±9%;p=0,04). P managed with Rv3 had lower mean ejection fraction values (44±9% vs 47±9% vs 42±8%;p=0,04). After multivariate analysis, stenosis severity, presence of LAD non culprit lesions and renal dysfunction persisted as independent variables that had been influencing Rv strategy choice. The incidence of primary endpoint was higher in P managed with Rv1 (34,9% vs 10,5% vs 28,6%; p=0,003). After multivariate analysis, this strategy persisted as an independent predictor of the clinical event studied (HR 1,9;CI 95%;p=0,02).
Conclusion: In P with STEMI and multivessel coronary disease the Rv of culprit artery only had a poorer 6m outcome when compared with complete staged or ischemia guided Rv. Stenosis severity, the presence of LAD non culprit lesions and renal dysfunction were the main determinants of Rv strategy choice in a real world population.

P4994 | BEDSIDE

Comparative effectiveness of primary percutaneous coronary intervention versus fibrinolytic therapy for ST-elevation myocardial infarction by time to treatment. A national cohort study

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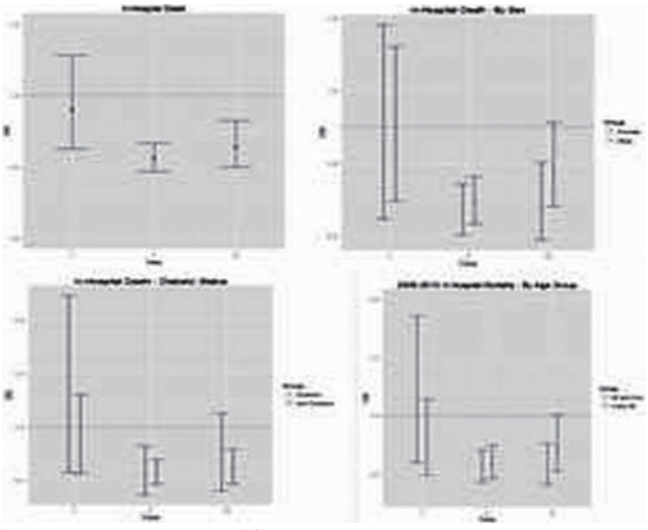
Introduction: Primary percutaneous coronary intervention (PCI) is reported to be better than fibrinolytic therapy (FT) for acute STEMI. However, it is not know if this is upheld in patients who present early to hospital.
Methods: Nationwide population-based cohort study (243 hospitals, 78,343 patients, 2006–10) using data from the Myocardial Ischaemia National Audit Project (MINAP). We used inverse weighted propensity score regression analysis for use of primary PCI to compare the effectiveness (in-hospital mortality from any cause) of primary PCI versus FT for STEMI by call to treatment (CTT) time.
Results: Overall 52.7% of patients received primary PCI and 47.3% in-hospital FT. CTT times were shorter for FT than primary PCI (difference in medians 43 minutes). Primary PCI was associated with a lower risk of death than FT for CTT times between 1 and 2 hours (in-hospital mortality adjusted odds ratio (aOR) 0.56, 95% confidence interval 0.48 to 0.67) and between 2 and 12 hours (in hospital mortality aOR 0.64, 0.50 to 0.8) but was no better than FT for CTT times ≤1 hour (in-hospital mortality aOR 0.90, 0.63 to 1.28). For CTT times between 2 and 12 hours, the effectiveness of primary PCI over FT was greater in males (aOR 0.52, 0.38 to 0.80), age >80 years (aOR 0.55, 0.41 to 0.76) and those without diabetes (aOR 0.61, 0.47 to 0.80).



Risk of in-hospital death for primaryPCI

Conclusion: For patients hospitalised with STEMI, primary PCI is equally effective as in-hospital FT for CTT times ≤1 hour, but is associated with reduced in-hospital mortality for CTT times between 1 and 12 hours. For longer CTT times, the effectiveness of primary PCI over FT is greater in males, the elderly and those with diabetes.

ADVANCES IN CARDIAC COMPUTED TOMOGRAPHY IMAGING

P4995 | BEDSIDE

Aortic valve calcium volume predicts paravalvular regurgitation and the need for balloon post-dilatation after transcatheter aortic valve implantation

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Background: Paravalvular regurgitation (PVR) remains a frequent complication of transcatheter aortic valve implantation (TAVI) that has been shown to be associated with increased morbidity and mortality.
Purpose: This study sought to evaluate the impact of aortic valve (AV) and left ventricle outflow tract (LVOT) calcium on PVR and need for balloon post-dilatation after TAVI.
Methods: A total of 131 patients submitted to TAVI were included in the study. AV and LVOT calcium volumes were estimated from contrast-enhanced multislice computed tomography imaging, using a dedicated software and 3 thresholds for calcium detection [650 Hounsfield units (HU), 850 HU and 1050 HU]. Post-procedural PVR was graded by transthoracic echocardiography, according to Valve Academic Research Consortium-2 (VARC-2) criteria.
Results: A self-expandable prosthesis was implanted in 64.1% of patients and a balloon-expandable prosthesis in the remaining 35.9%. Seventy patients (53.4%) presented post-procedural PVR, which was mild in 45.8% and moderate in 7.6%. The greatest discriminatory value for PVR ≥ mild was seen at 850 HU threshold, with an area under the curve of 0.72 (95% CI 0.64–0.80, p<0.001) for AV and of 0.63 (95% CI 0.54–0.72, p=0.008) for LVOT. At this HU threshold, the calcium volume cut-off with the highest sum of sensibility and specificity for PVR was 157 mm^2 (sensibility 72%, specificity 67%) for AV and 0.6 mm^2 (sensibility 47%, specificity 80%) for LVOT. In a multivariate logistic regression analysis that included aortic valve calcium ≥157 mm^2, LVOT calcium ≥0.6 mm^2 and annulus area ≥ prosthesis area, the presence of aortic valve calcium ≥157 mm^2 was the sole independent predictor of mild or greater PVR (OR 4.2, CI 95% 1.8–9.7, p=0.001). Aortic valve calcium ≥267 mm^2 (using a threshold of 850 HU) was also the only independent predictor of the need for balloon post-dilatation (OR 11.3, CI 95% 1.2–103.1, p=0.03).
Conclusion: AV calcium was the only independent predictor of mild or greater PVR and of the need for balloon post-dilatation in patients submitted to TAVI. The best calcium volume cut-offs were 157 mm^2 and 267 mm^2, respectively. Pre-procedural imaging study should include systematic assessment of AV calcium volume.

P4996 | BEDSIDE

Coronary artery calcium and metal stent subtraction by 320-row cardiac-CT: fact or fiction?

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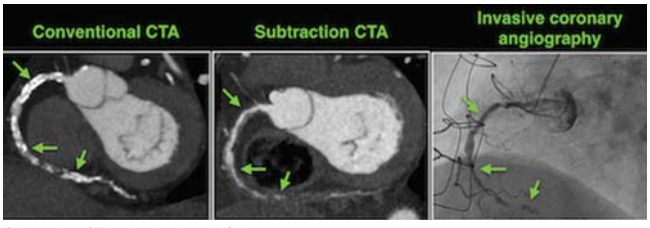
Background and purpose: Coronary CT angiography (CTA) reliably detects coronary artery disease (CAD), but its diagnostic accuracy is reduced in patients with highly calcified or previously stented vessels. In this study we investigate the feasibility and diagnostic accuracy of subtraction CTA using a recently developed software, on a series of patients with these features, as compared to invasive coronary angiography (ICA).
Methods: Selected were 23 patients with calcified or stented CAD shown at a previous ICA. CTA exams were performed using 320-row CT with an acquisition protocol that includes 2 studies (non-contrast and contrast) obtained during the same breath-hold. The non-contrast CT is subtracted from the contrast CT to remove the calcium/metal signal in the vessels. A subjective image quality score was assigned at each coronary segment using a 4-point scale (1: unreadable to 4: good image quality).
Results: A total of 129 coronary artery segments were analyzed. There was significant improvement in image quality in subtraction compared to conventional CTA (3.3±0.9 vs 2.7±0.9; p<0.01), although in those segments with motion artefact it was not significant (2.7±1.2 vs 2.4±1.2; p=0.23). Metal subtraction from stented segments led to significantly improved image quality (3.3±0.9 vs 2.7±0.9; p=0.01), while in those stents <3 mm of diameter this improvement was not significant (2.7±0.9 vs 2.1±0.8; p=0.17). Diagnostic accuracy to detect stenosis >50% by subtraction CTA significantly improved in comparison with conventional CTA (AUC 0.91 vs. 0.83; p=0.05).



Subtraction CTA of a dominant RCA

Conclusion: Subtraction CTA is a promising tool to overcome limitations of conventional CTA due to calcium/metal artefacts, which significantly improves the CTA diagnostic accuracy, particularly when no motion artefact are present.

P4997 | BEDSIDE

Diagnostic Accuracy of Rapid Kilovolt Peak-Switching Dual-Energy CT Coronary Angiography in Patients with High Calcium Score

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Background: Although good diagnostic performance of coronary CT angiography has been widely demonstrated, beam-hardening artifacts resulting from heav-

ily calcified plaques may preclude high-quality images and diagnostic accuracy. Recently, a new CT technology that combines dual-energy CT (DECT) with rapid peak kilovoltage (kVp) switching (gemstone spectral imaging, GSI) and allows to reconstruct material decomposed images (MDI) was introduced in clinical practice.

Objectives: To evaluate the diagnostic accuracy of coronary CT angiography using DECT with monochromatic images and calcium removal by MDI vs. simulated conventional polychromatic images evaluation as standard of reference (sSTD).

Methods: We enrolled 75 patients referred for clinically indicated invasive coronary angiography who had a coronary calcium score (CCS) >400 and underwent coronary CT angiography with prospective ECG-triggering without padding. In all patients, 77 KeV mono-chromatic images used to simulate a conventional 120 kVp poly-chromatic images (sSTD) and the corresponding MDI (Iodine minus calcium) were reconstructed from a GSI Cardiac exam. Two independent blinded experienced readers interpreted all studies for both STD and GSI reconstructions

Results: The mean CCS was 606±253.Twenty patients had a 1-vessel disease (>50% stenosis), 26 patients had a 2-vessel disease, 5 patients had a 3-vessel disease. Coronary evaluability (number of coronary segments evaluable/total number of coronary segments), in a segment-based model, was significantly higher with MDI vs. sSTD (98% vs.95%, $p<0.0001$). A significantly lower number (6 vs. 46, $p<0.0001$) of beam-hardening artifacts (large coronary calcifications impairing accurate evaluation of the lumen)was observed with MDI vs. sSTD. In a segment-based analysis, specificity, positive predictive value and accuracy for >50% coronary stenosis identification were significantly higher with MDI vs. sSTD (99%, 94% and 99% vs. 96%, 66% and 96%, respectively, $p<0.001$). The sensitivity was 100% in both groups. Similarly, in a patient-based analysis, specificity, negative predictive value, positive predictive value and accuracy were significantly higher with MDI vs. sSTD (89%, 100%, 94% and 96% vs. 11%, 50%, 65% and 64%, respectively, $p<0.001$).

Conclusions: DECT with MDI improves coronary CT angiography evaluability and diagnostic accuracy in patients with suspected CAD and high CCS.

P4998 | BEDSIDE

Relationship between adverse coronary plaque characteristics, coronary CT angiography and fractional flow reserve: comparison of proximal and total vessel based analyses

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Background: An association between adverse plaque characteristics (APC) as assessed by coronary CT angiography (CTA) and ischemia by fractional flow reserve (FFR) has recently been demonstrated. This association has only been evaluated for APC proximal to the FFR sensor. However, it may be difficult in practice to determine a priori the exact vessel location in which APC are "proximal-to-FFR".

Objective: To evaluate a "proximal-to-FFR" versus "total" vessel based model to a standard coronary CTA stenosis assessment in discriminating lesion-specific ischemia.

Methods: In 254 patients (mean age 64±10 years, 64% males) suspected of coronary artery disease, coronary CTA and FFR were performed in 484 vessels in a prospective multicenter trial. Coronary CTA lumen reduction >50% was considered obstructive. Lesion-specific ischemia was defined by FFR ≤0.80. We quantified non-calcified plaque (NCP), low-density NCP (LD-NCP), calcified (CP) and total (TP) plaque volumes, remodeling index (RI), lesion length (LL) and contrast density difference (CDD, maximum percent attenuation difference/proximal cross-section) by semi-automated software (AutoPlaq); spotty calcification (SC) was visually assessed from standard CTA images. Plaque analyses were performed in a "proximal-to-FFR" (proximal to FFR sensor located 10–20mm distal to lesion) and "total" vessel (entire vessel>2mm) fashion. Univariate and multivariate analyses of APC for prediction of ischemia were performed. Models combining coronary CTA stenosis and APC independently predictive of ischemia from multivariate analyses were created. Receiver operating curve (AUC) for coronary CTA were compared to coronary CTA + "proximal-to-FFR" or coronary CTA + "total" vessel APC models.

Results: In 80 patients (100 vessels) FFR ≤0.80. In univariate analyses, "proximal-to-FFR" and "total" vessel NCP, LD-NCP, TP volumes, RI (only for total), LL and CDD were predictors of FFR ≤0.80 (all, $p<0.02$), however in multivariate analyses, only "proximal-to-FFR" and "total" vessel LD-NCP and CDD (all, $p<0.0001$) remained independent predictors of FFR ≤0.80. The AUC for coronary CTA + "total" vessel APC had higher discrimination for ischemia than coronary CTA + "proximal-to-FFR" APC (AUC 0.85 (0.81–0.90) vs 0.83 (0.78–0.88), p=0.03), both models superior to coronary CTA (AUC 0.79 (0.74–0.85), both, $p\leq0.003$).

Conclusions: Coronary CTA and "total" vessel APC provided the highest discrimination of lesion-specific ischemia, incremental to coronary CTA and "proximal-to-FFR" APC model, and to coronary CTA alone. "Total" vessel APC thus should be the preferred plaque analysis strategy.

P4999 | BEDSIDE

Gender differences in computed tomography measurements before transcatheter aortic valve implantation

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Background: Very little data exist on the impact of gender on computed tomography (CT) measurements in patients referred for TAVI.

Purpose: To evaluate gender-specific differences in CT measurements of patients with severe aortic stenosis (AS) referred for transcatheter aortic valve implantation (TAVI).

Methods: In our cohort of 442 patients (80±8.5 years), there were 239 women and 203 men with severe AS who underwent 256-slice CT before TAVI. We assessed the impact of gender on aortic annulus cross-sectional area (CSA), perimeter (Perim), Sino-tubular junction (STJ), sinus of valsalva (SOV), ellipticity index (EI), and the distance of left and right coronary artery ostia from the aortic annulus plane. In a subgroup of 73 patients we evaluated the impact of gender on the aortic valve calcification (AVC), which was quantitatively evaluated by CT.

Results: Women had significantly smaller CSA (404±73 vs. 506±112 mm^2), Perim (71.8±7.6 vs. 80.1±8.6 mm), STJ, (27.3±29.4 mm), and SOV (32.5±3.7 vs. 35.6±4.6 mm) versus men; $P<0.001$ for all, even after adjustment of the small body surface area in women. The EI was comparable between women and men (1.24±0.12 vs. 1.25±0.12, P=0.7), and the mean left and right coronary artery ostia height were lower in women versus men (12.4±2.7 vs. 13.9±3 mm, $P<0.001$; 14.8±2.6 vs. 17±3.2 mm, $P<0.001$). AVC was borderline lower in women versus men (12±6.7 cm^3 vs. 14.3±6.8 cm^3, P=0.1).

Conclusion: In this large severe AS population, women had smaller annulus, shallow SOV and STJ, and lower-lying coronary ostia, even after indexing for their smaller body size. The aortic annulus shape was similar in women and men and the valvular calcification in women had a trend towards lower value compared to men.

P5000 | BEDSIDE

Epicardial adipose tissue expansion and differentiation status predict myocardial redox state and coronary calcification

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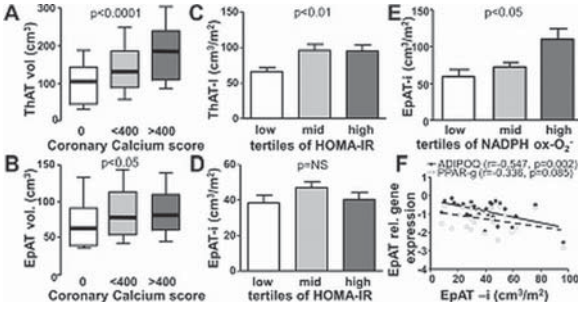
Background: Epicardial adipose tissue (EpAT) may exert paracrine effects on the heart, affecting major biological processes in the myocardium and the coronary arteries.

Purpose: To explore the role of EpAT expansion in the regulation of myocardial redox state and coronary calcification.

Methods: In 220 patients undergoing coronary CT angiography (CTA), the volume of EpAT and thoracic (ThAT) adipose tissue were quantified. In 38 additional patients undergoing cardiac surgery, CTA was used to calculate EpAT and ThAT volume, and right atrial appendage/EpAT biopsies were obtained at surgery. Myocardial NADPH oxidase activity was assessed by lucigenin chemiluminescence and EpAT was used for gene expression profiling. Plasma malonydialdehyde (MDA, marker of oxidative stress) was measured fluorometrically.

Results: Coronary calcium score (CCS, A) was strongly related with ThAT volume while its association with EpAT volume was modest (B). ThAT-i (ThAT vol. adjusted for body surface area (BSA)) but not EpAT-I (D) was positively associated with body mass index (BMI, r=0.295, $p<0.05$) and insulin resistance (HOMA-IR index, C). MDA was not associated with EpAT-i or ThAT-i, but there was a significant association between myocardial NADPH oxidase activity and EpAT-i (E) (not ThAT-i). EpAT-i was associated with reduced adiponectin and PPAR-γ gene expression in EpAT samples from the same patients (F).



Conclusions: Increased EpAT-i is associated with increased NADPH oxidase activity and superoxide radicals production in the human myocardium, as well as increased CCS. Quantification of EpAT volume in CTA offers valuable information on the underlying cardiovascular biology, with important clinical implications in cardiovascular diagnostics.

P5001 | BEDSIDE

German cardiac CT registry: Indications, procedural data and clinical results of cardiac computed tomography in 7061 patients

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Cardiac Computed Tomography permits coronary artery visualization to identify coronary calcium and to detect and rule out coronary artery stenoses. It furthermore allows anatomic and functional imaging of the heart. Data concerning indications, acquisition parameters, results and clinical consequences of cardiac computed tomograph are not available on a large scale.

Methods: The German Cardiac CT Registry includes 13 experienced clinical sites using at least 64-slice computed tomography systems. Between 2009 and 2014, 7061 consecutive cardiac CT examinations were included in the resgistry. Patient parameters and procedural data, indications and clinical consequences of the test result were recorded in a systematic fashion.

Results: Mean patient age was 61±12 years, 63% were male. 63% of cases were performed on outpatient basis, 37% in inpatients. 91% were scheduled electively and 9% as an emergency. In 9% of cases, only coronary calcium imaging was performed (n=630), in 17% (n=1163) only coronary CTA, and in 57% (n=4043) coronary calcium and coronary CTA. Other cardiac CT examinations were performed on 16.5% of patients (n=1162). Specific indications are listed in table 1. Coronary calcium scoring was performed using prospective tiggering in 79% of cases (21% with retrospective gating), 120 kV tube voltage was used in 98% and mean dose-length product (DLP) was 42 mGy*cm (estimated effective dose 0.6 mSv). Coronary CTA was prospectively triggered in 76% (24% retrospective gating), 100 kV tube voltage was used in 31% of cases, mean DLP was 256 mGy*cm (3.6 mSv). As a consequence of CT, invasive coronary angiography was avoided in 42% of cases. Testing for ischemia was recommended in 5% of cases, invasive coronary angiography in 15%, and a change of medication in 20%.

Table 1. Indications for cardiac CT

Coronary caclcium	Coronary CT angiography	Other cardiac CT
Prior to coronary CTA (59%)	Rule out coronary stenoses (68%)	Pulmonary veins (66%)
Risk stratification (41%)	Risk stratification (29%)	Pre-TAVI (29%)
Other (4%)	Other (4%)	Evaluation implant (4%)

Conclusion: The majority of cardiac CT examinations are performed to rule out or detect coronary artery stenoses. With a low average radiation dose, further diagnostic testing – including invasive coronary angiography – can be avoided in a high percentage of patients.

CARDIOVASCULAR DYSFUNCTION AND REPAIR – ROLES OF INFLAMMATION AND IMMUNE CELLS

P5002 | BENCH

Sphigosine-mono-phosphate (S1P) induces the migration of Muse cells but not non-Muse cells toward the rabbit post-infarct heart and contributes to the improvement of cardiac function and remodeling

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Background: It has been reported that the S1P-S1P receptor is a critical mediator of stem/progenitor migration towards damaged tissue, and that S1P is elevated in the ischemic heart. Pluripotent stem cells, multilineage-differentiating stress-enduring (Muse) cells, which have S1P receptor type 2 (S1PR2), may be attracted to the ischemic heart. We investigated whether serum and cardiac tissue levels of S1P increase after AMI in the rabbit, and whether Muse cells, but not non-Muse cells, could be mobilized to the ischemic myocardium and decrease the myocardial infarct size and improve the cardiac function.

Methods: Bone marrow mesenchymal stem cells from Japanese white rabbits were cultured and expanded, and then Muse cells were isolated by FACS as SSEA-3(+) cells. In a 30-minute coronary occlusion and reperfusion rabbit model, 3x100000 of autologous Muse cells (Muse group, n=10), saline (control group, n=10), or 3x100000 of autologous non-Muse cells (non-Muse group, n=10) were intravenously infused at 24 hours after MI. The MI size, cardiac function, and general pathology of the heart were evaluated at 2 weeks post-MI. We measured the serum and cardiac tissue S1P levels after AMI in the rabbit, and examined the in vitro migration ability of Muse and non-Muse cells toward the serum and cardiac tissue of the AMI rabbit using a matrigel invasion chamber. We then examined whether Muse cell migration is directly mediated by S1P-S1PR2.

Results: The MI size as a percentage of LV by Masson trichrome staining was significantly smaller in the Muse group (14.1±1.3%) than that in the control (31.7±1.3%) and non-Muse (23.0±1.8) group. A smaller infarct size, smaller left ventricular (LV) dimensions, an increased LV ejection fraction, and increased ±dP/dt were seen in the Muse group compared with the other groups at 2 weeks post-MI. The S1P levels in serum and cardiac tissue of the AMI rabbit were higher compared to those of the healthy rabbit. Large numbers of Muse cells migrated toward the serum and cardiac tissue of the AMI rabbit compared to those of non-Muse cells. Muse cells migrated positively toward the S1PR2 agonist, while non-Muse cells did not.

Conclusions: The post-infarct administration of Muse cells reduces the myocardial infarct size and improves cardiac remodeling and functioning. S1P-S1PR2 is one of the relevant axis enabling Muse cells to actively migrate toward the AMI heart.

P5003 | BENCH

Perivascular accumulation of M1 macrophages elicits the development of immature vascular formation

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Background: The formation of immature vascular structure underlies the development of cardiovascular diseases including atherosclerosis and tumor progression. The molecular mechanisms of immature angiogenesis, however, are still unclear. Hematopoietic cells such as macrophages are believed to play a key role in vascular remodeling. Recently, macrophages can be broadly classified into two subpopulations, pro-inflammatory M1 macrophages and anti-inflammatory M2 macrophages. In this study, we aim to elucidate the roles of each macrophage subpopulation in vascular remodeling.

Methods: We established murine Lewis Lung Carcinoma Cells (LL/2) xenograft model as an immature angiogenesis model and characterized M1 and M2 macrophage surface markers by Flow cytometry (FACS) analysis. We also performed pimonidazole FACS analysis, and investigated the intratumoral localization of macrophages, perivascular (pimo low) and intratumoral (pimo high).

Results: We examined the surface markers of the macrophage subpopulations in tumor tissue, and classified M1 macrophages as Ly6c high, and M2 as Ly6c low. Ly6c high macrophages expressed CCR2 and inducible nitric oxide synthase, whereas Ly6c low cells express arginase1 and CD206. FACS analysis using pimonidazole showed that M1 macrophages accumulate in perivascular area (pimo low), whereas M2 macrophages intratumoral (pimo high). Importantly, perivascular M1 macrophages expressed higher level of VEGF-A expression, one of the most potent angiogenic factors. To explore the role of M1 macrophages in vascular remodeling, we searched for a chemokine receptor which expressed exclusively in M1 macrophages. Among the chemokines, we found that Flt-1 expressed in M1, but not in M2 macrophages. We subsequently generated myeloid cell specific Flt-1 deficient (LysM/Flt-1 flox) mice. Intriguingly, M1 macrophages accumulation was strikingly attenuated in LysM/Flt-1 flox mice, whereas M2 cells recruitment unchanged. Histological study showed that tumor vasculature in LysM/Flt-1 flox mice were less tortuous with greater pericyte coverage. Moreover, tumor xenograft in LysM/Flt-1 flox mice grew faster, which were consistent with the vascular normalization in myeloid cell specific VEGF-A deficient mice.

Conclusion: Collectively, we showed that the accumulation of VEGF-A expressing M1 macrophages to the perivascular area underlies the development of immature vascular formation. We also identified that Flt-1 plays a key role in M1 macrophage recruitment. These data suggest that targeting Flt-1 signaling can be a therapeutic target to reestablish well organized vasculature.

P5004 | BENCH

Animal experimental evaluation of growth adaptation in in vivo tissue-engineered "biotube" vascular grafts

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Purpose: Size mismatch between implanted artificial vascular grafts and native vessels that is caused by the growth of recipients remains a problem to be solved in pediatric surgery. Biotubes, autologous connective tissue tubes, formed by "in body tissue architecture" technology, which is a novel and practical approach of regenerative medicine based on the tissue encapsulation phenomenon, can be vascular reconstructed within several months of implantation. Therefore, the growth potential of the biotubes was expected. However, the rapid growth of animals prevents evaluation in an animal model. This study aimed to evaluate the growth potential of biotubes by examining their caliber adaptation to growing native arteries after transplantation. Allogenic transplantation of pre-prepared biotubes was performed in adult to juvenile beagles.

Methods and results: Biotubes (3 mm in internal diameter) were prepared in adult beagles (age, 1 year; weight ca. 10 kg) subcutaneous embedding silicone molds (outer diameter 3 mm) for 2 months. After treatment with argatroban, allogenic transplamtation of the biotubes (n=6) was performed by end-to-end anastomosis manner to the common carotid arteries (internal diameter, 2 mm) of the

juvenile beagles (12 weeks old; weight ca. 3 kg). After 3-month transplantation all biotubes were patent without any stenosis or aneurysm formations, and vascular reconstruction including endothelialization was achieved. In this period, angiographic observation revealed that the diameter of the host arteries was gradually dilated from 2 to 3 mm, in tandem with body growth. However, little change was observed in the diameter of the transplanted biotubes. Thereafter, monthly angiographic evaluation revealed that the biotubes were continuously expanded in diameter, similarly to the growth of the native arteries with little size-mismatching in all cases. At 5 months of transplantation (weight ca. 8 kg) both vascular diameters reached 4 mm.
Conclusion: After vascular reconstruction within several months of transplantation, biotubes could be dilated according to the growth of native arteries. This is the first study to confirm the growth adaptation of biotubes in an animal experiment model. Based on our results, biotubes have a high potential usefulness in pediatric surgery.

P5005 | BENCH
Chronic cardiac allograft rejection after heterotopic rat heart transplantation: effects of antibody-based targeted delivery of interleukin-10 in a preventive and a therapeutic approach

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Background: Chronic cardiac rejection causes severe complications and limits long-term survival of heart transplant recipients. Clinical management is challenging since there are no sufficient preventive or therapeutic strategies. Chronic rejection leads to an overexpression of ED-A fibronectin (ED-A+ Fn). The human monoclonal antibody F8, specific to ED-A+ Fn, may serve as a vehicle for targeted delivery of bioactive payloads like interleukin 10 (IL-10), an anti-inflammatory cytokine, which might reduce chronic rejection.
Purpose: The aim of this study was to investigate the preventive and therapeutic effects of F8-interleukin-10 (F8-IL10) administration in a rat model of chronic cardiac rejection.
Methods: A heterotopic rat heart transplantation model was used to induce chronic rejection within 70 days. For therapeutic interventions, F8-humanIL10 (F8-huIL10), F8-ratIL10, KSF-humanIL10 (KSF-huIL10, control) and PBS (control) were used. Treatment was performed every week (1mg/animal) for 10 weeks starting at day 7 (preventive approach) or day 70 (therapeutic approach) after transplantation.
Results: In the preventive approach, treatment with F8-huIL10 or F8-ratIL10 revealed a significant increase in allograft weights, rejection score, alpha-smooth muscle actin (a-SMA) expression, immune cell infiltration (CD4+, CD8+ and CD68+ cells) and serum brain natriuretic peptide (BNP) levels compared to control groups. In the therapeutic approach, administration of F8-IL10 was neither capable to stop progression of chronic rejection nor to reverse its tissue manifestations.
Conclusions: This is the first study focussing on the antibody-based targeted delivery of IL-10 in an animal model of chronic cardiac rejection. All observed intervention effects were transplantation-specific since the ED-A+ Fn is not expressed in healthy hearts. A clear targeting effect of F8-IL10 could be evidenced, since the administration of KSF-IL10 did not induce any alterations. In the experimental settings used in this study, treatment with F8-IL10 was neither capable to inhibit chronic rejection development nor to stop or reverse the process. However, the results are encouraging since it could be proven in vivo that ED-A+ Fn qualifies as an excellent target for an F8 based delivery of bioactive payloads in cardiovascular diseases.

P5006 | BENCH
In vivo inhibition of microRNA-155 attenuates experimental septic cardiomyopathy

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Background: Septic cardiomyopathy remains a leading cause of death in critically ill patients. We have previously demonstrated that microRNA-155 knockout mice have attenuated sepsis-associated mortality and cardiovascular dysfunction, however, constitutive deletion of microRNA-155 may alter baseline inflammatory signaling pathways and cellular response to inflammation.
Purpose: The present study evaluated the effect of miR-155 pharmacological inhibition in experimental septic cardiomyopathy.
Methods: Experimental sepsis was induced using endotoxin injection (LPS) or cecal ligation and puncture (CLP) models. Pharmacological inhibition was evaluated by intravenous injection of anti-miR-155 (AM) or scrambled (SC) LNA probes. Cardiac function was assessed through echocardiography; mortality analysis was also performed. Quantification of myocardial miR-155, pro-inflammatory cytokine mRNA profile (IL-1β, IL-6, TNF-α and MCP-1), miR-155 target (SOCS1, SHIP1), apoptosis (BAX/Bcl-2), cellular adhesion proteins (VCAM-1, ICAM-1 and e-selectin) and activation of pro-inflammatory intracellular signaling pathways (STAT3 and NF-kB) were assessed.
Results: Myocardial miR-155 levels were increased in septic SC groups, compared with Ctrl SC groups. Anti-miR-155 LNA probe injection decreased myocardial miR-155 levels by 74% and 82%, in LPS and CLP models, respectively, compared with septic SC groups. Septic SC groups presented with with decreased ejection fraction (EF) and cardiac output (CO) and increased diastolic LV diameter (LVDd). AM groups presented with preserved EF, CO and LVDd, compared with SC; this was accompanied by $\sim$50% mortality reduction. Experimental sepsis in SC groups induced downregulation of SOCS1, myocardial cytokine upregulation, increased apoptosis and adhesion protein expression as well as pro-inflammatory transcription factor activation, all of which were attenuated AM.
Conclusions: Pharmacological inhibition of miR-155 attenuated sepsis-induced cardiac dysfunction, blunted pro-inflammatory activation and reduced mortality. This suggests miR-155 as a potential target in human sepsis-associated cardiac dysfunction.

P5007 | BENCH
Whole blood omega-3 fatty acid content predicts recurrent venous thromboembolism and death in elderly patients with acute venous thromboembolism

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Background: Venous thromboembolism (VTE) is a leading cause of cardiovascular disease (CVD) and death. Omega-3 fatty acids (n-3 FA) have been shown to reduce the risk of CVD as well as mortality due to their antiinflammatory and antithrombotic properties. Inflammation, activation of platelets and coagulation are key mechanisms of VTE. Elderly patients with previous VTE are at particular risk for recurrent VTE due to their frequent proinflammatory and prothrombotic comorbidities. We therefore hypothesized that increased n-3 FA are associated with a lower risk of recurrent VTE and death in this elderly population with previous VTE.
Methods: We determined baseline whole blood fatty acid composition by gas chromatography in 826 patient samples from The Swiss Cohort of Elderly Patients with VTE (SWITCO65+), a prospective multicenter cohort study of in- and outpatients aged $\geq$65 years with acute VTE. We categorized n-3 FA into low, medium, and high levels based on the 25th and 75th percentile (low: 2.7–4.9%, medium: 4.9–6.6%, high: 6.6–11.6%). Associations between n-3 FA and the primary composite endpoint of recurrent VTE or death and the secondary endpoint of major and non-major bleeding within six months were assessed by ordinary Cox-regression and competing risk regression, respectively. Cumulative incidences of recurrent VTE or death and bleedings were estimated by the Kaplan-Meier method and compared using the logrank test. Recurrent VTE or death was adjusted for age, gender, overt PE, cancer, heart failure, chronic lung disease, BMI, provoked VTE, prior VTE, and periods of anticoagulation. Bleeding was adjusted for age, cancer, history of major bleeding, overt PE, antiplatelet therapy, and periods of anticoagulation.
Results: The cumulative incidence of recurrent VTE or death was significantly different among levels of n-3 FA ($p<0.001$). A high level of n-3 FA was significantly associated with a reduced risk of VTE recurrence or death after six months (adjusted HR for high versus low level: 0.36, 95% confidence interval 0.20–0.67, p=0.001). In contrast, n-3 FA were not associated with major and non-major bleeding.
Conclusion: Our findings demonstrate that increased levels of whole blood omega-3 fatty acids are strongly associated with a reduced risk of recurrent VTE or death from any cause in patients with previous VTE. Anti-inflammatory and anti-coagulant mechanisms may mediate this effect. Total n-3 FA was not associated with risk of major and non-major bleedings.

P5008 | BENCH
Periodontal bacteria promote systemic immune responses and persistence of intramural hematoma in experimental abdominal aortic dissection/aneurysm

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The occurrence of silent bacteraemia from periodontal pockets is associated with abdominal aortic aneurysm (AAA) in patients but the putative pathogenic link remains to be elucidated. The aim of this study was to assess whether Porphyromonas gingivalis (Pg), a usual periodontal bacteria, in the circulating blood could affect the immune response involved in the physiopathology of AAA.
Twenty-seven week-old male apolipoprotein E knockout mice were submitted to

chronic angiotensin II infusion, a common model of aortic wall dissection followed by AAA formation. The presence of AAA was validated by Doppler tissue echography and mice were thereafter randomly assigned to the intravenous weekly injection of Pg (n=13, 1.108 CFU) or of the vehicle (n=14), for 4 weeks. Plasma, spleen and aortic wall samples were collected at the end of the study.
The intramural hematoma was partially resorbed in 4 out of 13 Pg-injected mice vs 10 out of 14 control mice (χ^2, p=0.01). Total as well as Pg-specific IgM, IgE plasma concentrations were consistently increased in Pg-injected mice. Flow-cytometry analysis of the spleen leukocytes revealed an enrichment of CD19+CD95highIgMlow germinal center B cells and CD69+ activated CD4+/CD8+ T cells. These findings were consistent with the enhanced levels of plasma CC19 and CXCL13 chemokines. Finally, IL-2, IL-10, IL-12 and IFN-gamma were also found enriched in the plasma of Pg-injected mice.
This study provides evidence of a systemic activation of the immune system triggered by Pg bacteraemia, which could be involved in the pathological processes leading to the persistence of intramural hematoma AAA.

OUTCOMES AFTER TAVI

P5009 | BEDSIDE
Aortic stiffening is a strong determinant of heart failure after transcutaneous valve replacement

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Background: In the presence of aortic stenosis, left ventricular afterload involves not only a valvular load but also a vascular load. After transcutaneous aortic valve replacement (TAVR), the vascular load becomes the prevailing feature and may prolong the impairment of cardiac function leading to heart failure (HF)
Objectives: The principal objective of this study was to examine the impact of aortic stiffening on the risk of HF after TAVR; two indices were used: ascending aorta calcifications (AAC) and pulse pressure (PP). They were compared to the gold standard pulse wave velocity (PWV) in a subset of patients.
Methods: In 141 patients treated by TAVR, AAC was measured by computed tomography and expressed either as a crude variable or corrected for Aortic Volume (AV). PWV was measured before TAVR in a subset of patients. The primary outcome was a composite of deaths and hospitalizations related to HF.
Results: The survival rates in the two highest AAC tertiles were lower than that in the first tertile (p[log-rank]=0.031). A similar trend was observed according to AAC/AV albeit not significant (p[log-rank]=0.259). PP did not change across AAC tertiles and was not predictive of HF in univariate analysis (hazard ratio; 1.01 [0.99–1.03], p=0.399). In multivariable Cox regression models adjusted for major confounders including EuroSCORE, AAC remained predictive of the primary outcome (tertiles 2 and 3 vs. 1 hazard ratio: 2.42; 95% CI: 1.16 to 5.06; p=0.019). When expressed as a continuous variable, +1 Log increment of ACC increased the risk of the primary outcome (hazard ratio: 1.55; 95% CI: 1.00 to 2.40; p=0.049). In a subset of patients, AAC was correlated with PWV (r=0.356, p=0.068) while PP was not (r=0.207, p=0.311). Using the C-index approach, AAC significantly improved risk prediction.
Conclusions: AAC is a strong predictor of HF after TAVR. This is probably because AAC reveals aortic stiffness (probably more than pressure related indices) and thus maintains a high left ventricular afterload. AAC measurement should be implemented in the routine work-up of patients referred for TAVR in order to refine risk stratification and help in the difficult decision-making process.

P5010 | BEDSIDE
Incidence and predictors of coronary obstruction following transcatheter aortic valve implantation in the real world

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Aims: Symptomatic coronary obstruction (CO) is a rare but serious complication of transcatheter aortic valve implantation (TAVI). The Edwards SAPIEN 3 (S3) is a low profile, new-generation, percutaneous aortic valve, with increased height and larger struts designed for easier access to the ostium of both the right and left coronary arteries. There are very limited data regarding CO following TAVI, especially with the S3 valve. The aim of this study was to evaluate the baseline and procedural characteristics, the outcomes of patients who suffered CO and the impact of the valve type on the outcomes.
Methods and results: Between October 2006 and December 2014, 1120 TAVI cases were performed in our institution. Measurement of the coronary height using MSCT for screening was carried out in 728 cases. The Edwards SAPIEN/SAPIEN XT (S/XT) was used in 433 (59.5%) patients, the CoreValve in 227 (31.2%) cases and S3 in 68 (9.3%). CO occurred in 8 (1.1%) cases. Patient age and logistic EuroSCORE were similar (84.8±6.4 vs 83.2±6.5 yrs and 21.7±13.7 vs 18.8±11.6%) in the CO and non-CO group respectively. There was a greater number of female patients in the CO group (63% vs 48%, p=0.453). The mean height of the left coronary artery (LCA) ostium was significantly lower in the CO group (11.2±1.7 vs 13.4±2.5, p=0.009). All CO occurred at the LCA ostium. Among S/XT cases, the ratio of valve height and distance between the annulus and the coronary ostium was significantly higher in the CO group than in the non-CO group (1.53 vs 1.30, p=0.036). By using a receiver-operating characteristic analysis with the area under curve (AUC) as a measurement of accuracy, the ratio had moderate accuracy in predicting the incidence of CO (AUC=0.786, p=0.009) among S/XT cases. The frequency of CO tended to be lower in recipients of the CoreValve compared with the S/XT (0.4% vs 1.6%, p=0.260). Furthermore, the frequency of CO was significantly decreased in S3 cases compared to S/XT (0% vs 1.6%, p=0.022). Percutaneous coronary intervention was attempted in 5 (62%) patients, 3 of whom underwent successful revascularization, but 2 patients required emergency cardiac surgery. The 30-day mortality was very high in cases of CO (37.5% vs 6.7%, p=0.001).
Conclusions: CO tended to occur more frequently in women at the ostium of LCA. The frequency of CO tended to be higher in recipients of the S/XT valve compared with the CoreValve. The preliminary data showing that CO has not occurred in patients receiving the S3 despite the increased height need further confirmation.

P5011 | BEDSIDE
Pre- and postprocedural mitral regurgitation and mortality following transcatheter aortic valve replacement for severe aortic stenosis - an interaction with aortic regurgitation (POL-TAVI registry)

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Background: Polish Transcatheter Aortic Valve Implantation Registry (POL-TAVI) 2013 contained detailed clinical characteristics, procedural results and mid-term follow up (1 month, 6 months and 1 year) of patients undergoing TAVI. It included 105 patients with significant mitral regurgitation (MR), giving an opportunity to supplement data concerning an impact of pre- and postprocedural MR on mortality following TAVI with an interaction with aortic regurgitation (AR).
Methods: Transthoracic echocardiograms were performed prior to the procedure, post-procedure and at 1 month follow-up. To assess an interaction between MR and AR we compared survival of patients (i) without both significant MR and AR vs (ii) with either significant MR or significant AR vs (ii) with significant both MR and AR, all postprocedure.
Results: 381 patients were enrolled into registry, including 166 males (43.6%) and 215 females (56.4%) aged 78.8±7.4 years (Medtronic Corevalve prosthesis was implanted in 209 (54.9%), Edwards-Sapien XT in 133 (34.9%), and other valve types in remaining patients). Follow-up was 118,4±97,5 days. In-hospital and overall mortality were 6.6% and 10.2% (25 and 39 patients). Significant (grade 3/4) MR was present in 27,6% at baseline, in 16% prior to discharge, in 8.7% patients at 1-month and in 2.9% patients at 6 months follow-up ($p \leq 0.0001$ for all vs baseline). 31 patients (8.1%) had significant AR post procedure, including 12 patients with both significant MR and AR (3.1%). Patients with significant versus insignificant AR immediately post procedure differed significantly with respect to mortality (log rank Mantel Cox p=0.004). This difference was not apparent in a subgroup of patients without significant MR post procedure (Log rank p=0,78). Similarly in a subgroup of patients without significant AR post procedure there were no significant differences in mortality between individuals with vs without significant MR (Log rank p=0,43). Significant MR and AR post procedure had a significant impact on mortality only when associated with each other (log rank $p < 0.001$). At multivariate Cox regression modeling in the overall group concomitant significant MR and AR post-procedure was independently associated with mortality (OR 7.3, 95% CI 1.6–33.6, p=0.01).
Conclusion: Significant MR or AR post procedure, when isolated, had no impact on mid-term survival. Volume overload resulting from combined MR and AR had a significant impact on prognosis. Particular attention should be paid to the occurrence of paravalvular AR in patients with significant MR.

P5013 | BEDSIDE
Type of atrial fibrillation and clinical outcomes in patients undergoing transcatheter aortic valve implantation

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Background: Atrial fibrillation (AF) is a major risk factor for stroke and death after transcatheter aortic valve implantation (TAVI). However, there is paucity of data regarding the association between AF clinical type, anticoagulation therapy, and clinical outcomes after TAVI.
Methods: We analyzed data from a single center TAVI registry, including 325 consecutive patients with severe aortic stenosis. Patients were divided into 3 groups based on their history of AF type: sinus rhythm (SR), paroxysmal AF (PAF) or non-paroxysmal AF (NPAF, including persistent AF and permanent AF). We also analyzed the effects of oral anticoagulation (OAC) treatment on outcome in these groups. The primary endpoint was stroke or death.
Results: There were 215 (66%), 57 (18%), and 53 (16%) patients in the SR, PAF and NPAF groups, respectively. The cumulative risk for stroke or death at 2 years was highest among patients with NPAF (38%), but similarly low in PAF (15%) and SR patients (17%, $p < 0.001$, Figure). By multivariate analysis, patients

with NPAF demonstrated a significantly higher risk of stroke or death (HR=2.36, 95% CI 1.35–4.13, p=0.003), as compared with SR. By contrast, patients with PAF compared with SR had a similar risk of stroke or death (HR=0.69, p=0.306). Patients with NPAF not treated with OAC demonstrated an 8-fold (HR=8.19, 95% CI 3.32–20.17, p<0.001) increased risk of stroke or death, whereas patients with PAF not treated with OAC had a similar risk of stroke or death compared with the SR group (HR=1.07, p=0.875).

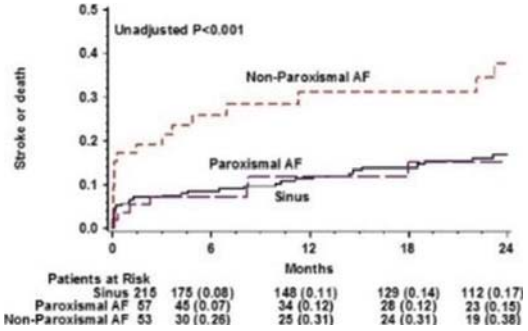

Figure 1

Conclusions: History of NPAF, but not PAF, is associated with a significant increased risk of stroke or death compared with sinus rhythm in patients undergoing TAVI. This finding may be helpful to estimate the risk-benefit of anticoagulation therapy in patients undergoing TAVI.

P5014 | BEDSIDE
Seven-year outcome after TAVI

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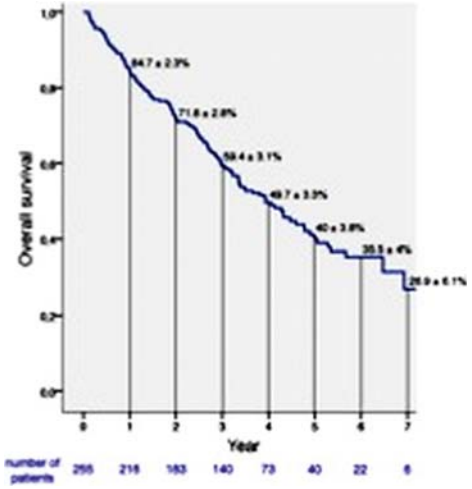
Background and aim: TAVI is increasingly used but few data exist on long-term outcome. We analyzed 7-year outcome after TAVI and its predictive factors.
Methods: Between 2006 and 2011, 289 consecutive high-risk patients (EuroScore 23±14%) underwent TAVI in our institution. Mean age was 82±9 years and 85% were in NYHA class III–IV.
Results: Procedural success was achieved in 265 pts (92%). At 30 days, 34 patients died (congestive heart failure in 14, peri-procedural death in 10 and septic shock in 10). We focused on the 255 patients discharged alive after TAVI to analyze long-term outcome. Follow-up was complete in 100% of patients. During a mean follow-up of 4.1±0.2 years, 139 patients died, half of deaths being non-cardiac.
Overall 7-year survival rate was 26±9%. We identified 5 preprocedural predictive factors of late mortality in multivariate analysis: cancer (p=0.001), diabetes under insulin therapy (p=0.02), NYHA class III-IV (p=0.03), atrial fibrillation (p=0.04), higher creatinin level (p<0.0001) and 2 post-procedural factors: higher systolic PAP (p=0.02) and arrhythmias (p=0.02). Whereas conduction disorders are more frequent after TAVI (29% of cases in this series) and may often lead to pacemaker implantation, only post-TAVI arrhythmias (supraventricular in 32 patients or ventricular in 4) were predictive of late mortality.
Finally, in the 116 survivors, 70% were in NYHA class I-II at last follow-up.



7-year survival after TAVI

Conclusions: At 7-year follow-up after TAVI, the survival rate was 27% and most patients have few or no symptoms. The predictive factors of late mortality emphasized the weight of comorbidities. Particular awareness is needed toward the occurrence of post-TAVI arrhythmias which identifies high-risk patients.

P5015 | BEDSIDE
Changes in the pacemaker rate after transition from Edwards Sapien XT to Sapien 3 transcatheter aortic valve implantation are primarily related to the implantation height

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Background: The introduction of the Edwards Sapien-3 valve (S-3) for transcatheter aortic valve implantation (TAVI) has led to a marked reduction of paravalvular regurgitation. However, it remains unclear whether the increase in stent length and the additional seal may result in a higher risk of conduction abnormalities (CA) and pacemaker (PM) requirement. The aims of this study were to compare the PM rate after TAVI using S-3 versus Sapien XT valves (XT), and to explore risk factors for the development of CA after S-3 implantation, considering in particular the implantation height (IH).
Patients and methods: The first 206 patients treated in our institution with S-3 were compared to 371 preceding patients treated with XT. After exclusion of patients with a previously implanted PM or ICD, transapical and valve-in-valve procedures, 162 S-3 patients (age 82±6 yrs., 38% male) and 287 XT patients (age 82±6 yrs., 37% male) were analyzed. All patients were monitored for 7 days with continuous ECG-telemetry. Previous and new CA in both groups were documented and the prosthesis IH was assessed in the S-3 group.
Results: There were no significant differences in baseline characteristics between the groups. The developement of new CA was, however, significantly higher in the S-3 vs. the XT group (39.0% vs. 28.9%, p=0.022). The PM rate was also significantly higher in the S-3 group (19.0% vs. 12.2%, p=0.049). Previous CA were significantly more frequent in patients who required a PM after TAVI (48.4% vs. 28.2%, p=0.03). No other differences in clinical characteristics were found. The mean IH in the S-3 cohort was, however, significantly lower in patients requiring a PM (66%/33% vs. 73%/27% aortic/ventricular, p=0.001). On multivariate logistic regression analysis IH was the only independent predictor of the need for PM implantation (OR 0.95 [95% CI 0,91–0,99], p=0.008). In order to analyze the temporal trend of IH and PM implantation rate in our series, we compared the first 50% of the cohort (n=81) to the second half (n=81). A significant increase in IH from 68%/32% to 75%/25% aortic/ventricular (p<0.0001) was associated with a significant decrease in the PM implantation rate from 25.9% to 12.3% (p=0.028) which did no longer differ from the PM rate in the XT group (12.2%).
Conclusions: The incidence of PM implantation after TAVI is higher with Sapien 3 than with Sapien XT and is independently associated with the implantation hight. This increase in PM rate can apparently be eliminated by optimizing the implantation hight with keeping the extension of the stent into the left ventricular outflow tract short.

ADVANCING THE CLINICAL APPLICATION OF BIOMARKERS

P5016 | BENCH
Prognostic value of circulating MicroRNAs in patients with coronary artery disease - results from the AtheroGene study

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Introduction: Stratification for subsequent coronary events among patients with coronary artery disease (CAD) is of considerable interest because of the potential to guide secondary preventive therapies. MicroRNAs (miRNAs) are a class of small noncoding RNAs found to be involved in cardiovascular pathophysiology. In a previous study -using a three-phase approach of (i) miRNA profiling in patients with unstable angina pectoris and controls groups; (ii) replication of significant miRNAs in an independent patient cohort, (iii) validation of a multi-miRNA panel for clinical application, we identified eight miRNAs facilitating diagnosis of acute coronary syndrome (ACS). This study aimed to evaluate the potential role of the identified miRNAs as prognostic biomarkers for cardiovascular disease.
Methods: Plasma levels of eight candidate miRNAs - miR-19a, miR-19b, miR-132, miR-140–3p, miR-142–5p, miR-150, miR-186, and miR-210- were measured by real-time quantitative polymerase chain reaction (RT-qPCR) at baseline in a cohort of 1,112 patients with documented CAD including 430 ACS patients and 682 patients with stable angina pectoris (SAP). Cycle threshold (Ct) values were normalized to cel-miR-39 using the formula $2^{-(Ct[miRNA]-Ct[cel\text{-}miRNA\text{-}39])}$ for Ct <40 and 2^{-40} in the case Ct ≥40. Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction.
Results: Spearman analyses yielded a strong positive correlation of all miRNAs among each other (all >0.5). During a median follow-up of 4.0 years, most miRNAs reliably predicted cardiovascular death in ACS patients. Cox regression analyses indicated a predictive value of mir-132 (HR 2.85 per one standard deviation [SD] increase, p=0.007), miR-140–3p (HR 2.88 per one SD increase,

p=0.006), and miR-210 (HR 3.10 per one SD increase, p=0.029) for cardiovascular death. miR-140–3p (HR 1.60 per one SD increase, p=0.016) was also a powerful predictor of the combined endpoint cardiovascular death and myocardial infarction. Finally, all three miRNAs clearly improved various model performance measures, including c-statistics (AUC [area under the receiver-operating-characteristic curve] for miR-132: 0.842; AUC for miR-140–3p: 0.848; AUC for miR-210: 0.835).
Conclusions: This is the largest study so far evaluating the prognostic value of circulating miRNAs in cardiovascular disease. Our study shows that single miRNAs derived from peripheral blood could be valuable biomarkers for risk estimation in CAD.

P5017 | BEDSIDE
Association between high-sensitive troponin I and coronary artery calcification in a healthy Danish background population

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Background: High-sensitive cardiac troponin I (hs-TnI) is clinically used to diagnose acute myocardial infarction (AMI). Hs-TnI is also an important individual risk marker for prediction of future cardiovascular disease (CVD) in the general population. The development of an AMI is most often precipitated by atherosclerotic plaques in the coronary arteries.
Purpose: To investigate the relationship between hs-TnI and coronary artery calcification (CAC) in a healthy background population.
Methods: 1257 randomly selected subjects, 50 or 60 years old, underwent a clinical examination as well as a non-contrast cardiac-CT scan for determination of CAC. The magnitude of CAC was measured using Agatston score. Cardiac troponin I was detected using a high-sensitive assay. Subjects with known CVD were excluded. The relationship between hs-TnI and CAC was assessed using multivariate regression analyses adjusted for cardiovascular risk factors including age, sex, diabetes, family history of CVD, BMI, hypercholesterolemia, hypertension and smoking. Receiver operating characteristic curves were plotted and the area under curve (AUC) was calculated.
Results: A total of 1173 subjects were included in this study, 52% were female and 48% were 50 years old. Concentrations of hs-TnI above the limit of detection (1.9 ng/L) were measured in 87% of all subjects, 80% in women and 95% in men. Hs-TnI above the 99th percentile of 24 ng/L was detected in 25 subjects (2.1%). Presence of CAC (Agatston score >0) was detected in 29% in the lowest hs-TnI quartile compared with 55% in the highest, with a stepwise increase over the quartiles. In fully adjusted regressions with dichotomous CAC outcomes, hs-TnI was able to predict presence of CAC (OR: 1.25, 95% CI: 1.03–1.51, p=0.03) and an Agatston score >100 (OR: 1.36, 95% CI: 1.08–1.71, $p<0.01$). Subjects in the fourth hs-TnI quartile had an increased risk for presence of CAC (OR: 1.56, 95% CI: 1.06–2.26, p=0.02) and for an Agatston score >100 (OR: 1.82, 95% CI: 1.04–3.18, p=0.04), when compared with the lowest quartile. When stratified by gender, hs-TnI was associated with presence of CAC in men (OR: 1.48, 95% CI: 1.10–2.00, $p<0.01$) but not in women (OR: 1.11, 95% CI: 0.85–1.45, p=0.46). Addition of hs-TnI to a traditional risk score (HeartScore) for prediction of CAC presence improved the AUC from 0.67 to 0.70 ($p<0.01$).
Conclusion: Hs-TnI is associated with CAC in a middle aged background population without known CVD. The association is apparent in men but not in women. This is a step towards understanding the use of hs-TnI in primary cardiovascular preventive medicine.

P5018 | SPOTLIGHT
Circulating aldosterone predicts future cardiorenal and metabolic disease in the general community

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Background: Plasma aldosterone increases sodium and water reabsorption and mediates inflammation. We recently reported in the general community that aldosterone, even within the normal range, is strongly associated with hypertension (HTN), obesity, and chronic kidney disease (CKD). It is undefined whether aldosterone can actually predict new onset cardiorenal and metabolic diseases in the general community underscoring its role as both biomarker and disease mediator.
Purpose: We sought to analyze whether: 1) Aldosterone at a first visit (V1) predicts new onset disease at a second visit (V2) four years later; 2) An increase of aldosterone between V1 and V2 predicts new onset disease; and 3) Aldosterone at V2 remains associated with cardiorenal and metabolic disease.
Methods: We defined correlations between aldosterone at V1 and V2, with cardiorenal and metabolic diseases and medications at V2, in n=1368 randomly selectid subjects from Olmsted County, MN. Associations were adjusted for age, sex and BMI.
Results: After 4 years, log-transformed aldosterone at V1 predicted new onset of central obesity (p=0.0113, OR=1.36, CI: 1.07–1.73), HTN (p=0.0012, OR=1.36, CI: 1.13–1.63) and use of antilipemic drugs (p=0.0119, OR=1.25, CI: 1.05–1.48) at V2. Aldosterone levels in the 3rd tertile at V1 predicted new onset of type 2 diabetes (T2DM) (p=0.0392, OR=1.96, CI: 1.03–3.70), use of antilipemic therapy (p=0.0162, OR=1.59, CI: 1.09–2.31) and HTN (p=0.049, OR1.44, CI: 1.00–2.08) at V2. We also observed that an increase in aldosterone between V1 and V2 predicted new HTN at V2. In addition, we found that aldosterone levels at V2, even within the normal range, remained associated with HTN, obesity and CKD, when analyzed as log-transformed aldosterone and when in the 3rd tertile.
Conclusions: In the general community, aldosterone predicts new onset HTN, central obesity, T2DM and use of antilipemic therapy in a 4-year follow-up. Importantly, the increase of aldosterone between V1 and V2 also predicts new onset HTN. Finally, we replicated our findings from V1 and observed significant and sustained associations between aldosterone at V2 with HTN, obesity and CKD as observed at V1. This study strongly advances the use of measuring aldosterone to identify high-risk subjects in the general community who may develop future cardiorenal and metabolic disease, as well as it provides support for the use of therapeutic agents targeting aldosterone to delay disease onset and progression.

P5019 | BEDSIDE
Cardiac biomarkers and the prediction of primary CVD events in two cohort studies: results from the BRHS and MIDSPAN family study

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Background: There is intense interest in the potential use of cardiac biomarkers to improve existing cardiovascular disease (CVD) risk scores. However, it is not clear whether current efforts to lower thresholds for statin prescription might impact utility of these biomarkers across the age ranges relevant for screening.
Purpose: To assess the ability to predict primary CVD events by N-terminal B-type natriuretic peptide (NT-proBNP), high sensitivity troponin T (hsTnT), and mid-regional pro-adrenomedullan (MR-proADM) in the British Regional Heart Study (BRHS) of men aged 60–79 years recruited in 1998–2000, and the MIDSPAN Family Study of Scottish men and women aged 30–59 recruited in 1996.
Methods: Cardiac biomarker measurement was complete in 2810 and 1884 participants without prior CVD or prior statin prescription in BRHS and MIDSPAN respectively. Over 10 years of follow-up 395 and 62 primary CVD events occurred in each cohort respectively. Cardiac biomarkers were related to CVD using Cox models after adjusting for a range of classical and non classical CVD risk factors. Improvement in QRISK2 (in BRHS) and ASSIGN (in MIDSPAN) based risk scores on addition of cardiac biomarkers was tested using Harrell's C-index and net reclassification index across a binary threshold of 0–10% and 10+% 10-year risk, as per new UK national guidelines.
Results: A 1 standard deviation increase in log-transformed NT-proBNP, hsTnT and MR-proADM was associated with a HR of 1.46 (95% CI 1.28–1.66), 1.27 (1.14–1.41) and 1.22 (1.06–1.41) in BRHS and 1.31 (1.00–1.73), 1.19 (1.02–1.40), and 1.25 (0.92–1.69) in MIDSPAN respectively. In BRHS, a QRISK2 based risk score yielded a C-index of 0.670, which was improved +0.019 ($p<0.001$), +0.014 ($p<0.001$), and +0.005 (p=0.14) by cardiac biomarkers respectively. Addition of both NT-proBNP and hsTnT improved the C-index +0.007 (p=0.007) compared to the addition of NT-proBNP alone. NT-proBNP improved risk classification 2.8% (1.4%-4.2%), but addition of other cardiac biomarkers did not further improve classification. In MIDSPAN the ASSIGN based score yielded a C-index of 0.795. Addition of NT-proBNP resulted in borderline improvement +0.011 (p=0.10), but was not further improved by addition of other cardiac biomarkers, and none of the biomarkers improved risk classification.
Conclusion: Addition of cardiac biomarkers to CVD risk scores moderately improved prediction in both BRHS and MIDSPAN, but evidence of improvement in risk classification that would change clinical decision making at the emerging lower global risk thresholds for statin prescription was modest.

P5020 | BENCH
Effects of combined cognitive and physical training on telomere length in patients with mild cognitive impairment

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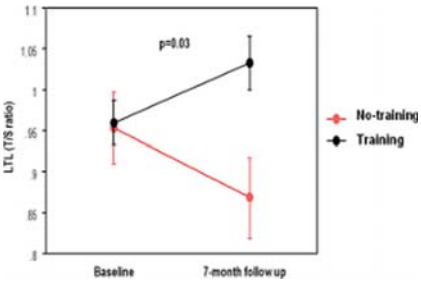
Background: There is increasing evidence to support the benefits of regular physical activity and training on the vascular impairment in Mild Cognitive Impairment (MCI), but the molecular mechanisms underlying these benefits remain unknown.
Purpose: To evaluate the efficacy of combined cognitive and physical training on leukocyte telomere length (LTL), a consolidated biomarker of vascular and cellular aging.
Methods: Within the open-label clinical trial called "Train the Brain", 94 MCI

(44 males; 75.1±5.1 years) and 37 age- and sex-matched controls (21 males; 73.2±4.6 years) were enrolled in the study. Fifty patients with MCI were randomly placed in a 3-h environmental enrichment therapy 3 times a week for 7 months, consisting of tailored, stepwise physical, cognitive and social training. A no-training group of 27 patients received standard treatment. LTL was evaluated by real-time PCR before and after 7-month intervention period.
Results: Patients with MCI and controls had a similar prevalence of traditional cardiovascular risk factors. The relative telomere length (T/S) ratio was significantly reduced in MCI group compared with controls (0.95±0.23 vs. 1.07±0.3, p=0.02). In multiple linear regression analysis, only age (β=–0.013, se= 0.005, p=0.006) and MCI (β=–0.115, se= 0.051, p=0.02) had a significant effect on telomere length. After 7-month follow-up period, patients in training group showed a significant increased LTL when compared to baseline (0.97±0.21 vs. 1.03±0.23, LTL change=+0.06, p=0.03). An opposite trend was observed in no-training group (0.92±0.26 vs. 0.87±0.26, LTL change = –0.05, p=0.1) (Figure).



Conclusions: LTL is shortened in patients with MCI, but telomere shortening is attenuated by environmental enrichment therapy, consisting of cognitive and physical training.

P5021 | BEDSIDE
Associations of estradiol, sex hormone-binding globulin and testosterone with circulating levels of amino-terminal pro-B-type natriuretic peptide in postmenopausal women: The Rotterdam Study

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Background: Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) has a well-documented prognostic value for cardiovascular disease and sex-hormones are suggested to modulate NT-proBNP levels. However, little data is available on the association of sex-hormones with NT-proBNP in postmenopausal women. Furthermore, age and years since menopause may play a role on these associations, but have not yet been investigated.
Objectives: To assess the relationships between sex-hormones and NT-proBNP in postmenopausal women and whether these associations differ by age and years since menopause.
Methods: We measured estradiol, total testosterone (TT), sex hormone-binding globulin (SHBG) and NT-proBNP in 3139 postmenopausal women (free of cardiovascular disease) participating in the prospective population-based Rotterdam Study. Free androgen index (FAI) was calculated as ratio of TT to SHBG concentration. TT, SHBG, FAI and NT-proBNP were natural log transformed. Regression coefficients and 95% Confidence Intervals (CI) were calculated using multivariable linear regression models adjusting for confounders.
Results: After adjustment for age, body mass index, years since menopause, serum total cholesterol, hypertension, alcohol intake, physical activity, smoking and prevalent diabetes, higher levels of estradiol (per SD increase, β=0.04; 95% CI: 0.01 to 0.07) and SHBG (per SD increase, β=0.17; 95% CI: 0.13 to 0.20) were positively associated with NT-proBNP concentrations. In contrast, TT (per SD increase, β=–0.06; 95% CI: –0.08 to –0.03) and FAI (per SD increase, β=–0.13; 95% CI: –0.16 to –0.10) were inversely associated with circulating NT-proBNP (both p<0.001). These associations were independent of insulin resistance, C-reactive protein or fatty liver. However, significant interactions were found between estradiol, age (p-interaction=0.002) and years since menopause (p-interaction=0.01). After stratification by median-age (68.5 years), the positive association between estradiol and NT-proBNP was present in women 68.5 years or older (per SD increase, β=0.10; 95% CI: 0.04 to 0.16) whereas no association was observed in women younger than 68.5. Similarly, the stratification analysis by years since menopause (median) revealed that the positive association between estradiol and NT-proBNP was significant only in women 20 years or further from menopause (per SD increase, β=0.06; 95% CI: 0.01 to 0.11).
Conclusions: These findings suggest an association between estradiol, SHBG, and testosterone with circulating NT-proBNP levels among postmenopausal women. This association seems to be modified by age and years since menopause.

P5022 | BEDSIDE
Homoarginine predicts outcome in patients with acute chest pain and coronary syndrome

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Background: The endogenous amino acid homoarginine is an alternative substrate for nitric oxide (NO) synthesis. NO exhibits antiatherosclerotic effects. Low concentrations of homoarginine have been linked to an increased risk of adverse cardio- and cerebrovascular outcome and mortality as well as to clinical phenotypes of vascular remodelling.
Purpose: The present study aimed to investigate the associations between homoarginine and cardiovascular outcome and its relationship to clinical phenotypes in patients with acute chest pain and coronary syndrome (ACS).
Methods: Patients with acute chest pain were consecutively enrolled from January 2007 through December 2008. On admission, plasma concentrations of homoarginine, brain natriuretic peptide (BNP), and mid-regional pro-adrenomedullin (MR-proADM) were measured. Patients were followed for major adverse cardiovascular events (MACE), including all-cause death, myocardial infarction or stroke.
Results: In total 1,649 patients (66% men) were included in the analysis of whom 589 (36%) were diagnosed with ACS. During a median follow-up of 183 days, 60 MACE were registered in the overall study population and 43 MACE in the ACS subgroup. Multivariable Cox regression analyses adjusted for age, sex, body mass index, current smoking, diabetes mellitus, hypertension, and dyslipidemia revealed that an increase of one SD plasma log-transformed homoarginine (0.37) was associated with a hazard reduction of 25% (HR 0.75 [95% CI: 0.58–0.97]) for incident MACE. Likewise, in the subgroup of ACS patients the hazard reduction related to an increase of homoarginine was 34% (HR 0.66 [95% CI: 0.50–0.88]). Homoarginine was not only correlated with biomarkers representing cardiovascular function, i.e. MR-proADM and BNP, but also with with QTc duration (P<0.001 for all) and prevalent atrial fibrillation (OR 0.83 [95% CI: 0.71–0.95]).
Conclusion: Low homoarginine was identified as risk marker for incident MACE in patients with acute chest pain, in particular in ACS. Homoarginie was also associated with prevalent atrial fibrillation. Further investigation is needed to evaluate homoarginine as a therapeutic option for these patients.

UNDERSTANDING PATHOPHYSIOLOGY FROM IMAGING AND FUNCTIONAL ASSESSMENT

P5023 | BEDSIDE
Demonstration of the functional consequences of the coronary stenosis on the basis of the flow-pressure relations using 3D-QCA morphological data

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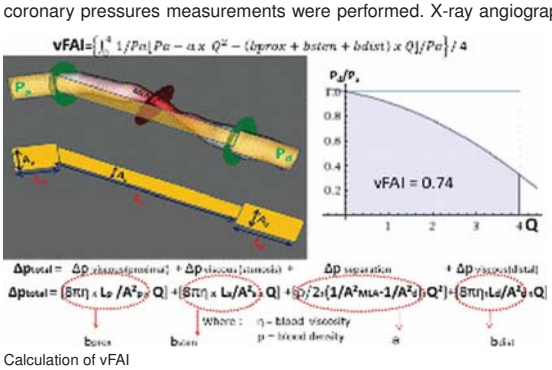
Background: The virtual functional assessment index (vFAI) has been suggested recently for demonstration the functional consequences of the coronary lesions. The vFAI was derived from the data of the flow-pressure curves generated by solving the Navier-Stokes equations using three-dimensional quantitative coronary angiography (3D-QCA) reconstructions. This new index showed good correlation with the fractional flow reserve.
Aims: To develop a smart model to calculate the vFAI using 3D-QCA data and the simple Hagen-Poiseuille and the Bordan-Carnot fluid dynamic equations as well as to compare these results to the measured FFR values.
Methods: A total of 45 coronary lesions of 33 patients were investigated. Intracoronary pressures measurements were performed. X-ray angiographic images



Calculation of vFAI

were recorded by flat panel systems. The lumen of the interrogated vessel segments from the origin of the target vessel to the pressure sensor was reconstructed in 3D using a dedicated 3D QCA software package.
Results: Significant tight correlation was found between the calculated vFAI and the measured FFR values (r=0.81; p<0.0001). The cut off value of the vFAI of 0.92 provided a good sensitivity (95%) with 71% specificity to predict the diagnostic FFR ≤0.8 values. The area under the curve was calculated to be 0.86 according to the ROC analysis.
Conclusions: The vFAI demonstrates comprehensively the pathophysiological consequences of the coronary lesions. The level of correlation between the vFAI values and the measured FFR values calculated using the simple approach developed by our team matches the performance of the previously described method that uses dedicated software and time-consuming fluid dynamic computations.

P5024 | BEDSIDE
Change in characteristics of the population receiving angiography in an era with decreasing cardiovascular incidence and mortality

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Background: Over the past 40 years, cardiovascular mortality in Northern Norway has decreased from 8‰, among the highest in Europe, to 1.7‰ - among the lowest. This is due to a large decrease in incidence, but lately also to >50% reduction in case fatality.
Purpose: Our aim is to describe how decreasing incidence and case fatality is reflected in the population receiving angiography in the last decade.
Methods: From 2005–2012, a total of 27,218 angiographies were performed by a sole provider of angiography for 479,000 people. Patient characteristics were entered into a clinical registry. Changes in trends were analysed by age-adjusted logistic regression analyses. Gender differences were tested with interaction terms. All the reported differences below had p<0.05.
Results: 19,923 patients (66% men and 34% women) had 25,232 admissions for angiography. Men were 64 years old and women were 67 at admission, of whom 62% vs 75% did not have former revascularisation. 25% of men were admitted more than once vs only 20% of women. 51% of men and 45% of women were admitted as acute coronary syndrome (ACS). In both genders, the total number of acute admissions increased by 1.5% per year vs 3.8% per year for elective admissions. Age of the admitted population increased 1 year from 2005 to 2012. ST-elevation myocardial infarction (STEMI) decreased from 24% to 18%, and prevalence of obstruction in either left main stem, proximal LAD or 3 vessels decreased from 22% to 20%. The number of ACS angiographies resulting in revascularisation decreased from 77% to 65% among those without former revascularisation vs from 63% to 51% among those with revascularisation. In the elective population, proportion with stable angina as referral cause decreased from 91% to 85%.The proportion resulting in revascularisation decreased from 62% to 36% among those without former revascularisation vs from 49% to 40% among those with either former percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). 63% of first diagnosis of obstructive coronary heart disease occurred during acute admission in both genders.
Conclusions: The dramatic drop in cardiovascular mortality in Norway was reflected in less obstructive pathology detected both in emergency and elective settings and with less severe pathology. Despite a high and increasing rate of elective angiography, most obstructive disease in need of revascularisation were diagnosed during acute admissions. This possibly reflects the difference in underlying pathology in stable angina and ACS with more vulnerable plaques in the latter.

P5025 | BEDSIDE
The impact of exercise therapy on coronary plaque

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Background: Although pharmacologic therapies have affected the coronary plaque components and improved the prognosis for patients with ischemic heart disease, but recurrent cardiovascular events occur. Exercise therapies also reduce cardiovascular event. The purpose of the present study is to assess the effect of exercise on coronary plaque component using intravascular ultrasound radiofrequency data analysis (VH-IVUS).
Methods: We investigated 110 non-culprit lesions of 82 patients, who underwent percutaneous coronary intervention (PCI) and received optimal medical treatment (OMT), with VH-IVUS at PCI and 7 months later. Following PCI, 18 patients performed aerobic exercise (30 minutes ergometer/day, 2 or 3 times a week) for 5 months in our hospitals (ET group, 28 lesions) and 64 patients received only OMT (OMT group, 82lesions).
Results: LDL cholesterol and high sensitive CRP equally decreased in both groups, and peak oxygen uptake significantly increased in ET group (17.0±5.5 to 18.6±4.9 ml/min/kg, P=0.03). Despite no significant changes of plaque volume from baseline in both groups, the changes of the relative plaque content were different between ET group and OMT group in fibrosis (%F) (0.6±6.9% vs –3.9±12.7%, P<0.01) and necrotic core (–0.3±6.9% vs 4.5±11.7, P=0.01). In only OMT group, %F was decreased (66.3±9.6 to 62.4±10.8%, P<0.01) and the relative plaque content of Dense calcium increased (4.6±4.3 to 6.8±4.9%, P<0.01).
Conclusion: Even without significant changes of plaque volume, the combination of aerobic exercise and optimal medical treatment may be able to prevent the progression of atherosclerosis.

P5026 | BEDSIDE
Association between serum levels of C-reactive protein and changes of plaque composition in non-infarct-related coronary arteries following high-intensity statin therapy. Results of the IBIS-4 Study

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Background: Levels of serum inflammatory markers associate with changes of coronary plaque burden and composition in statin-treated patients with stable coronary artery disease. Acute myocardial infarction is triggered by inflammatory bursts that may precipitate plaque progression. The association between inflammatory markers and changes of coronary plaque burden and composition in patients with ST-elevation myocardial infarction (STEMI) is unknown.
Objectives: To asses volumetric and compositional changes of coronary atheroma in relation to serum lipoprotein and high-sensitivity C-reactive protein (hsCRP) levels in patients with STEMI treated with high-intensity statin therapy.
Methods: In the IBIS-4 study 82 patients with acute STEMI underwent serial intravascular ultrasound (IVUS) and radiofrequency (RF) IVUS of the two non-infarct related epicardial coronary arteries following successful primary percutaneous coronary intervention and repeated imaging after 13 months of treatment with rosuvastatin 40mg. All patients recruited at Bern University (n=44) with serial hsCRP measurement are included in the present analysis.
Results: At 13 months, LDL-C decreased by 38% to 77mg/dl, HDL increased by 13% to 48 mg/dl and hsCRP decreased by 58% to 0.70 mg/L. Regression of percent atheroma volume (–0.99%, 95% CI –1.84 to –0.14, p=0.024) did not correlate with levels of hsCRP and was accompanied by reduction of fibro-fatty tissue (p=0.005), increase of dense calcium (p=0.016) and no significant change of necrotic core tissue (p=0.22). Changes of RF-IVUS-defined components did not correlate with LDL-C or HDL-C levels. In contrast, on-treatment hsCRP correlated with the change of necrotic core tissue, which decreased in patients with the lowest hsCRP tertile (–0.13mm^2, –0.23 to –0.04) and increased in patients across higher hsCRP tertiles (p=0.002). A per-lesion analysis showed lowest on-treatment hsCRP levels for thin-cap fibroatheromas (TCFAs) at baseline that progressed to non-TCFA lesions (0.03, 0.02 to 0.19 mg/L) and highest hsCRP levels for non-TCFA lesions that progressed to TCFAs at follow-up (1.75, 0.75 to 2.87 mg/L).
Conclusions: In this observationsl study of STEMI patients treated with high-intensity statin therapy, elevated on-treatment levels of hsCRP, but not of LDL-C, associated with serial increase of RF-IVUS-defined necrotic core. Increased levels of systemic inflammation may identify patients with progression of presumed high-risk indices of coronary plaque composition despite aggressive statin therapy. Larger studies are needed to determine potential prognostic implications of these associations.

P5027 | BEDSIDE
Contrast medium induced Pd/Pa ratio (CMR) versus FFR and adenosine-free indexes in the evaluation of intermediate coronary stenosis

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Aims: The need for adenosine administration to achieve maximal hyperaemia limits the widespread application of fractional flow reserve (FFR) in the real world. We previously demonstrated that Pd/Pa ratio registered during submaximal reactive hyperaemia induced by conventional non-ionic radiographic contrast medium (contrast medium induced Pd/Pa ratio: CMR) can be sufficient for the assessment of physiological severity of stenosis in the vast majority of cases. In this study we aimed to test the accuracy of CMR in predicting an FFR≤0.80 in comparison with other adenosine-free indexes, such as basal Pd/Pa and instantaneous wave-free ratio (iFR).
Methods and results: 323 patients with 373 intermediate coronary stenoses were prospectively and consecutively enrolled. FFR was measured after administration of adenosine, CMR was obtained after intracoronary injection of 6 ml of radiographic contrast medium, while Pd/Pa and iFR were measured at rest. Pd/Pa was measured in all 373 lesions, while CMR in 279 and iFR in 64. Although we found a significant correlation between FFR and all measured indexes, the strongest correlation was between FFR and CMR (r=0.92, p<0.001; r=0.77, p<0.001 for correlation between FFR and Pd/Pa; r=0.76, p<0.001 for correlation between FFR and iFR). ROC curve analysis confirmed these data, showing an excellent accuracy of CMR cut-off of ≤0.83 in predicting a positive FFR (AUC 0.98

[95% CI: 0.96–0.99], specificity 0.93, sensitivity 0.82). Moreover CMR was statistically superior than basal Pd/Pa≤0.92 (AUC 0.94 [95% CI: 0.91–0.97], specificity 0.93, sensitivity 0.82; p<0.001) and iFR ≤0.86 (AUC 0.89 [95% CI: 0.76–0.97], specificity 0.95, sensitivity 0.76; p=0.04) in predicting a positive FFR.
Conclusions: In the present study not only we confirm in a much larger population our previously published data, showing that CMR is accurate in predicting the functional significance of coronary stenosis but also we demonstrate its superiority over other adenosine-free indexes (Pd/Pa and iFR). This finding support the use of CMR in clinical practice, limiting the use of adenosine to doubtful cases only.

P5028 | BEDSIDE
Influence of optical coherence tomography on PCI strategy during bioresorbable scaffold implantation

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Background: The biomechanical differences in the structure of bioresorbable vascular scaffolds (BVS) compared to metallic scaffolds demand an optimal deployment. The combination of angiography with optical coherence tomography (OCT) during percutaneous coronary intervention (PCI) has been shown to improve safety of PCI. Its superiority in terms of spatial resolution allows for more accurate detection and quantification of BVS malapposition, underexpansion, tissue prolapse, edge dissection, stent fracture and thrombus. These issues may be associated with increased post-procedural mobidity and mortality.
Objectives: To evaluate the influence of OCT during PCI and its impact on stenting strategy.
Design: Consecutive patients undergoing PCI with OCT-guided scaffold implantation from April 2012 to October 2014 were reviewed. Angiography and OCT-images –were analysed, when available, before and after BVS implantation with respect to a change in PCI strategy.
Results: A total of 162 procedures were included. The median age of the patients was 62 (35–89) years, and 72.2% of patients were male. Indication for PCI was stable angina in 74.6%, STEMI in 9.8%, NSTEMI in 9.3%, unstable angina in 6.2% of the cases. OCT was performed in 87% (n=141) before deployment of the BVS. In 13.5% (n=19) it was decided againgst BVS implantation after OCT analysis due to heavy calcification (6.4%) or inadequate sizing (7.1%). In 19.7% (n=24) the pre-implantation OCT-analysis influenced the further strategy. This included the additional use of scoring devices (4.9%). In 10.7% the lesion length was underestimated. OCT analysis after BVS implantation, performed in 128 (79%) of the patients, led to additional interventions in in 33.6% (n=43) of the procedures. Specifically, further BVS implantation was performed in 11.7% (edge dissection 10.9%, BVS fracture 0.8%). Additinal balloon dilatation was needed in 20.3% of cases (thrombus 4.7%, underexpansion 3.1%, malapposition 10.9%, tissue prolaps 1.6%). In 1.6% of patients no further intervention was needed although angiography suggested so. In total, the OCT-images before the implantation influenced the PCI strategy in 30.5% and after BVS implantation in 33.59% (overall 53%) of the cases.
Conclusion: OCT guidance during BVS implantation was associated with changes in PCI procedure more than half of the cases. Thus, OCT guidance may minimise the presence and the impact of procedural issues during BVS implantation and potentially improve clinical outcome.

P5029 | BEDSIDE
Usefulness of optical coherence tomography in determining the mechanisms of myocardial infarction in patients without angiographically demonstrable coronary artery disease

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Background: Coronary angiography (CAG) generally allows us to identify culprit lesions in patients with myocardial infarction (MI) by a number of characteristic findings (e.g. obstruction, narrowing, and haziness). However, a substantial proportion of patients with MI have no angiographically demonstrable coronary artery disease (CAD), and it is occasionally difficult to determine the mechanism of MI in these patients.
Purpose: The aim of this study was to clarify the usefulness of optical coherence tomography (OCT) for determining the mechanism of MI in these patients.
Methods: We studied 441 consecutive patients with MI, diagnosed according to the third universal definition of MI, admitted to our hospital (mean age, 68.0±13.3 years; men, 78.8%). The culprit lesion morphologies by OCT were classified as follows: plaque rupture, OCT-calcified nodule, OCT-erosion, and others. The patients were divided into two groups according to the presence or absence of angiographically demonstrable CAD.
Results: Twenty-four patients (5.4%) had no angiographically demonstrable CAD (non-CAD group). Patients in the non-CAD group tended to be younger (63.0±16.3 vs. 68.0±13.3 years, P=0.055) and to have lower prevalence rates of diabetes mellitus and dyslipidemia (20.8% vs. 38.6%, P=0.08 and 37.5% vs. 56.3%, P=0.07, respectively) compared to those for patients in the CAD group. In the pre-intervention Thrombolysis in Myocardial Infarction (TIMI) flow grade classification, patients in the non-CAD group had a significantly higher frequency of TIMI 3 flow grade compared to that for patients in the CAD group (58.3% vs. 8.7%, P<0.01), although the rate of ST-segment elevation MI was similar between the groups (66.7% vs. 75.2%, P=0.40). Eighteen patients in the non-CAD group underwent OCT imaging. The incidences of plaque rupture, OCT-calcified nodule, OCT-erosion, and others were 22.2%, 5.6%, 27.8%, and 38.9%, respectively. The mechanisms of MI in patients classified as "others" by OCT included dissection, spasm, thromboembolism caused by atrial fibrillation, and thrombus formation triggered by dehydration or hypotension in the intact coronary artery.
Conclusion: The incidence of no angiographically demonstrable CAD in patients with MI was relatively high. Although it was difficult to determine where the culprit lesions were located or what the mechanisms of MI were using only CAG in these patients, we could confirm the mechanisms of MI by using OCT. Hence, OCT appears to be a useful modality for determining the mechanism of MI, especially in patients without angiographically demonstrable CAD.

OMINOUS SIGNS IN HEART FAILURE

P5030 | BENCH
Overexpression of phosphodiesterase-2 in mice reduces CaMKII-dependent enhancement of late sodium current through impared beta-adrenergic response

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In heart failure, late Na current (late INa) is increased and this has been shown to lead to arrhythmias and contractile dysfunction. Chronic β-AR stimulation promotes heart failure. CaMKIIδ, which can be activated by β-AR stimulation (via cAMP-Epac), increases late INa via phosphorylation. We hypothesized that overexpression of phosphodiesterase-2 (PDE2), which hydrolyses cAMP, can abolish activation of CaMKIIδ, thereby reducing phosphorylation of CaMKIIδ targets (such as late INa), even in the presence of β-AR stimulation. To evaluate this hypothesis we investigated ventricular cardiomyocytes isolated from PDE2-overexpression transgenic (TG) vs wild-type (WT) littermates. Late INa integral was measured using whole-cell patch clamp technique. CaMKIIδ was activated upon external application of either isoproterenol (100 nmol/L, ISO) or direct Epac activator 8-(4-chlorophenylth)-2'-O-methyladenosine-3', 5'-cyclic monophosphate (5 μmol/L, 8-CPT). In WT myocytes, both ISO and 8-CPT resulted in significant and comparable increases in late INa (control: –27.9±3.1 vs ISO: –81.6±4.7 vs 8-CPT: –78.6±8.3 A*ms*F-1, n=15 vs 16 vs 14; P<0.001 vs control). However, in myocytes from TG mice the ISO-dependent increase in late INa was completely abolished (control: –24.6±3.2 vs ISO: –28.0±3.6 A*ms*F-1, n=16 vs 17), while direct Epac activation by 8-CPT (–79.4±7.5 A*ms*F-1, n=12, P<0.001) led to enhancement of late INa. As hypothesized, preincubation with CaMKIIδ peptide inhibitor AIP (1μmol/L, 10 min) significantly reversed the ISO- and 8-CPT-dependent enhancement in late INa in WT myocytes (–26.7±3.4 and –24.7±7.9 A*ms*F-1 respectively, n=5 and 3), as well as the 8-CPT-dependent enhancement in late INa in TG mice (–30.4±5.5 A*ms*F-1, n=7). Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKIIδ-dependent phosphorylation of ryanodine-receptor. Preliminary data show that the low basal Ca-spark-frequency (CaSpF) could be significantly increased by superfusion with ISO in WT (0.09±0.03 vs 0.52±0.08 μm-1s-1, n=69 vs 66; P<0.001) but not in TG myocytes (0.03±0.02 vs 0.10±0.04 μm-1s-1, n=46 vs 48). Ongoing work in this mouse model is focussing on the effects of direct activation of Epac and inhibition of CaMKIIδ and on spark frequency.
In conclusion, overexpression of PDE2 in mice abolishes the effect of ISO on the proarrhythmic late INa via an Epac-CaMKIIδ-dependent pathway. Modulation of this pathway may have potential in the treatment of arrhythmias and heart failure.

P5031 | BEDSIDE
Risk related to diabetes and pre-diabetes in heart failure with reduced ejection fraction: Insights from PARADIGM-HF

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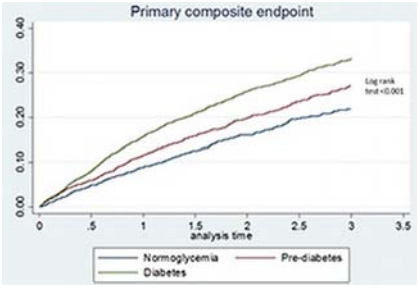
Background: Although the frequency of diabetes is well known in patients with heart failure and reduced ejection fraction (HF-REF), the prevalence of pre-diabetes and its consequences are not. We investigated this in the Prospective

Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF).
Methods: We examined clinical outcomes in 8399 patients during a median follow-up of 27 months according to history of diabetes and glycaemic status in the remainder, according to baseline hemoglobin A1c (HbA1c): normoglycaemia = <6.0%; pre-diabetes = 6.0–6.4% and diabetes = ≥6.5%. Cox regression models were used to adjust for known predictors of risk: age, sex, race, HF duration, NYHA class, LVEF, heart rate, KCCQ score, BMI, eGFR, NTproBNP, ischemic etiology, prior MI, stroke, and AF.
Results: At baseline, 2907 patients (35% of the total) had a history of diabetes, an additional 1106 patients (13%) had undiagnosed diabetes, and 2103 (25%) had pre-diabetes. Compared to the 2158 patients (26%) with normoglycaemia, the adjusted hazard ratio (HR) for the primary composite outcome of CV mortality or HF hospitalization (CV/HFH) was: 1.61 (95% CI 1.41–1.83) for known diabetes, 1.54 (1.35–1.74) for known diabetes or HbA1c ≥6.5% and 1.26 (1.09–1.45) for pre-diabetes (Figure). The benefit of LCZ696 compared with enalapril was consistent across the range of HbA1c studied.



Outcomes according to glycaemic status

Conclusion: In patients with H-REF, dysglycaemia is very common and compared with normoglycaemia, pre-diabetes, as well as diabetes, is associated with a higher risk of adverse cardiovascular outcomes. LCZ696 was similarly effective across the glycaemic spectrum.

P5032 | BEDSIDE
Respiratory syncytial virus infection is associated with acute decompensated heart in adult patients with congestive heart failure

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Respiratory syncytial virus (RSV) has been documented as an increased cause of severe respiratory infections in adults. Few studies have examined RSV infections in adults with chronic heart diseases.
The aim of this study was to evaluate the occurrence of RSV infection among chronic heart disease patients, their clinical characteristics and outcome.
During RSV season we assessed RSV respiratory illnesses in prospective cohorts of adults patients presenting with congestive heart failure (CHF). RSV infection was confirmed by Real-Time PCR technique performed on respiratory samples of outpatients and those who were hospitalized because acute decompensated heart failure.
A total of 99 patients, median age 57 years, were enrolled in a prospective surveillance including 45 outpatients recruited from the CHF ambulatory, and 52 inpatients, with a history of exacerbation of underlying heart disease without an evident cause.
Thirty percent (30/99) of all respiratory samples obtained of each subject were positive for RSV infection. A positive rate of 17.3% (9/52) was observed in hospitalized RSV infected cases and 46.6% (21/45) in infected outpatients. RSV infection generated respiratory symptoms more frequently in hospitalized patients than in infected outpatients (77.7% x 36.8%). In addition, RSV viral load analysis was significantly higher in hospitalized patients samples (2.8 log10 copies/mL) when compared to outpatients infections (1.9 log10 copies/mL) (p=0.02). The results of this pilot study suggest that RSV is a very frequent cause of infection in adult patients with heart disease. RSV can cause more severe disease among CHF patients and those with higher viral load are at higher risk of acute decompensated heart failure and hospitalization.
RSV infection surveillance should be intensified among CHF patients during seasonality. High-risk patients for hospitalization should be evaluated by RSV test. An effective RSV vaccine or antiviral may offer benefits for these patients.

P5033 | BEDSIDE
Development of major types of cancer in patients with heart failure

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Background: Patients with chronic heart failure (CHF) survive for extended periods thus increasing the clinical importance of comorbidity such as development of cancer. It is unknown, which types of cancer that are associated with CHF, and more knowledge is needed to prevent non-cardiac morbidity and mortality in CHF patients.
Purpose: The aim of this study was to assess the risk of major subtypes of cancer in a large Danish cohort with CHF compared to the total Danish background population using nationwide Danish administrative registries.
Methods: A total of 9.307 outpatients with verified CHF without prior diagnosis of cancer (27% female, mean age 68 years, 89% with LVEF <45%) were included in the CHF cohort from 2002 to 2009. A new diagnosis of cancer was obtained from the Danish National Patient Registry. Type specific risk of cancer was evaluated in Cox regression analysis adjusted for age and gender.
Results: With 975 new diagnosis of cancer in the CHF cohort and 330.843 in the background population the adjusted Cox regression analysis demonstrated an increased risk of any type of cancer in the CHF population with a hazard ratio (HR) of 1.51 (95% CI 1.42–1.61, p<0.0001). The subtype specific analysis demonstrated a HR of 1.81 (95% CI 1.54–2.12, p<0.0001) for lung cancer, which along with skin cancer with a HR of 1.84 (95% CI 1.57–2.15, p<0.0001) were the two most common malignant diagnosis in the cohort constituting proportions of 15.7% and 16.3%, respectively. The HR for cancer in the kidney and urinary system was 1.75 (95% CI 1.41–2.18, p<0.0001) and in the liver/biliary system 1.60 (95% CI 1.20–2.13, p=0.0015). The risk of lymph/blood cancer and colon/rectal cancer proved increased with a HR of 1.45 (95% CI 1.14–1.85, p=0.0027) and 1.24 (95% CI 1.04–1.49, p=0.0180), respectively. Women with CHF had an increased risk of breast cancer constituting a HR of 1.36 (95% CI 1.02–1.81, p<0.0001), while risk of prostate cancer was not increased for men in the cohort.
Time analysis with elimination of early diagnosis of cancer did not significantly change the incidence, thus increased surveillance does not likely explain the results.
Conclusion: Patients with CHF are of increased risk of major types of cancer, except for prostate cancer, compared to the background population. Increased awareness of development of cancer is warranted in patients with CHF.

P5034 | BEDSIDE
High prevalence of iron deficiency in heart failure with preserved ejection fraction

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Introduction: Anaemia and iron deficiency (ID) are common co-morbidities present in patients with heart failure with reduced ejection fraction (HF-REF) and treatment with iron replacement for those with ID has been shown to improve symptoms and quality of life. However, between 30–50% of all patients with HF have preserved ejection fraction (HF-PEF) and the prevalence and relevance of ID is uncertain among this group of patients.
Purpose: To determine the prevalence of ID and anaemia in patients with HF-PEF compared to those with HF-REF.
Methods: The PEOPLE study is a prospective observational study of patients with validated HF that aims to compare clinical outcomes for patients with HF-PEF to those with HF-REF. For the purpose of this substudy, baseline blood samples were evaluated for the presence of anaemia and ID. Anaemia was defined as Hb <13g/dl in men and <12g/dl in women. ID was defined as ferritin <100mcg/L (absolute ID [AbsID]) or ferritin 100–300mcg/l with a Tsat <20% (relative ID [RelID])
Results: Of the 774 patients, 492 (64%) had HF-REF and 282 (36%) had HF-PEF. Patients with HF-PEF were older and more likely to be female those with HF-REF:- 73.8yrs vs 66.7yrs respectively (p<0.001), 45% vs 22% female (p<0.001) Overall, 440 patients (57%) had ID, of whom 265 (34%) had AbsID and 175 (23%) RelID. Patients with HF-PEF had a higher prevalence of ID compared to those with HF-REF:- 64% vs 53% respectively (p<0.003). Among patients with HF-PEF 41% had AbsID compared with 30% of those with HF-REF (p=0.004). There were similar proportions of patients with RelID in the two groups (HF-PEF 23% and HF-REF 22%, p=0.83).
Overall, 257 patients (33%) had anaemia. Of those with HF-PEF 46% were anaemic, compared with 29% of those with HF-REF (p<0.001). Of the subgroup of patients with anaemia, 78% of those with HF-PEF had ID (53% AbsID, 26% RelID) compared with 68% of those with HF-REF (40% AbsID, 28% RelID) (p=0.069). Of those who did not have anaemia, ID was present in 54% of those with HF-PEF (33% AbsID, 21% RelID) and 48% of pateints with HF-REF (26% AbsID, 21% RelID) (p=0.24)
Conclusions: ID and anaemia are highly prevalent among patients with HF-PEF with two-thirds having ID and half anaemia. Importantly, ID, in particular AbsID,

was commonly present even in the absence of anaemia, in both groups of patients with HF. Treatment of ID has been shown to improve morbidity in patients with HF-REF, whether this also applies for patients with HF-PEF needs urgent evaluation.

P5035 | BEDSIDE
Time-related cumulative incidence of congestive heart failure after childhood cancer treatment; a DCOG LATER study

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Introduction: Cardiac events (heart failure (HF), cardiac ischemia, valvular disease, pericarditis and arrhythmia) are among the most serious late effects after childhood cancer treatment. HF is the most common cardiac event that develops even decades after treatment. Known cardiotoxic treatments are anthracyclines and radiation where the heart was in the field.
Purpose: To determine the incidence of and associated risk factors of HF after childhood cancer treatment, we performed a large nationwide cohort study in childhood cancer survivors.
Methods: In our nationwide cohort (n=6,168) of 5-year childhood cancer survivors, in the Netherlands (diagnosed between 1963 and 2002), questionnaires were sent to identify patients with HF and medical records were used to further define HF. The outcome of HF was classified as symptomatic HF needing medication, cardiac device implant, heart transplant or fatal HF. We used a competing risk analysis to calculate the cumulative incidence of HF (death due to other causes was a competing risk) and a multivariable Cox regression model for the risk factors analysis.
Results: We collected cardiac information of 5,307 (86.0%) 5-year survivors (of which 611 (9.9%) were deceased). Of the other survivors, 521 (8.4%) refused participation and 340 (5.5%) were lost to follow-up. After a median follow-up of 20.3 years (5–50.4) and at a median attained age of 27.9 year (6.8–65.2), 106 survivors developed HF (2.0%); of these HF patients, 11 survivors needed a cardiac device, 8 survivors needed a heart transplant and 22 survivors died due to HF.
The cumulative incidence of HF in all survivors at the age of 20 years was 0.7% (95% Confidence Interval (CI) 0.69%-0.70%), at the age of 30 was 2.0% (1.99%-2.01%), at the age of 40 was 3.6% (3.59%-3.62%) and at the age of 50 was 5.9% (5.85%-5.91%). Contributing risk factors for the development of HF were treatment with anthracyclines (Hazard Ratio (HR): 11.6; 95% CI 6.3–21.7), mitoxantrone (4.1; 2.0–8.3), high dose cyclophosphamide (>10,000 mg/m^2) (2.0; 1.2–3.3) and radiation to the heart (1.6; 1.0–2.5).
Conclusion: Survivors of childhood cancer have increasing risk of developing HF with time, starting even from young age. Especially those survivors treated with anthracyclines, mitoxantrone, cyclophosphamide and radiation to the heart. Our study has a high percentage of follow-up, and there for a low risk of bias.
Health care professionals need to be aware of these findings, and recognize the risk of developing HF in young people, even years after their childhood cancer treatment.

P5036 | BEDSIDE
Impact of diabetes mellitus on heart failure with reduced ejection fraction - a Swedish registry based analysis

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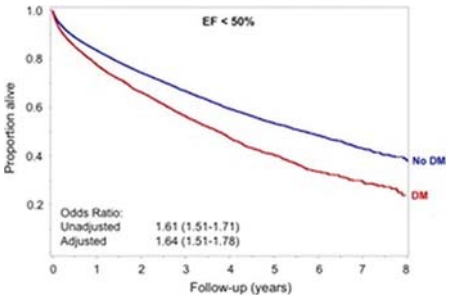
Purpose: Patients with diabetes mellitus are at increased risk of developing heart failure. We analyzed the impact of diabetes on longevity in patients with systolic heart failure in an everyday life setting.
Methods: Patients with EF<50%, with (n=5829) and without (n=18163) type 2 diabetes included in the Swedish Heart Failure Registry (S-HFR) 2003–2011 were followed for mortality until 30 September 2011 (median 22.5 months). Differences in background characteristics were adjusted for in a logistic regression model.
Results: Patients were on average 73 years old and 30% were women regardless of diabetes status. Patients with diabetes more frequently had known ischemic heart disease (68 vs. 50%; p<0.0001), hypertension (57 vs. 40%; p<0.0001), reduced renal function (58 vs. 48%; p<0.0001) and were more often revascularised (37 vs. 26%; p<0.0001). The proportion of patients with EF<30% was similar in both groups (38%), while NYHA class III and IV was more common if concomitant diabetes (53 vs. 41%; p<0.0001). Patients with diabetes had a compromised survival with a median survival time of 3.7 (range 3.6–3.9) years compared with 5.7 (5.5–5.9) years in those without (log rank, p<0.0001). The unadjusted and adjusted* ORs (95% CI) of mortality were 1.61 (1.51–1.71) and 1.64 (1.51–1.78).
Conclusion: These data support that diabetes remains as a strong independent predictor of mortality in patients with systolic heart failure despite the lack of a difference in EF. Ischemic heart disease was highly prevalent in heart failure patients with diabetes, but only 50% of them were revascularised.
* Adjusted for diabetes, gender, age, duration of heart failure, weight, blood pressure, ischemic heart disease, co-morbidities, revascularisation, eGFR class, Hb class, pharmacological treatments.



KM-survival in EF<50%, DM vs. no DM

HYPERTENSION AND COMORBIDITIES: A CHALLENGE OF TREATMENT

P5037 | BEDSIDE
Effect of Diosmin treatment on left ventricular systolic function in hypertensive patients with chronic venous insufficiency

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Introduction: Diosmin (D) has a demonstrated activity as venotonic agent. Although flavonoids have been studied for more than 50 years, there is no data explaining the effect on left ventricular function. No study has identified so far the role of D treatment over the left ventricular systolic function in patients with chronic venous insufficiency (CVI) and arterial hypertension.
Purpose: The aim of the study was to determine whether Diosmin treatment recommended for CVI influence left ventricular ejection fraction (EF) in patients with arterial hypertension.
Methods: Our 4-year study included 501 patients, aged 40–80, admitted to our cardiology department. They were all diagnosed with essential arterial hypertension and CVI according to CEAP classification. We assessed by echocardiography the left ventricular mass index (LVMI) and EF. The LVMI threshold was 95 g/m^2 in women and 115 g/m^2 in men. We divided the patients into two groups: one group with normal left ventricular mass index (LVMIN) (n=124) and one group with pathologic left ventricular mass index (LVMIP) (n=377). Each group was divided into two subgroups according to initiation of D treatment (500 mg twice per day): 1. LVMIN - D (n=78); 2. LVMIN + D (n=46); 3. LVMIP – D (n=250); 4. LVMIP + D (n=127). The groups were homogeneous according to age (62±10, 64±9, 63±9, 62±10 years) and body mass index (34±4.6, 35±4, 35.4±4.6, 35.7±5.6 kg/m^2). There were no statistical differences for EF (66.7±6.4, 63.5±7.3, 62.1±9, 62.2±8.3%). All patients were followed for 12 months according to LVMI and EF. The statistical analysis was performed in SPSS v 16.0.
Results: Comparing the four subgroups according to EF and CEAP classification after 1 year, we observed that in LVMIN + D subgroup, the EF became significantly lower in patients with CEAP class III-VI compared to CEAP class I-II (p<0.05). There were no significant results for EF in patients with LVMIP undergoing D treatment. As well, there were no correlations regarding EF between the treated or untreated subgroups.
Conclusions: The study highlights the important role of Diosmin treatment in maintaining the left ventricular systolic function in hypertensive patients with early stages of CVI (CEAP class I-II).

P5038 | SPOTLIGHT
Sitagliptin and risk of hypertension in patients with type 2 diabetes mellitus: meta-analysis of randomized trials

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Background: Recent reports of sitagliptin use have raised questions about whether the sitagliptin have beneficial effect on blood pressure of type 2 diabetes mellitus (T2DM) patients. The aim of this meta-analysis was to evaluate the effect of sitagliptin on hypertension.
Methods: We searched PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and product information sheets for randomized controlled trials, systematic reviews, and meta-analyses published through December 2012. Studies were included if they were randomized controlled trials of sitagliptin vs placebo or active comparator for T2DM patients also monitored hypertension. Relative risks of hypertension events were estimated using a fixed-effects meta-analysis.
Results: We analyzed 8 randomized controlled trials. Compared with placebo therapy and control therapy, sitagliptin had no significant increase in risk of hy-

pertension (n=46/2381 vs 39/2224; RR 0.99; 95% CI, 0.65 - 1.52; P=0.97). The risk of hypertension was slightly lower in the sitagliptin group than in the placebo group, but the difference was not statistically significant (n=27/1459 vs 19/694; RR 0.72; 95% CI, 0.40 - 1.29; P=0.27). Conversely, the risk of hypertension was slightly higher in the sitagliptin group than in the control therapy group, but the difference was not statistically significant (n=19/922 vs 20/1530; RR 1.48; 95% CI, 0.76 - 2.86; P=0.25). There was no evidence of substantial heterogeneity among the trials (I2 = 41%, I2 = 28%, and I2 = 46%, respectively).
Conclusions: Sitagliptin has no beneficial or harmful effect on hypertension in the treatment of T2DM.

P5039 | BEDSIDE
The effect of mineralocorticoid receptor antagonists in patients with hypertension and diabetes mellitus: a systematic review and meta-analyses

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Introduction: Hypertension and diabetes are established risk factors for cardiovascular morbidity and mortality. Although blood pressure (BP) control is important for diabetic patients in order to prevent cardiovascular events, attaining the target BP in these patients with a single drug is often difficult.
Purpose: We performed a systematic review and meta-analysis of published studies to evaluate the anti-hypertensive effects of mineralocorticoid receptor antagonists (MRAs) as add-on therapy to renin-angiotensin system (RAS) inhibitor(s) in patients with hypertension and diabetes.
Methods: A systematic literature search for eligible studies was conducted through October 2014 based on the Cochrane handbook. Studies were identified by searching MEDLINE, Embase, ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials. Search terms were hypertension, hypertensive, blood pressure, diabetes, diabetic, eplerenone, and spironolactone. The search was restricted to English articles of human studies, which were limited to randomised controlled trials or prospective, observational studies on the administration of MRA concomitantly with RAS inhibitor(s) in patients with type 1 or type 2 diabetes. Studies were stratified according to controlled vs. uncontrolled designs and analysed using random-effect models. Articles were excluded if mean systolic BP (SBP) was <130 mmHg before randomisation for comparative studies or at baseline for prospective cohort studies.
Results: We identified 9 eligible studies for analysis, involving a total of 486 patients and consisting of 5 randomized placebo-controlled trials, 3 randomized active-drug-controlled trials, and 1 single-arm observational study. In placebo-controlled trials, the mean difference between patients receiving MRA and the placebo group in office systolic and diastolic BP was –9.4 (95% confidence interval [CI], –12.9 to –5.9) and –3.8 (95% CI, –5.5 to –2.2) mmHg, respectively. Subgroup analyses, considering study type, age, baseline office SBP, and length of follow-up, did not show a difference from the main analysis in the SBP-lowering effects of MRA between the groups. In terms of safety, MRA demonstrated a mild increase in serum potassium (0.4 mEq/L; 95% CI, 0.3 to 0.5 mEq/L).
Conclusions: MRA contributed to further reduction of SBP and diastolic BP in patients with hypertension and diabetes who were already taking RAS inhibitors. Serum potassium levels should be checked regularly to prevent hyperkalaemia.

P5040 | BEDSIDE
Barnidipine compared to lercanidipine in addition to losartan on endothelial damage and oxidative stress parameters in patients with hypertension and type 2 diabetes mellitus

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Background: Hypertension causes endothelial damage revealed by higher levels of inflammatory markers.
Purpose: To evaluate the effects of barnidipine or lercanidipine, in addition to losartan, on some markers linked to endothelial damage and oxidative stress in patients with hypertension and type 2 diabetes mellitus.
Methods: We enrolled 151 hypertensive patients with mild systolic blood pressure (SBP) ≥140 and <180 mmHg and diastolic blood pressure (DBP) ≥90 and <105 mmHg, type 2 diabetes mellitus, normocholesterolemic. Patients were randomised to barnidipine, 20 mg/day, or lercanidipine, 20 mg/day, both in addition to losartan, 100 mg/day, for 6 months. We assessed BP monthly, in addition, patients underwent ambulatory blood pressure monitoring (ABPM) at baseline, and at the end of the study. We also collected blood sample to assess: fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), some adipocytokines linked to endothelial damage such as high-sensitivity C-reactive protein (Hs-CRP), tumor necrosis factor-alfa (TNF-alfa), metalloproteinase-2 (MMP-2) and -9 (MMP-9), soluble vascular adhesion protein-1 (sVCAM-1), soluble intercellular adhesion protein-1 (sICAM-1). We also evaluated some markers of oxidative stress such as isoprostanes and paraoxonase-1 (PON-1).
Results: One hundred and forty-three patients completed the study. Both barnidipine and lercanidipine resulted in a significant reduction in SBP and DBP, even if the blood pressure reduction obtained with barnidipine + losartan was greater than that obtained with lercanidipine + losartan ($p<0.05$). Data recorded with ABPM showed a similar trend. Barnidipine + losartan reduced the levels of Hs-CRP and TNF-alfa ($p<0.05$ vs baseline and vs lercanidipine + losartan). There were no significant differences between the two treatments on the levels of MMP-2 and -9. Barnidipine + losartan significantly reduced the levels of sVCAM-1 and sICAM-1, both compared to baseline and to lercanidipine + losartan ($p<0.05$ for both). The levels of isoprostanes were reduced by barnidipine + losartan ($p<0.05$ vs baseline and vs lercanidipine + losartan), while the levels of PON-1 remained unchanged.
Conclusions: Other than giving a greater reduction of blood pressure, barnidipine + losartan gave an improvement of some parameters linked to endothelial damage and oxidative stress in diabetic and hypertensive patients.

P5041 | BEDSIDE
Vascular function and atherosclerosis are similar in patient with idiopathic hyperaldosteronism and essential hypetension

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Introduction: Primary aldosteronism (PA) is a major cause of secondary hypertension. PA is characterized by autonomous aldosterone hypersecretion, and it has been reported that patients with PA exhibit higher incidents of cardiovascular and cerebrovascular diseases than those with essential hypertension. There is two major subtypes of PA; aldosterone-producing adenoma and idiopathic hyperaldosteronism (IHA), but the risk of IHA alone is unclear. The purpose of this study is to clarify the vascular damage of IHA, comparing essential hypertension (EH).
Methods: 316 consecutive patients consulted our hospital with hypertension were included. All patients proposed to check plasma aldosterone concentration and plasma renin activity. Renovascular hypertension was checked by contrast computed tomography or renal artery ultrasonography. 231 patients were diagnosed EH, 1 was renovascular hypertension, 1 was pheochromocytoma, 2 were subclinical Cushing syndrome and 78 were diagnosed PA. PA was diagnosed according to The Japan Endocrine Society guideline. 53 patients of PA (68% of PA) underwent adrenal vein sampling and 47 patients were diagnosed IHA who were proven bilateral adrenal excessive secretion of aldosterone. The patients with IHA and EH enrolled. Marker of vascular health was assessed as brachial artery flow-mediated vasodilation (FMD), carotid intima-media thickness (IMT), cardio-ankle vascular index (CAVI) and coronary artery calcium (CAC) score. FMD and carotid IMT were measured with B-mode ultrasound, CAVI was measured with a CAVI instrument and CAC score was measured with computed tomography.
Results: No patient was treated with aldosterone antagonist in both groups. Systolic blood pressure was similar in IHA and EH group (146±17 vs 142±22mmHg). Age was significantly lower in IHA group than in EH group (57±11 vs 64±11). FMD, Carotid IMT, CAVI and CAC score was similar in IHA and EHT group (FMD: 3.2±3.3% vs 2.8±2.3%, IMT: 0.72±0.18 mm vs 0.76±0.23 mm, CAVI: 8.0±1.4 vs 8.5±1.5, CAC score: 118±283 vs 255±553).
Conclusion: These findings suggest that vascular function and atherosclerosis were similar between IHA and EH. IHA may treat with conventional medical therapy, not with aldosterone antagonist.

P5042 | BEDSIDE
Diverge responses of cardiac autonomic function to beta-blocker therapy depending on chronic kidney disease

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Introduction: Although in patients (pts) with chronic kidney disease (CKD), who have high risk of cardiac death, the sympathetic activation is elevated, the renal-protective effect and the preventive efficacy of beta-blocker (BB) therapy against sudden cardiac death for CKD pts remain controversial. We investigated the difference of BB effect on the cardiac autonomic function utilizing heart rate variability (HRV) between individuals with and without CKD.
Methods: Twenty-four-hour Holter monitor was conducted in 122 non-diabetic CKD pts (65 males, 70±11 years, 29 with BB) and 278 non-diabetic controls without CKD (123 males, 59±16 years, 31 with BB). Both the time-domain and the frequency-domain HRV analyses were performed. The proportion of NN50 (pNN50; reflecting parasympathetic activity), the high-frequency component (HF; reflecting parasympathetic activity), and the low-frequency to high-frequency ratio (L/H ratio; reflecting sympatho-vagal balance) were evaluated. The natural logarithmic transformation (Ln) was performed if the indices were not normally distributed. To evaluate the contribution of CKD and related comorbidities (hypertension, dyslipidemia, Hb, ischemic heart disease, hyperuremia, age, sex) to the cardiac autonomic fluctuation, the night-time (10PM-8AM) and day-time (8AM-10PM) segments were arbitrary adopted during regression analysis.
Results: The BB therapy significantly reduced the heart rate in each cohort ($P<0.05$). Although the BB therapy enhanced Ln pNN50 in controls only during

day-time (P=0.01), the BB therapy made no significant differences in Ln pNN50 during night-time in controls and throughout 24 hours in CKD pts (P>0.05). The BB therapy did not significantly affect the Ln LF throughout 24 hours in each cohort (P>0.05). The Ln HF was significantly enhanced due to BB therapy only during day-time in controls (P<0.01), in contrast, it was significantly enhanced with BB therapy only during night-time in CKD pts (P=0.02). Though the Ln L/H ratio showed significant reduction with BB as compared to without BB throughout almost 24 hours in controls (P<0.05), the BB therapy made no difference in Ln L/H ratio in CKD pts (P>0.05). The regression analysis demonstrated that these significantly different responses to BB therapy depending on the presence of CKD were maintained after the adjustment for comorbidities above.
Conclusion: The effect of BB on the cardiac autonomic function is different according to the presence of CKD. The controversial efficacy of BB in CKD pts may derive from this divergent effect on the cardiac autonomic function.

P5043 | BEDSIDE
Implementation of hypertension guidelines recommendations in primary care improves detection of silent renal damage

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Background: Subclinical renal damage in hypertension is often underestimated. Identification of hypertensive patients at high risk, at which further target organ damage development or cardiovascular events can be prevented by strict control of blood pressure and of multiple risk factors, needs to be improved in primary care.
Purpose: To analyze the results of active detection of subclinical renal damage made by trained general practitioners in comparison with untrained and to analyse the factors correlated with renal damage in hypertension.
Methods: During 2013–2015 we performed a cross sectional study on 3145 hypertensive patients from 12 family medicine offices of Timiş County. After exclusion of diabetes and manifest renal disease, 2516 cases of primary hypertension remained. Detection of subclinical renal damage was made by presence of microalbuminuria (MAU), estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 and a slightly elevated serum creatinine. Screening for MAU was made actively at the family doctor's office on 1154 cases (45.8%) with Arkray test strips from spot urine samples. Afterwards patients with subclinical renal damage performed ambulatory blood pressure and echocardiography.
Results: Detection of subclinical renal damage consisted in MAU was present in 277 cases (11%), of which 162 cases (14.8%) in the active detection group vs. 115 (8.44%) in the second group (p<0.05). eGFR ≤60 ml/min/1.73 m^2 was present in 542 (21.5%) cases (25.95% vs.17.47%) and mild elevated creatinine levels documented in 46 (1.8%) patients (2.68% vs. 1.18%). The mean age of patients with subclinical renal damage was 56±13.1 years and the mean duration of hypertension was 6±5.3 years. Twenty six patients with MAU (9.38%) had mild, 108 (38.9%) moderate and 143 (51.6%) severe hypertension. A high cardiovascular risk profile was present in 219 cases with MAU (79.8%). Left ventricular mass index (LVMI) was 125±28 g/m^2 in the hypertensive group without MAU and 157±56 g/m^2 in the MAU group (<0.04). According to a logistic regression analysis, the values of systolic and diastolic office blood pressure, 24 h systolic blood pressure, weight and LVMI were the main predictors of MAU (p<0.001 for all determinants).
Conclusions: Better compliance of general practitioners with the recommendations of hypertension guidelines results in superior detection of kidney injury in early stages, when the damage process can be regressed and complications prevented. A larger use of this standpoint in the diagnostic work-up of hypertensive patients is recommended in primary care.

HYPERTENSION TREATMENT

5075 | BEDSIDE
Effects of antihypertensive therapies on primary and secondary prevention of stroke: systematic review and network meta-analysis

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Background: Hypertension is the most important risk factor for stroke and stroke recurrence. However, the preferred antihypertensive therapy for these patients has yet to be determined
Methods: We performed a systematic review, network meta-analysis, and meta-regression of randomized controlled trials that investigated the effect of antihypertensive therapies on primary prevention of stroke or secondary prevention for previous stroke patients of any vascular event. Trials were identified from searches of published hypertension guidelines, electronic databases, and clinical trial registries.
Results: For primary prevention (39 trials, 283529 patients), all antihypertensive agents, except alpha-blocker, outperformed placebo in preventing any stroke events. By using probability ranking for mixed treatment comparisons, angiotension receptor blocker may be the most preferred agent for primary prevention of stroke. For secondary prevention (10 trials, 40496 patients), only diuretics significantly outperformed placebo for preventing any adverse vascular events, and should be the class of choice for patients with previous stroke. Moreover, for primary prevention trials, the meta-regression analysis showed that 1 mmHg decrease of BP was associated with an 0.12% absolute risk reduction of (95% confidence interval 0.061–0.170; p=0.00012) for any stroke.
Conclusions: Evidence from randomized controlled trials supports the use of antihypertensive agents in lowering blood pressure for the primary prevention of stroke and secondary prevention of vascular events in patients with previous stroke. Although angiotension receptor antagonist and diuretics may be the most preferred strategies for primary and secondary prevention, repectively, the final achieved BP may be the key element in the effective risk reduction for primary prevention of stroke.

5076 | BENCH
A novel blood pressure lowering and renal enhancing designer peptide: acute MANP in experimental hypertension

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Background: Hypertension remains the key risk factor for cardiovascular and renal diseases with an unmet need for novel blood pressure (BP) lowering and organ protective therapies. We recently engineered MANP as a designer ANP-like therapeutic peptide with enhanced renal and BP lowering properties which go beyond native ANP. The biological actions of MANP are mediated by its guanylyl cyclase A receptor (GC-A) and the second messenger cyclic guanosine monophosphate (cGMP). Compared to ANP, MANP is also resistant to degradation by peptidases highly expressed in the kidney. The acute actions of MANP in lowering BP and modulating renal function in an animal model of essential hypertension are undefined.
Purpose: We sought to evaluate the BP lowering and renal actions of acute infusion of MANP in spontaneously hypertensive rats (SHRs).
Methods: We randomized n=12 SHRs in 3 groups: group 1 received MANP 300 pmol/kg/min, group 2 MANP 100 pmol/kg/min and group 3 received vehicle (saline 0.9%). We infused MANP/vehicle for 75' in anesthetize rats. At the end of the protocol we collected blood and urine. We measured BP using intra-carotid catheter, and glomerular filtration rate (GFR) using the clearance of inulin. Non-parametric one-way analysis of variance (ANOVA) was used for comparison. p-value significant when <0.05.
Results: See Table.

BP lowering and renal actions of MANP

SHRs parameters	MANP 300 pmol/kg/min	MANP 100 pmol/kg/min	Saline 0.9%	p-value
ΔMAP mmHg	29±4	16±5	8±7	0.001
UcGMPV pmol/min	190±61	46±20	23±6	<0.0001
GFR ml/min	3±1	1.7±0.4	1.8±0.3	0.004
UNaV uEq/min	1.7±0.4	1.3±0.5	0.8±0.5	0.06
DFRNa %	97±1	97±0.6	99±2	0.06

Values are mean±SD. ΔMAP is the difference in blood pressure between the beginning and end of the drug infusion.

Conclusions: MANP significantly reduced BP through GC-A activation as demonstrated by the marked increase in urinary cGMP excretion (UcGMPV). Importantly, despite the reduction in BP, MANP increased GFR and showed a trend for increase in natriuresis (UNaV) with a reduction of distal fractional sodium reabsorption (DFRNa) in the treated group. These results support MANP as BP lowering and renal enhancing therapeutic peptide. Further studies are needed to evaluate the long-term effects of MANP in hypertension.

5077 | BEDSIDE
Impact of a custom-made mandibular repositioning device (MRD) on blood pressure in obstructive sleep apnea (OSA) patients noncompliant with continuous positive airway pressure (CPAP)

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Background: Prevalence of arterial hypertension (HTN) is high in pts with Obstructive Sleep Apnea (OSA). Guidelines recommend Mandibular Repositioning Devices (MRD) as first-line treatment in mild-to-moderate OSA and second-line therapy for OSA pts noncompliant with continuous positive airway pressure (CPAP). MRD treatment may improve blood pressure in OSA pts with HTN.
Purpose: ORCADES, a French prospective multicenter cohort study is evaluating the long-term effects of a custom-made MRD in OSA pts who refused or did not tolerate CPAP. Interim data are presented at 3-month follow-up.

Methods: Eligible OSA pts have been fitted with a CAD/CAM MRD. Objective sleep data (polygraphy or polysomnography), clinical symptoms, arterial blood pressure (BP), quality of life and side effects are evaluated at baseline and during follow-up (FU) visits. MRD treatment success is defined by a reduction of 50% or more in Apnoea-Hypopnoea Index (AHI) from baseline. Patient was hypertensive (HTN) if office systolic and/or diastolic BP were respectively ≥140 and ≥90 mmHg.
Results: 77 HTN and 222 nonHTN pts treated with MRD were analysed. Sex ratio (75% male), age (53±11y) and AHI (29±15/h) were similar in both groups. In HTN group, body mass index was higher and nadir SpO2 was lower. Therapy success was higher in non-HTN group (84% vs. 66%, p=0.0012). Improvement in oxygen saturation, sleepiness or quality of life was equivalent in both groups with no weight change. In HTN group, SBP and DBP were reduced significantly (see table) and BP was normalized in 59% of pts. SBP decrease was correlated with mean SpO2 improvement (ρ=–0.30, p=0.022). Only 8% of pts stopped MRD due to side effects and mean usage was similar in both groups (6.7 hours/night).

Evolution of BP under MRD therapy

Group	BP	Baseline	3 month FU	Δ	P
HTN	SBP, mmHg	140.3±7.8	133.3±12.0	–7.6±12.7*	<0.0001
Non-HTN	SBP, mmHg	122.3±9.0	123.5±13.2	1.5±12.8	NS
HTN	DBP, mmHg	88.6±8.0	81.8±9.1	–6.8±10.2*	<0.0001
Non-HTN	DBP, mmHg	74.1±7.6	75.4±9.7	1.5±10.4	NS

HTN, arterial hypertension; Non-HTN, no arterial hypertension; DBP, diastolic blood pressure; SBP, systolic blood pressure. *p<0.0001 vs. non-AHTN.

Conclusion: Custom-made CAD/CAM MRD is effective in OSA pts noncompliant with CPAP with additional benefits on blood pressure.
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5078 | BEDSIDE
Lack of evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people

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Background: Treatment of hypertension with antihypertensive medication has been shown to reduce stroke, cardiovascular events and mortality in those aged 80 and over, but there is concern that such treatment may not be appropriate in frailer individuals. To investigate whether there is an interaction between the effect of treatment for hypertension and frailty in older adults, we calculated a frailty index for all available participants from the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placebo controlled study of antihypertensives in people with hypertension aged 80 and over, and obtained frailty adjusted estimates of the effect of treatment with antihypertensive medication on risk of stroke, cardiovascular events and mortality.
Methods and findings: Participants in HYVET were randomised 1:1 to active treatment with indapamide sustained release (SR) 1.5mg +/– perindopril 2–4mg or to matching placebo. The FI was calculated at entry, based on fifty seven potential deficits. The distribution of FI was similar to that seen in population studies of adults age 80 years and over (median FI=0.17; IQR 0.11–0.24). Cox regression was used to assess the impact of FI at entry to the study on subsequent risk of stroke, total mortality and cardiovascular events. Models were stratified by region of recruitment and adjusted for age at entry and sex. Extending these models to include a term for a possible interaction between treatment for hypertension and FI provided a formula for the treatment effect as a function of FI. For all three models the point estimates of the hazard ratios for the treatment effect decreases as FI increases, although to varying degrees and with varying certainty.
Conclusions: We found no evidence of an interaction between effect of treatment for hypertension and frailty as measured by the FI. Both the frailer and the fitter older adults with hypertension appeared to gain from treatment.
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5079 | BEDSIDE
Effect of a short term antihypertensive treatment on retinal arterioles evaluated with adaptive optics camera

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Objectives: Antihypertensive treatment Long-term administration can correct retina arteriolar remodeling. A recently developed adaptive optics (AO) fundus camera enables high reproducible repeated measurements of retinal arteriolar morphology. Our objective was to assess arteriolar changes after a short-term antihypertensive treatment prescription.
Methods: Two groups of non-diabetic hypertensive patients were included. Group 1 consisted in treated or untreated subjects with uncontrolled blood pressure (BP) and group 2: treated subjects with controlled BP. In group 1, ARB or Calcium antagonist was added to the prescription and subjects with Systolic BP (SBP) decrease >10 mmHg were followed-up. Wall thickness (WT) and lumen diameter (LD) were measured directly using the RTX1® AO camera and a semi-automated analysis software. They were used to calculate Wall-to-Lumen Ratio (WLR) and Wall Cross Sectional Area (WCSA). AO examination was performed by the same trained orthoptist on the same arteriolar branch and at the same distance from the optical disk at baseline and after one month.
Results: We included 30 patients in group 1 and 20 in group 2 (50±13 years, 57% men). In group 1, BP and WLR significantly dropped when LD increased. No changes were observed in group 2. Univariate analysis showed significant regression between WLR and SBP absolute decrease (R^2=0.18, p=0.01).

Table 1

	Group 1		Group 2	
	Baseline	1 month follow up	Baseline	1 month follow up
Systolic BP, mmHg	154.8±4.9	128.6±4.9‡	120.8±5.1	119.4±5.3
Diastolic BP, mmHg	87.6±71.2	76±2.8	71.2±3.3	71.9±3.0
WLR	0.329±0.012	0.294±0.01†	0.312±0.013	0.301±0.01
Lumen diameter, μm	73.09±2.51	76.5±2.37*	76.36±2.59	77.03±2.45
Wall thickness, μm	23.8±0.99	22.08±1.12*	23.99±1.02	23.12±1.16
Wall cross sectionnal area, μm^2	3206±222	3100±224	3379±229	3292±232

Data are expressed as mean ± SD. BP, blood pressure. *p<0.05, †p<0.01, ‡p<0.001 between baseline and follow-up with bilateral Wilcoxon test on matched pairs.

Conclusion: AO can visualize retinal arteriolar morphology short-term modifications. Although WLR reduction could be ascribed to eutrophic remodeling, the observed LD increase without change in WCSA suggests a short-term effect of antihypertensive treatment on arteriolar tonus.

5080 | BEDSIDE
Effect of allopurinol on serum uric acid and endothelial function in patients with essential arterial hypertension optimally treated

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Background: Serum uric acid (SUA) is involved in cardiovascular (CV) disorders and the hypouricemic agent allopurinol (ALLO) has proven effective in improving endothelial dysfunction (ED), a major contributor to the development and progression of arterial hypertension (AH). The effect of ALLO on ED in relationship with the severity of AH has not been well studied.
Purpose: The aim of the study was to analyse: 1) the relationship between SUA, ED and CV risk and 2) the effect of ALLO on SUA and ED in relation to the severity of AH in patients (pts) with essential AH optimally treated.
Methods: The study group consisted of 103 pts (mean age 62±14 years; 52% men) with essential AH (grade 2–28%, grade 3–66%), optimally treated (average blood pressure on 24 hour ambulatory monitoring 136.57±13.80/83.89±10.04 mmHg). We determined for all pts target organ damage (heart, peripheral arteries, kidney, brain), endothelial function by flow-mediated vasodilation (FMD) using two-dimensional vascular ultrasound of the brachial artery and SUA level. ALLO 300 mg/day was randomly administered in 46 pts, regardless of the SUA level (ALLO+ group). SUA level and FMD were reassessed in all pts (ALLO+/ ALLO- groups) after one month (mo) and after 3 mo.
Results: SUA level (mg/dl) was 5.62±1.96 in ALLO+ and 5.18±1.73 in ALLO- (p=0.6) and correlated with: the number of risk factors-r=0.34 (p=0.0004), the total CV risk category (low, moderate, high, very high)-r=0.32 (p=0.001), the total CV risk calculated by SCORE model-r=0.32 (p=0.001), target organ damage-r=0.35 (p=0.0003), left ventricular mass- r=0.32 (p=0.0022) and FMD-r=–0.61 (p=0.044). In ALLO+ SUA (mg/dl) significantly decreased after one mo to 3.3±1.4 (p<0.0001) and remained low after 3 mo: 3.63±0.79 (p=0.14). In ALLO- SUA had no significant change after 1 mo: 5.3±1.7 (p=0.94) or after 3 mo: 5.54±1.47 (p=0.64). ED was significantly improved in all pts in ALLO+, FMD (%) increasing after 1 mo from 8.98±4.53 to 9.42±4.40 (p<0.0001) and reaching 10.91±4.01after 3 mo (p<0.0001). In ALLO- FMD (%) did not change significantly from 10.60±4.79 at baseline to 10.73±4.77 after 1 mo (p=0.09) and 10.64±4.21 after 3 mo (p=0.43). The improvement of ED in ALLO+ was more important than in ALLO- in pts with high (p=0.0011) and very high risk (p<0.0001). FMD variation did not correlate with SUA variation after 1 mo-r=–0.20 (p=0.22), or after 3 mo-r=0.075 (p=0.66).
Conclusions: 1) SUA levels correlate with ED, CV risk and target organ damage in AH and 2) ALLO improves ED, even more important as the CV risk is higher, independent of lowering SUA level.

5081 | SPOTLIGHT
Effects of angiotensin-II receptor blocker or calcium channel blocker on abdominal aortic aneurysm growth at presurgical stage

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Introduction: Patients with smaller-size abdominal aortic aneurysm (smAAA) receive no survival benefit by surgical intervention, thus, smAAA patients at presurgical stage are followed by medical therapy mainly with anti-hypertensives. How-

ever, it is unknown what type of drugs can effectively delay the enlargement of smAAA. Preclinical studies suggest that angiotensin II induces aortic aneurysm formation that is inhibited by angiotensin-II receptor blocker (ARB). In a small cohort study, ARB slowed the rate of aortic-root dilation in young patients with Marfan's syndrome. Thus, ARB may be useful to slow down the enlargement of smAAA. We, thus, examined the effects of ARB, candesartan, on the growth rate of smAAA in comparison with a common anti-hypertensive drug, amlodipine, a calcium channel blocker.
Methods: In this randomized, multicenter and prospective study (UMIN #2216), patients with presurgical smAAA (n=128) and inoperative AAA (n=4) (mean AAA diameter, 3.9±0.7 mm) were assigned to either candesartan (n=67, CAN) or amlodipine (n=64, AML) group with 5 minimization factors (statin use, smoking, age, gender, renal function). Primary endpoint was the % changes in AAA diameter at 24 mo of the follow-up measured by plain multislice computed tomography and its difference between the two groups was evaluated based on the mixed-effect model repeated measure. Secondary endpoint was the incidence of time to surgical repair that was compared using multivariate Cox regression analysis by intention to treat.
Results: There was no statistical difference in the blood pressure time course between the CAN and AML (p=0.800) groups. The % change at 24 mo of AAA diameter did not differ between the CAN and AML groups [8.4% for CAN (95% CI, 6.23 to 10.59%) and 6.5% for AML (95% CI, 3.65 to 9.43%) and the difference of 1.87% (95% CI, −1.22 to 4.95%; p=0.233)]. The hazard ratio for surgical repair of the AML arm relative to those CAN was 2.615 (95% CI, 0.721 to 9.492; p=0.144). The use of b-blocker had no additional effects on smAAA growth and incidence of surgery.
Conclusion: Candesartan and amlodipine had comparable efficacies on both blood pressure and the growth rate of smAAA size.

5082 | BENCH
Chronic treatment with orally active angiotensin-(1-7) formulation decrease oxidative damage and improve hemodynamic parameters in spontaneously hypertensive rats

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Background: Renin-angiotensin (RAS) system has been implicated in the pathogenesis of cardiovascular diseases. The cardioprotective Angiotensin-(1–7)/Mas axis has an important role in cardiovascular regulation once that Ang-(1–7) exerts beneficial effects mainly due to antihypertensive and antioxidative properties. Furthermore, low levels of Ang-(1–7) have been evidenced in cardiovascular diseases mainly associated with changes in blood pressure (BP) such as in hypertension. Oxidative stress, characterized by increased reactive oxygen (ROS) production, seems to be an important mechanism in hypertension and due to this antioxidative interventions have shown some cardiovascular benefits.
Purpose: To assess the effect of a chronic treatment with orally active formulation of Angiotensin-(1–7) (HPβCD/Ang-(1–7)) in cardiac oxidative stress and hemodynamic parameters in SHR.
Methods: Male spontaneously hypertensive rats (SHR) (15 weeks) treated by gavage with tap water (C) or HPβCD/Ang-(1–7) (A) (30 ug/kg), once a day for 10 weeks (n=8/group). After treatment systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and heart rate (HR) were recorded from a femural catheter (Windaq/2Hz). At the end of hemodynamic measurements hearts were collected for biochemical assays: cardiac lipid peroxidation by chemiluminescence (CL) initiated by t-BOOH, superoxide dismutase (SOD) antioxidant enzyme activity and superoxide anion (O2-) analysis.
Results: Chronic treatment with the orally active Ang-(1–7) reduces SAP, DAP, MAP, HR in treated group (in C and A respectively; SAP=216,2±5,09 and 195,4±4,15, DAP= 147±1,90 and 134,6±3,17, MAP=180,2±3,48, and 162±3,18mmHg, HR=353,5±9,95 and 299,9±6,54 bpm; $P<0.05$). Oxidative damage was decreased in Ang-(1–7) treated SHR (CL=4870±968 and 1693±622,7 cps/mg protein; O2-= 9,48±0,40 and 5,40±0,43 mmoles/mg $P<0.05$). Regard to SOD antioxidant enzyme activity there were no significant differences related to Ang-(1–7) chronic treatment (SOD=19,29±0,67 and 18,33±1,42 U/mg protein; $P<0.05$)
Conclusion: Our results show that the oral treatment with Ang-(1–7) was able to improve relevant cardiovascular parameters which are altered in hypertension, such oxidative damage and arterial pressure values, improving cardiac function and oxidative metabolism and reinforce the pharmacological potential of orally active Ang-(1–7) in hypertension therapy.

5083 | BEDSIDE
The influence of antihypertensive therapy with amlodipine and telmisartan on serum adiponectin level in the metabolic syndrome

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Background: The central obesity and arterial hypertension (AH) are associated with the basic pathogenetic mechanism of metabolic syndrome (MS) - insulin resistance (IR). Adiponectin - the adipose tissue hormone plays an important role in blood preassure (BP) regulation and AH and IR pathogenesis in MS.
Purpose: To find out the influence of antihypertensive therapy in MS patients with AH on the adiponectin level.
Methods: 65 persons included in the study were divided into two groups: the main group - 40 patients (15 men and 25 women) with AH and MS, mean age 50,7±4,7 years, and the control group - 25 healthy people (11 men and 14 women), mean age - 43,7±7,2 years. The main group was randomized into two subgroups: 20 patients of the first subgroup were treated by angiotensin II receptor blocker telmisartan (40–80 mg per day) and 20 patients of the second subgroup – by calcium-channel blocker amlodipine (5–10 mg per day) during 12 weeks. The anthropometrical measurements, biochemical blood analyses, fasting serum insulin and leptin levels estimations (by the enzyme-linked immunosorbent assay) were carried out in both groups before and after the therapy. IR index was evaluated by Homeostasis Model Assessment 2 (HOMA2) calculator.
Results: The statistically significant decrease of systolic BP (SBP) and diastolic BP (DBP) was observed in both subgroups: ΔSBP= - 18,35±8,9 mmHg and ΔDBP = –6,95±5,1 mmHg in telmisartan group and ΔSBP= - 23,65±9,6 mmHg and ΔDBP = - 5,35±3,9 mmHg in amlodipine group ($p<0,001$). The mean baseline adiponectin levels were reliably lower in both subgroups compared to control group (13,9±2,9 ng/ml and 17,25±4, ng/ml, $p<0,001$). There was revealed the increase of its levels in both groups, but just in telmisartan subgroup these changes were statistically reliable (Δ=+16,66±6,8 ng/ml, $p<0,001$ and Δ=+3,47±1,94 ng/ml, $p>0,05$ for telmisartan and amlodipine, respectively). IR-HOMA2 that was significantly increased in both subgroups at baseline also reliably decreased after treatment only in the first subgroup (Δ IR-HOMA2 = –0,73±1,25, p=0,017).
Conclusions: The antihypertensive therapy with telmisartan leads to IR-HOMA2 decrease and serum adiponectin level increase that can demonstrate the pathogenetic effects of telmisartan in MS, while amlodipine doesn't influence significantly those parameters.

5084 | BEDSIDE
Predicting prognosis in patients with hypertensive left ventricular hypertrophy during thirteen years

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Introduction: Left ventricular hypertrophy in hypertensive patients predicts cardiovascular morbidity and mortality. It is important to find out which of other non-invasive parameters are the best predictors for bad outcome in these patients.
Purpose: The aim of the study was to examine the correlation between non-invasive parameters and outcomes in patients with essential arterial hypertension (AH) and left ventricular hypertrophy (LVH) during the thirteen years of follow-up. Patients used regular medicament therapy according to the European guidelines during the period of follow-up.
Methods: 104 patients were examined (55.3±8.4 years; 61 male and 43 female) with AH and LVH. All patients were examined by means of echocardiography (two independent examiners - Acuson-Sequoia), exercise testing, 24-h Holter monitoring, 24-h ambulatory blood pressure monitoring, heart rate variability and QTc interval dispersion.
Results: Average left ventricular mass index (LVMI) was 170.8±32.1 g/m^2 and duration of hypertension was 12.5±7.7 years. During the thirteen years period of follow-up in 33 (31.7%) patients occurred cardiovascular and cerebrovascular adverse events (AE). At the beginning of the study patients with AE had greater: LVMI (188.9±37.9 g/m^2 vs. 162.4±25.1 g/m^2; $p<0.001$), left ventricular mass (362.0±85.6 g vs. 321.3±64.0 g; $p<0.02$), septum thickness (14.3±2.9 mm vs. 13.2±2.0 mm; $p<0.05$), posterior wall thickness (12.1±1.2 mm vs. 11.6±1.0 mm; $p<0.05$) and left atrial diameter (41.4±6.0 mm vs. 39.0±4.5 mm; p=0.05). In patients with AE QTc dispersion was greater than in patients without AE (72.5±20.5 ms vs. 53.8±19.2 ms; $p<0.001$). AE occurred in 21 (55.3%) of 38 patients with QTc dispersion greater than 65 ms and in 12 (18.2%) of 66 patients with QTc dispersion lower than 65 ms (odds ratio 2.66; 95% CI 1.63 to 4.33). Patients with AE had frequent premature ventricular beats per hours ($p<0.05$) in 24-hours holter monitoring. Using multiple linear regression analysis the best predictors of worse prognosis were QTc dispersion and LVMI (standardized coefficient beta: for QTc dispersion 0.381; $p<0.0001$ and for LVMI 0.351; $p<0.0001$ and for the model: R=0.534, R^2 = 0.285, adjusted R^2 = 0.271, standard error of the estimate = 0.40252; $p<0.0001$).
Conclusions: Patients with greater QTc dispersion, especially greater than 65 ms, and greater left ventricular mass index have worse outcome during the thirteen years in spite of regular medical treatment.

ACUTE INTENSIVE CARDIOVASCULAR CARE

5085 | BEDSIDE
Direct comparison of the safety and efficacy of two rule-out strategies for AMI: combination of 1h-algorithm and undetectable levels at presentation versus 2h-accelerated diagnostic protocol

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Purpose: Addressing the increasingly recognized, yet unmet clinical need for rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) T at presentation) in combination with hs-cTnT 1h-algorithm versus 2h-ADP rule-out strategy (0h and 2h levels≤99th percentile, no significant ECG changes and TIMI Score of ≤1).
Methods: In a prospective international multicentre diagnostic study enrolling 1697 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: LOD <5ng/l; 1h algorithm: 0h<12ng/l and Δ0–1h<3ng/l and 99th percentile =14ng/l; hs-cTnI Abbott: LOD<2ng/l; 1h-algorithm 0h <5ng/L and Δ0–1h<2ng/l; 99th percentile=26.2ng/l) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial ECG, STEMI patients were excluded from the analysis.
Results: Acute myocardial infarction was the final diagnosis in 16% of patients. The safety was very high and comparable with both algorithms (LOD+1h-Algorithm NPV 99.9%, 95% CI 99.5–100% versus 2h ADP: NPV 100%, 95% CI 99.4–100% p=ns). Regarding efficacy, 1h-algorithm +LOD allowed rule-out in 60%of patients versus 38% with 2h ADP (p<0.001). Using hs-cTnI, the safety was very high and comparable with both algorithms (LOD+1h-Algorithm NPV 99.4%, 95% CI 98.6–99.9% versus 2h ADP: NPV 100%, 95% CI 99.3–100% p=ns). Regarding efficacy 1h-algorithm +LOD allowed rule-out in 53%of patients versus 38% with 2h ADP (p<0.001).
Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI. However the combination of LOD+1h-algorithm has a significantly higher efficacy allowing the rule out of more than double of patients and has the obvious advantage of allowing rule-out already after 1h and without the need of TIMI Score calculation.

5086 | BEDSIDE
Inaccurate treatment and poor outcome in patients with ACS and atypical symptoms

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Purpose: We explored clinical characteristics and outcome associated with atypical chest pain (CP) in patients with diagnosis of ACS.
Methods: Data of 8947 patients (32.4% women) from the International Survey of Acute Coronary Syndrome in Transitional Country (ISACS-TC) were reviewed in our comprehensive coordinating center. Only patients with admission and discharge diagnosis of ACS were considered.
Results: There were 778 patients with atypical CP for the index event. These patients were significantly (p<0.001) older than those with typical CP (68 vs. 63 years) and they were more likely to be female (41.3% vs. 31.6%). More frequently (p<0.01), they had history of diabetes (33.2% vs. 25.6%) and hypertension (73.7% vs. 68.6%), but less smoking (21.7% vs. 35.6%) and hypercholesterolemia (39.2% vs 43.6%). Peripheral artery disease (5.3% vs. 3.1%), chronic kidney disease (11.9% vs. 5.6%) and history of stroke (10.7% vs 4.7%) were more frequently (p<0.001) in patients without then with typical CP. Moreover, a greater number (p<0.001) of patients without typical CP compare to those with typical CP had a delay >12 hrs to arrive to hospital; absence of typical CP doubled the probability (OR: 2.18; CI: 1.89–2.55) to late hospital presentation. Interestingly, patients without typical CP were significantly more likely to exhibit signs of heart faliure (42.8% vs. 22.1%), although they less frequently had STEMI as index even. In-hospital mortality rate was in the overall cohort 8.2% (STEMI: 9.1%, NSTEMI: 8.8%, UA: 2.1%). Yet, the mortality was significantly greater for patients with atypical CP (STEMI: 19.8%, NSTEMI: 19.3%) than for those with typical CP (STEMI: 6.7%, NSTEMI: 7.1%). It should be noted, however, that patients with atypical CP were less likely (p<0.001) to receive medications (aspirin 90.4% vs. 96.2%; beta-blockers 66.9% vs. 78.9%) and invasive procedures (21% vs. 47.6%) than patients with typical CP.
Conclusions: ACS without typical CP is not a rare experience and it is associated many co-morbidity and poor outcome, both in women and men. Strategies to avoid underestimation of atypical symptoms represent potential opportunities for improving the outcome of these patients.

5087 | BEDSIDE
A comparison of biomarkers and risk scores on risk stratification for patients with acute coronary syndrome

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Background: Accurate and efficient risk stratification for patients with acute coronary syndrome (ACS) remains a significant problem. Validated risk scores including Global Registry of Acute Coronary Events [GRACE], Thrombolysis In Myocardial Infarction [TIMI], and the Platelet IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy [PURSUIT]) have two significant problems. One is these algorisms are complicated, and second is that these algorithms were established before the drug-eluting stent era, which has dramatically improved the prognosis in patients with ACS. Few investigations have compared the usefulness of multiple biomarkers and these risk scores for predicting the risk of cardiovascular events.
Methods: This study is a prospective, multicenter, observational study of patients with ACS (n=562, 66.9±12.1 years old, 76% male) admitted to hospitals in Japan from 2010 to 2013, inclusive. We measured N-terminal pro B-type natriuretic peptide (NT-proBNP), high sensitive troponin T (hsTnT), high sensitive C-reactive protein (hsCRP) and heart-fatty acid binding protein (H-FABP), respectively. We calculated the validated risk scores simultaneously. The primary end point was death from cardiovascular events during one year of follow-up. We excluded persons who had serum creatinine levels greater than 2.0 mg/dL. Area under the receiver operator characteristic curve (AUC) and net reclassification improvement were used to compare incremental contributions of each marker.
Results: During the follow-up period, 31 participants (5.5%) died from cardiovascular events. In analyses adjusting for conventional risk markers, NT-proBNP, H-FABP levels, and GRACE score were significantly associated with the incidence of cardiovascular death (odds ratio [OR]); 2.23, (95% confidence interval [C.I.]), 1.24 to 4.03, OR; 2.92, C.I.; 1.44 to 5.90, and OR; 1.02, C.I.; 1.01 to 1.02; p<0.01, respectively). The AUC of NT-pro BNP, H-FABP levels, and GRACE score were 0.76 (0.66–0.88), 0.73 (0.62–0.85) and 0.79 (0.68–0.90), respectively. The combination of NT-pro BNP and H-FABP improved the AUC to 0.80 (0.67–0.83).Adding NT-pro BNP and H-FABP to GRACE improved the area under the curve from 0.80 to 0.84 (p<0.01).
Conclusions: For assessing risk in ACS patients, the GRACE score is still a useful risk score for ACS patients even in the drug eluting stent era. Measuring NT-pro BNP and H-FABP provides useful prognostic information equal to the GRACE risk score. Biomarkers result in a high reclassification rate in the ACS cohort, demonstrating the benefit of prognostic value.
Acknowledgement/Funding: Grant-in-Aid for Scientific Research

5088 | BEDSIDE
Kinetics of high-sensitive cardiac troponin T and I differ in patients with ST-segment elevation myocardial infarction treated by primary coronary intervention

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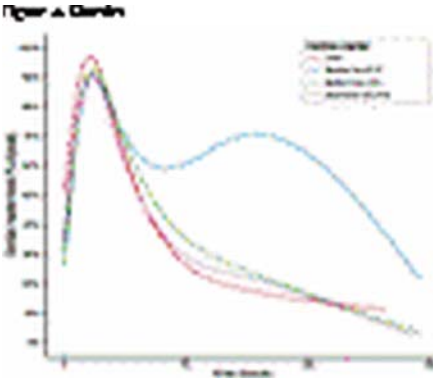
Purpose: Cardiac biomarkers including troponins are the cornerstone of the biological definition of acute myocardial infarction (AMI). New high-sensitive cardiac troponin T (hs-cTnT) as well as I (hs-cTnI) raises concerns because of their unclear kinetics following the peak.
Aims: This study aims to compare kinetics of creatine kinases (CK), hs-cTnT and hs-cTnI in patients with AMI treated by percutaneous coronary intervention (PCI).
Methods: We prospectively studied 106 consecutive patients admitted in our institution for AMI and treated with PCI. We evaluated for all the patients simultaneously kinetics of CK, hs-cTnT (Roche) and two different hs-cTnI (Abbott and Siemens). Modelling of kinetics was realized using mixed effects with cubic splines.
Results: Kinetics of markers showed a first peak at 10.7h (8.0–12.0) for CK, 11.8h (10.4–13.3) for hs-cTnT (Roche); 11.8h (10.7–11.8) for cTnI from Abbott and 10.2h (8.7–11.6) for cTnI from Siemens, respectively. This peak was followed by a nearly log linear decrease for cTnI and CK by contrast to hs-cTnT which appeared with a biphasic shape curve marked by a second peak at 76.9h (69.5–82.8). The analysis of the decrease in percentage of the peak value showed at 77h that hs-cTnT follows a twice lower decrease than other markers.
Conclusion: Kinetics of hs-cTnT and hs-TnI differ significantly with a linear decrease regarding the hs-cTnI contrasting with a biphasic shape curve for hs-cTnT.



This is of importance for clinical management of patients in routine settings especially follow-up after AMI including the suspicion of reinfarction.

5089 | BEDSIDE
Epidemiology of cardiogenic shock in French reanimations: incidence, etiologies, outcome and evolution on 15 years (a report from the CubRea database)

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Rationale: Most of data reporting epidemiology of CS concern patients with acute myocardial infarction admitted in intensive care unit of cardiology (ICUC). However, CS patients managed in Reanimation have often multiorgan failure and seem to have different characteristics and outcome.
Aim: The aim of study is to analyse incidence, etiologies, outcome and evolution on 15 years of CS managed in reanimation in the French hospital setting.
Methods and results: We queried the 1997–2012 database of Parisian area intensive-care units (ICUs)-the CubRea (Intensive Care Database User Group) database to identify all hospital stays with a principal or an associated diagnosis of CS (National classification of disease R 570). The evolution of CS was studied dividing the study period in 4: 1997–2000, 2001–2004, 2005–2008 and 2009–2012.
Among 303 314 hospital stays, 17 494 (5.8%) were CS. The patients were managed in 60% of cases in universitary centers. Mean age of patients was 64.3±17.0. Men accounted for 11047 (63.1%) hospital stays. Mean IGS II was 62.0±24.3. Among CS, only 535 (3.06%) were acute myocardial infarctions whereas 2685 (15.3%) were cardiac arrests and 858 (4.9%) were drug intoxications.
Mechanical ventilation was required in 12967 (74.1%) of cases, inotropic drugs in 14640 (83.7%) of cases and renal support in 3886 (22.2%) of cases.
Mean duration of hospital was 19.1 days ± 24.7.
Intrahospital Mortality was high (46.2%). In multivariate analysis, older age, high IGS II, cardiac arrest, drug intoxications were independent correlates of increased intrahospital mortality whereas study period, management in universitary center, use of inotropic drugs, mechanical ventilation and hemodialysis were associated with decreased mortality.
Over the 15-year period, mortality decreased (49.8% in 1997–2000, 49.1% in 2001–2004, 45.4% in 2005–2008 and 42.7% in 2009–2012, $p<0.001$) whereas the patients were more critically ill (IGS II 58.8±25.4 in 1997–2000 vs 64.2 8±23.6 in 2009–2012, $p<0.001$)). The management changed: more patient received hemodialysis whereas the use of inotropic drugs decreased.
Conclusion: It is the first study reporting the prevalence, determinants and prognostic factors of cardiogenic shock patients managed in reanimation. The etiologies of these patients are different from those of ICUC patients. These patients are very critically ill, need often hemodynamic and ventilator supports and their mortality is high. However over the 15-year period, even if these patients are more and more critically ill, early mortality decreased.

5090 | BEDSIDE
Iron metabolism in acute myocardial infarction complicated by cardiogenic shock - a biomarker substudy of the IABP-SHOCK II-trial

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Background: Catalytic iron (CI) is free iron with the potential to generate reactive oxygen species with further deleterious vascular effects. In acute coronary syndrome high levels of CI were linked to all-cause mortality. In cardiogenic shock (CS) no data exists on the prognostic impact of CI and further iron metabolism.
Methods: In 185 patients, blood samples collected at baseline and after two days were analyzed. Immediately after sample drawing, the blood was centrifuged and the serum frozen (–87° C). CI levels were measured using a modified bleomycin detectable iron assay. Furthermore levels of free hemoglobin (fHb), total serum iron (SI), transferrin (TF), total iron binding capacity (TIBC), ferritin and transferrin saturation (TS) were assessed.
Results: As shown in table 1 significant different levels between survivors and non-survivors at 30 days for CI, TF, TIBC and TS were observed. Patients with CI levels in the highest quartile had a worse outcome in Kaplan-Meier-analysis (Day 1: HR 1.91 [1.11–3.31], p=0.005; Day 3: HR 2.15 [1.06–4.34], p=0.01). After multivariable adjustment baseline CI remained an independent predictor of 30-day mortality (HR per 10LOG 2.08 [1.25–3.47], p=0.005) together with age, development of acute kidney injury and bleeding events on days 1 and 2. Predictors of CI levels on day 3 were baseline CI, bleeding events, acute kidney injury and baseline troponin T.

Table 1

	Day 1			Day 3		
30 day-	survivors	non-survivors	P	survivors	non-survivors	P
CI	0.37 (0.30; 0.58)	0.48 (0.35; 1.18)	0.007	0.35 (0.30; 0.41)	0.41 (0.32; 0.74)	0.01
SI	74 (65; 86)	71 (63; 83)	0.26	71 (61; 81)	67 (61; 75)	0.14
fHb	4.4 (2.8; 10.3)	6.6 (2.8; 22.1)	0.07	3.7 (1.7; 7.2)	4.4 (2.7; 11.0)	0.11
Ferritin	194 (68; 487)	350 (152; 655)	0.04	238 (117; 443)	351 (202; 552)	0.12
TF	176 (140; 212)	143 (90; 184)	<0.001	152 (114; 200)	104 (79; 133)	<0.001
TIBC	241 (192; 292)	196 (123; 245)	<0.001	208 (149; 275)	143 (109; 183)	<0.001
TS	32 (24; 41)	40 (30; 53)	<0.001	33 (27; 44)	44 (36; 71)	<0.001

Conclusions: Increasing CI levels were associated with increased short-term mortality in CS complicating acute myocardial infarction. Rise of CI at day 3 is associated with bleeding, acute kidney injury and myocardial injury.

5091 | BEDSIDE
Blood hyperosmolarity and mortality in patients after an acute coronary syndrome: how does dehydration affect prognosis?

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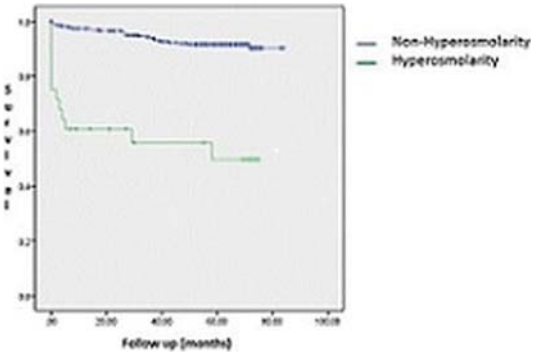
Background: Electrolyte and osmolarity disturbances are common in patients admitted for acute coronary síndrome (ACS). Blood hyperosmolarity development and its influence on the prognosis of these patients has not yet been studied. The aim of the study was to assess how dehydration affects outcomes of patients after ACS.
Methods: We created a registry of consecutive patients admitted due to ACS in Acute Care Unit (ACU) of our hospital for 18 months. Peak blood osmolarity value during hospitalization was retrospectively obtained in these patients.
Results: Of a total of 397 patients with ACS, third suffered ST-elevation ACS. The mean age was 65.2 years, 77,1% were men, 56.8% and 12.3% of patients were diagnosed with previous kidney failure. During long term follow up 88 patients died (22%). Total population was divided into two strata according to peak osmolarity during hospitalization: peak osmolarity <290mM/l (94%) (normal range 260–290mM/l) and>290 mM/l (6%). In-hospital mortality, all-cause mortality and cardiovascular (CV) mortality after a follow-up of 52±24 months, were significantly higher in patients with peak osmolarity>290 mM/l ($p<0.001$). In an univariate analysis it was strongly associated with diuretic use and development of renal failure. After adjusting for potential confounders (age, sex, history of renal insufficiency, renal failure development, diuretic therapy or need for renal replacement therapy), blood hyperosmolarity during hospitalization (>290mm/l) remained an independent predictor of all-cause, CV and in-hospital mortality at short and long term.



Conclusion: Hyperosmolarity is an independent predictor of all-cause and CV mortality after four years of an ACS. We might pay more attention to excessive water loss and be cautious with diuretic therapy.

5092 | BEDSIDE

Urinary output predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery

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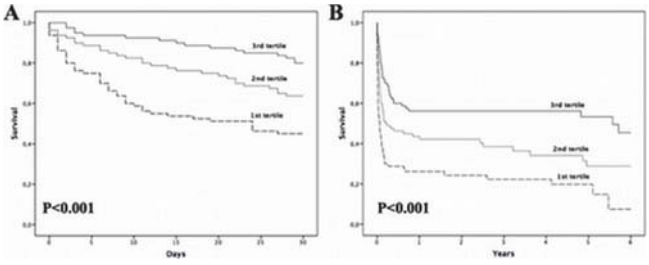
Background: An optimized risk evaluation in patients undergoing extracorporeal membrane oxygenation (ECMO) support may have important implications both for evaluating further therapeutic strategies and clinical judgment of prognosis. We therefore analyzed the prognostic significance of urinary output (UO) within 24-hour after ECMO initiation on mortality in adult patients undergoing veno-arterial ECMO support following cardiovascular surgery. We further aimed to refine established risk prediction models by implementation of UO.
Methods: We prospectively included 240 patients undergoing veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center into our registry.
Results: In the univariable Cox regression analysis 24hour urinary output was the strongest predictor of outcome among renal function parameters with a HR per 1-SD of 0.55 (95% CI 0.42- 0.71;P<0.001) for 30-day mortality and for long-term mortality with a HR per 1-SD of 0.63 (95% CI 0.53- 0.76; P<0.001). UO lead to a substantial improvement in the C-statistic of the SAPS3 score for 30 day mortality (SAPS3: 0.52 vs. SAPS3 & UO: 0.64; P=0.003) and for long-term mortality (SAPS3: 0.54 vs. SAPS3 & UO: 0.63; P=0.01). An improvement in individual risk stratification with combined assessment of SAPS3 score and UO was confirmed by a significant improvement of the NRI with 44% for 30-day mortality (P=0.001) and 46% for long-term mortality (P<0.001) compared with the SAPS3 score alone.



Kaplan-Meier analysis by tertiles of UO

Conclusion: We identified UO as a strong and easily available predictor of mortality in patients undergoing ECMO therapy following cardiovascular surgery.

5093 | BEDSIDE

Clinical impact of delirium and antipsychotic therapy on patients admitted to the coronary care unit

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Purpose: The impact of delirium on patients admitted to the coronary care unit (CCU) has not been well characterized. Moreover, the safety of short-term antipsychotic therapy remains controversial. This study aimed to evaluate (1) the association between delirium and mortality (2) the association between antipsychotic therapy and a prolonged QTc interval and ventricular arrhythmia.
Methods: A pre-study Confusion Assessment Method (CAM)–ICU criteria was implemented in screening 11,097 consecutive patients admitted to a referral CCU from 2004 to 2013. Death status was prospectively ascertained.
Results: The incidence of delirium was 8.5%. Delirium increased the risk of in-hospital (adjusted OR 1.45, 95% CI 1.06–2.01; P=0.02) and 1-year mortality (adjusted HR 1.46, 95% CI 1.13–1.88; P=0.01). A total of 792 doses of haloperidol (5 [3–10] mg/day) or quetiapine (25 [13–150] mg/day) were given in 244 patients with delirium. Clinical characteristics of delirium patients who did or did not receive antipsychotics were not different (baseline QTc interval 460±61 ms vs. 457±58 ms, respectively; P=0.57). In comparison to baseline, mean QTc intervals after first dose and third dose of antipsychotics were not significantly prolonged in haloperidol (445±44, 458±57 and 450±50 ms, respectively) or quetiapine groups (459±54, 467±68 and 462±46 ms, respectively) (P>0.05 for all). Additionally, in-hospital mortality (adjusted OR 0.67, 95% CI 0.42–1.04; P=0.07) and ventricular arrhythmia (adjusted OR 0.87, 95% CI 0.17–3.62; P=0.85) were not different in delirium patients irrespective of whether they received antipsychotics or not.
Conclusions: CCU delirium was associated with an increase in both in-hospital and 1-year mortality. Low dose of haloperidol and quetiapine appeared to be safe without side effects on prolonged QTc intervals or sudden cardiac death in carefully monitored patients.

5094 | BEDSIDE

The impact of multidisciplinary team approach with critical care specialist and cardiologist co-management style on the clinical outcomes of cardiac intensive care unit patients

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Background: There is increased complexity of patients' care in intensive care units that has motivated the involvement of critical care trained physicians as a part of multidisciplinary approach in medical, surgical and neurological ICUs. Multidisciplinary care has been less common in cardiac care units (CCUs).
Purpose: To determine whether a multidisciplinary team approach with a critical care specialists and cardiologist co-management style will impact the clinical outcomes of CCU patients.
Methods: A formal protocol was implemented starting July 2012 in a hospital whereby a medical intensivist integrated with the multidisciplinary team. This team included a cardiologist, a medical intensivist, a cardiology fellow, internal medicine residents and interns, ICU nurses, ICU pharmacist and respiratory therapists. Responsibilities were delineated in a fashion such that the intensivist primarily managed non-cardiac issues, deferring primary cardiologic issues to the cardiologist. Patients were divided to low, intermediate and high risk depending on their mortality risk based on APACHE III score.
Results: 2475 patients were included with 916 patients admitted in the 12 months before and 1516 admitted in the 12 months after intervention. Patients admitted after the intervention had a higher morbidity rate expressed by a higher mean APACHE III (56.26 vs. 53.87; P<0.001), SAPS II (44.49 vs. 41.49; P<0.001). Results showed that the implementation of the intensivist multidisciplinary team model was associated with a significant decrease in both CCU Mortality (3.52 vs. 5.85%; odds ratio OR=0.59; 95% CI (0.39–0.88); P=0.01) and in-hospital mortality (4.37 vs. 11.13%; OR=0.37; 95% CI (0.26–0.52); P<0.0001). Furthermore; there was also a significant reduction in both CICU length of stay (LOS) (2.46±3 vs. 2.84±3 days; P=0.006), hospital LOS (7.03±4.5 vs. 7.53±4.5 days; P=0.006) and days on ventilation for intubated patients (1.96±1 vs. 4.32±2.8; P=0.0001). The reduction in mortality and LOS was noticed mainly in intermediate and high risk patients, while the reduction in days on ventilation was seen in all subgroups.
Conclusion: The implementation of a multidisciplinary team approach where an intensivist and cardiologist co-manage the critical care of CCU patients is associated with reduced ICU and in-hospital mortality, ICU and in-hospital LOS and duration of mechanical ventilation

DIABETES MANAGEMENT: THE WAY TO CONTROL ATHEROSCLEROSIS

5123 | BENCH

Fresh fruit consumption in relation to mortality and incidence of vascular events among 26,000 individuals with diabetes: a 7-year prospective study

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Purpose: Although consumption of fruit is generally recommended in various health guidelines for patients with diabetes, concerns persist among both patients and healthcare professionals about the potential health risk posed by the relatively high levels of sugar contained in fruit. To date, there is little direct evidence about the associations of fresh fruit consumption with mortality and incidence of macro- and micro-vascular complications among people diabetes.
Methods: We analysed prospective data of 26,162 individuals with diabetes (about a half each for self-reported and screen-detected), but free of cardiovascular disease and cancer, who were enrolled into the China Kadoorie Biobank (CKB) Study from 10 diverse localities across China. During ~7 years of follow-up, there were 2453 deaths, 7291 incident vascular events, and 956 microvascular complications (i.e retinopathy, neuropathy and nephropathy) identified through linkages with mortality and morbidity registries as well as with hospital records. Cox proportional hazard models were used to yield adjusted hazards ratios (HRs) relating habitual fresh fruit consumption to disease risks, with adjustment for potential confounders including anti-diabetic treatment.
Results: The overall mean age of study participants was 57 years and 28% reported consuming fresh fruit on most days (regular consumers) and 12% never/rarely (non-consumers). The percentage of non-consumers in self-reported diabetes was ~3 times that in those with screen-detected diabetes. Fruit consumption was inversely associated with mortality, with the adjusted HRs for regular versus non-consumers as 0.69 (95% CI 0.62–0.77), 0.76 (0.64–0.90), and 0.45 (0.33–0.61) for all-cause mortality, CVD mortality, mortality from diabetes per se. The associations with incident vascular events, CVD, and microvascular complications were also significant, HRs being 0.88, 0.84, and 0.62 respec-

tively (Figure). All these observed associations were slightly stronger in those with screen-detected diabetes.
Conclusions: In Chinese adults with diabetes, higher consumption of fresh fruit was associated with lower risks of early death and incidence of macro- and microcardiovascular complications, suggesting fresh fruit consumption should be promoted universally irrespective of diabetic status.

5124 | BEDSIDE
The different impact of different statins on insulin resistance in Asian population: a propensity score matched analysis

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Objectives: There are limited data regarding impact of statin on the insulin resistance. The present study aimed to investigate the influence of statin and compare the difference from different statins on insulin resistance which was denoted by homeostasis model assessment (HOMA-IR).
Methods: A total of 5041 cardiovascular patients (pts) were enrolled and followed up for 5.04±1.64 years, among which 1500 pts were not treated with statin. The other 3541 were prescribed with lovastatin (66), fluvastatin (136), pravastatin (553), pitavastatin (274), rosuvastatin (456), simvastatin (1005) and atorvastatin (1051). The HOMA-IR were compared with repeated general linear model in propensity score matched cohort between statin group and non-statin group, and different statin groups as well.
Results: HOMA-IR increased significantly by 0.66±2.53 in non-statin group, and 0.87±4.46 in statin group ($p<0.001$). Compared to non-statin group, statin group has significantly higher increase ($p=0.023$, Fig 1). Dissimilar effect showed in different statin group ($p=0.003$). Among them, rosuvastatin was associated with significant elevation in HOMA-IR ($p<0.001$) compared to non-statin group (Fig 2).

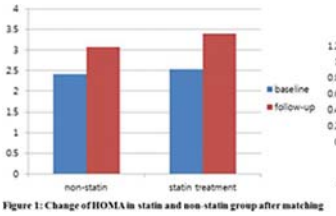

Figure 1: Change of HOMA in statin and non-statin group after matching

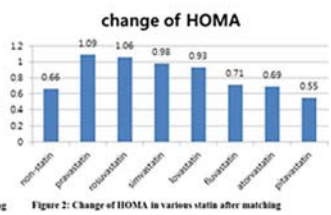

Figure 2: Change of HOMA in various statin after matching

Conclusions: Statin treatment was associated with worsening of insulin resistance, and the impact of rosuvastatin was significantly profound on HOMA-IR among different statins.

5125 | BEDSIDE
Insulin and acute myocardial infarction in diabetic patients with chronic kidney disease and end-stage renal disease undergoing dialysis: a national cohort study

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Introduction: Diabetes and chronic kidney disease (CKD) are a high-stakes combination for cardiovascular disease. Patients with decreased kidney function (CKD stage 3 to 5) and end-stage renal disease (ESRD) have increased risk of hypoglycemia when attaining HbA1c less than 7%, leading to elevated odds of myocardial infarction (MI). For these patients, what anti-diabetic drugs could be associated with higher risk of MI is not clear.
Methods: We identified patients from a nation-wide database called Registry for Catastrophic Illness, which encompassed almost 100% of the patients receiving dialysis therapy in Taiwan from 1995 to 2008. Patients with diabetes and CKD stage 3 to 5 and progressing to ESRD were selected as the study cohort. Propensity score adjustment and Cox's proportional hazards regression model were used to estimate hazard ratios (HRs) for MI.
Results: Among 15,161 patients, 39% received insulin, 40% received sulfonylureas, 18% received meglitinides and 3% received thiazolidinedione (TZD). After a median follow-up of 1,357 days, the incidence of myocardial infarction was significant increased in patients taking sulfonylureas (HR = 1.523, 95% confidence interval [CI] = 1.331–1.744), meglitinides (HR= 1.251, 95% CI = 1.048–1.494) and TZD (HR=1.515, 95% CI = 1.071–2.145) when treated patients receiving insulin as reference. The risk of MI remains higher in other three groups in subgroup analyses.
Conclusions: Among diabetic patients with decreased kidney function, the use of sulfonylureas, meglitinides and TZD are associated with higher risk of MI when compared with insulin.

LEADS EXTRACTION

5145 | BEDSIDE
Major transvenous lead extraction complications - occurrence and outcomes. An analysis of 1767 procedures

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Device-assisted transvenous lead extraction (TLE) may result in cardiac and vascular tears and other complications with different degree of severity. Immediate cardio-surgical (C-S) intervention may solve the problem The aim of the study: Analysis of appearance and management effect of major TLE complications (MC). Retrospective analysis of our 8-year TLE data-base.
Methods: Using conventional mechanical systems we have extracted 2963 leads in 1767 pts. Mean dwell implant time was 85,1 months. In 28 (1,6%) MC were noted. Results are presented in the table.
Cardiac tamponade determined 70% of MC. Other MC were less frequent. Pericardiocenthesis with drainage was effective in 40% cases only. In 60% C-S intervention was necessary. Positive outcome was achieved in every TLE procedure performed in C-S operating room. Delayed intervention resulted in 60% periprocedural mortality. Cardiac tamponade appeared more frequently during RAA lead extraction (15/1049=1,1%) than RVA (4/1405=0,3%).

Major complications (28/1767 = 1,58%)			Good outcome		Fatal outcome	
Hemopericardium - cardiac surgery	13	46,4%	7	26,9%	6	17,8%
Hemoperic - pericardiocenthesis - effective drainage	9	32,1%	9	32,1%	0	0,0%
Hemothorax - pleural drainage	1	3,6%	1	3,6%	0	0,0%
Hemothorax - thoracic surgery	1	3,6%	1	3,6%	0	0,0%
Brain embolia - stroke - rehabilitation	1	3,6%	1	3,6%	0	0,0%
Gradual decrease of contractility and delayed death (no structural damage)	1	3,6%	0	0,0%	1	3,6%
Fenoral arteria damage - vascular surgery	1	3,6%	1	3,6%	0	0,0%
Pulmonary embolism - cardiac surgery	1	3,6%	0	0,0%	1	3,6%
All patients wit major complications	28	100,0%	20	71,4%	8	24,9%

Cardiac tamponade: lead location & management					TLE in operating theathre		TLE in EPS laboratory		
Fatal lead location	No	%	Dreine ge only	Open chest cardiac surgery	Operatin g c.surg. room	Good c. surgery outcome	EPS Laboprat ory	Good c. surgery outcome	Death
RAA	15	68%	8	7	3	3	4	1	2
RVA	4	18%	1	3	1	1	2	1	2
CS/CSO	3	14%	0	3	0	0	3	1	2
All	22	100%	9	13	4	4	9	3	6
Important percentage			41%	59%		100%		33%	66%

Results

Conclusions: 1. Cardiac tamponade is the most frequent major TLE complication. 2. TLE is much more safe if performed in cardiac surgery operating theatre with trained cardiac surgeon presence. 3. Old RAA leads seem to generate higher risk of tamponade than RVA leads. 4. Use of conventional mechanical systems determines lower freqeuncy of vascular tears comparing with other reports.

5146 | BEDSIDE
Chronic venous obstruction during cardiac device revision: incidence, predictors and efficacy of percutaneous techniques

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Purpose: In the last few years upgrading and revision procedures became increasingly frequent and challenging procedures due probably to a dramatic increase in pacemaker and impiantable cardioverter defibrillator (ICD) implantation. Some degree of venous stenosis is relatively frequent and may represent a serious obstacle to a successful procedure. Aim of our study was to evaluate incidence of venous obstruction after chronic transvenous system implantation, to identify its predictors and to evaluate efficacy and safety of percutaneous techniques to overcome stenosis itself.
Methods: We considered 177 consecutive patients admitted for system revision due to device upgrading (76%), lead malfunction (23%) or infection (1%) between January 2004 and July 2014. All patients underwent ipsilateral contrast venography. Venous obstruction was classified as significant stenosis (>75%), sub-occlusion or total occlusion.
Results: Venous obstruction was found in 38 (21,4%) patients: 7,9% as complete occlusion, 7,3% as near occlusion and 6,2% as significant stenosis (>75%). We found as predictors of venous stenosis the number of existing lead, in particular 3 (p=0,04) and 4 (p=0,03) existing leads, a previous cardiac resynchronization therapy with defibrillator (CRT-D) system (p=0,004) implanted and a previous cardiac surgery. All procedures were successful. Different techniques were performed to obtain venous access: 8 percutaneous transluminal vein angioplasty, 19 distal venous puncture, far from the stenosis and one lead extraction with laser technology. In 10 cases there weren't any difficulties to advance cardiac leads according to standard methods. Transluminal vein angioplasty was performed both in complete and near occlusion, with a 6x40 mm balloon, inflated at 8–10 atm for 5–10 minutes; no complications occurred during procedures and electrical parametres of existing leads remained stable after procedure and during follow up-period.
Conclusions: Venous obstruction is a relatively frequent finding during cardiac device revision;the number of existing leads, devices complexity and previous cardiac surgery have emerged as predictors of stenosis. Percutaneous techniques, like transluminal vein angioplasty and distal venous puncture, are safe and effective approach, allowing ipsilateral transvenous lead placement.

5147 | BEDSIDE

Cardiac device infections- survival after transvenous leads extractions procedure

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Background: Cardiac device infections (CDI) are divided into infections of the generator pocket (PI) and lead-dependent infective endocarditis (LDIE)/Transvenous leads extraction (TLE) is a key procedure in patients with CDI. Survival after TLE in this population was rarely analyzed up to now.
Methods: Comparative analysis of clinical data of 1426 patients underwent TLE in single Center in years 2006–2013 due to CDI (619 pts) and noninfectious indications (NI-807pts) was conducted. Mean five years survival after TLE was assessed
Results: Patients with CDI were older (67,3±14,2 vs 62.3±17,4 p=0,001),with higher number of the leads (mean 2,1±0,8 vs 1,9±0,8 p=0,0001), especially inactive leads (mean 0,3±0,7 vs 0,2±0,5 p=0,0001), loops of the leads (20,9% vs 17,1% p=0,04) more frequent previous procedures prior to TLE (mean 2,2±1,3 vs 1,7±1,1 p=0,0001) and abrasion of the leads (30,4% vs 20,6% p=0,001). Leads dwell time was longer in NI patients (88,3±65,6 vs 79,4±59,5 p=0,008). Full procedural success and clinical success were comparable (respectvely: 93,7% vs 92,2% p=0,28; 98,4% vs 97,7% p=0,33).
Mean five years survival patients with LDIE was demonstrated on the figure 1.

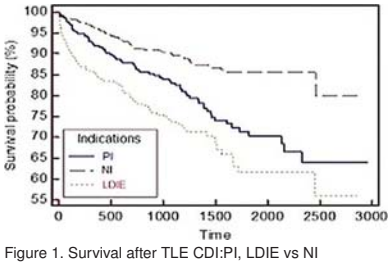

Figure 1. Survival after TLE CDI:PI, LDIE vs NI

Conclusions: Patients underwent TLE due to CDI represented more potential procedural risk factors (older age, higher number of the leads especially inactive leads and loops of the leads). Nevertheless the full procedural and clinical success of TLE was high and comparable to NI group- probably younger age of the leads in CDI patients decided on efficacy of procedures in this patients. Despite the very successful early effect of TLE, the long term five years mortality of CDI patients is very high: 45% for LDIE and 35% for PI in comparison of 20% for NI patients ($p<0,001$).

WHAT IS NEW IN MITRAL VALVE DISEASE

5210 | BEDSIDE

The Relationship Between Mitral Annular Calcification and Red Cell Distribution Width: A Cross Sectional Study

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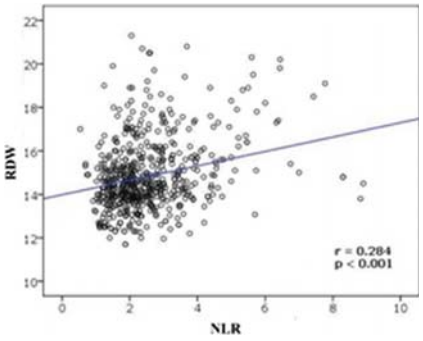
Objectives: Mitral annular calcification (MAC) and atherosclerosis are similar in regard to risk factors and pathogenesis. Increased red blood cell distribution width (RDW) has been shown to be associated with atherosclerotic diseases in previous studies. However, there was no data evaluating the association of MAC with RDW. In this cross sectional study, we aimed to investigate the relationship between the MAC and RDW among patients with various cardiovascular risk factors.



Study design: A total of 623 patients [n=413 MAC(+) group and n=201 control group] who admitted to our cardiology outpatient clinics were enrolled in between March 2014 and November 2014. Demographical, clinical and laboratory parameters of all participants were recorded. RDW were analyzed from complete blood samples in all study participants.
Results: Patients in MAC(+) group showed older age and higher rate of hypertension. The mean RDW value was significiantly higher in MAC(+) group as compared to control group (15.3±1.4% vs. 13.9±1.4%, $p<0.001$). In Pearson correlation analysis, there was a statistically significant and positive correlation between the neutrophil-lymphocyte ratio and RDW ($r=0.284$, $p<0.001$). In multivariate logistic regression analysis, age (OR: 1.04, $p<0.001$), hypertension (OR: 1.54, p=0.036), RDW (OR: 2.63, $p<0.001$) and mean platelet volume (OR: 1.19, p=0.046) were found as the independent predictors of MAC.
Conclusion: Our results showed that RDW levels were significantly increased in patients with MAC and RDW was found as the independent predictor for the presence of MAC. Therefore, increased RDW can be used as a marker of the continuing inflammatory process in patients with MAC.

5211 | BEDSIDE

The pan-inflammatory process may cause mitral valve deterioration in systemic autoimmune disorder patients: a transthoracic echocardiography study

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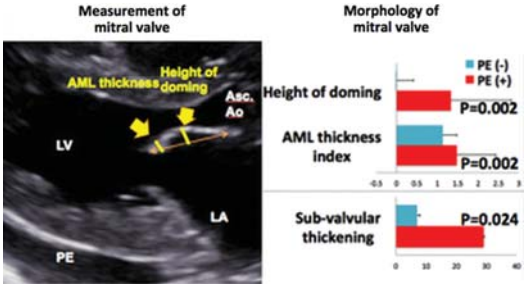
Background: Pericardial effusion (PE) occurs frequently in patients with systemic autoimmune disorder (SAD), and suggests a pan-inflammatory process.
Purpose: We evaluated the relationship between deterioration of the mitral valve and PE in SAD patients using transthoracic echocardiogram (TTE).
Methods: Seventy-five SAD patients (53 female; mean age, 53±11 years; systemic lupus erythematosus, 23%; vasculitis, 23%; scleroderma, 12%, polymyositis/dermatomyositis complex 10%, mixed connective tissue disease 9%, rheumatoid arthritis 3%, and polyarteritis nodosa 1%) underwent TTE (Vivid E9, GE Healthcare or iE33, Philips). We analyzed mitral leaflet motion and leaflet thickening by measuring the height of doming and anterior mitral leaflet (AML) thickness in addition to presence of significant PE. Furthermore, we qualitatively evaluated mitral valve calcification and sub-valvular thickening. AML thickness index was calculated as the ratio of AML thickness to that of the posterior aortic wall.
Results: Seventeen patients (23%) had PE. Four patients (5%) had moderate mitral regurgitation (MR) (2 with PE and 2 without PE). Patients with PE showed significantly greater height of doming of the AML (1.33±1.49 mm vs. −0.003±0.96 mm, p=0.002), AML thickness index (1.47±0.42 vs. 1.13±0.35, p=0.002), and frequency of sub-valvular thickening (29% vs. 7%, p=0.024) than patients without PE. There were no significant differences in the frequency of MR and serum c react-ive protein between patients with or without PE.



Measurement and morphology of MV

Conclusions: Mitral valve and sub-valvular deterioration were frequently detected in SAD patients with PE. The pan-inflammatory process may affect mitral valve and sub-valvular deterioration simultaneously, and careful follow up of these findings using TTE should be considered.

5212 | BEDSIDE

Appropriation of current recommendations for the optimal timing of surgery in patients with degenerative severe mitral regurgitation

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Background: In patients with severe degenerative mitral regurgitation (MR), current international guidelines recommend mitral valve surgery whenever patients become symptomatic (class I), develop LV dysfunction (class I), experience atrial fibrillation (AFib, class IIa) or exhibit pulmonary hypertension (PHT, class IIa). The aim of the present study was to evaluate the appropriateness of these recommendations using both natural history and postoperative data from a large prospective registry.
Methods: Between 1990 and 2005, 527 consecutive patients (mean age 66±14 years) with severe degenerative MR diagnosed by echocardiography were in-

cluded into this registry. Ten-year overall survival was assessed using the Kaplan Meier method in subgroups with and without operative triggers, i.e. symptoms, LV dysfunction, Afib and PHT. Natural history was assessed by censoring patients at the time of surgery. Postoperative survival was analyzed starting on the day of surgery.
Results: Survival in the absence of surgery (natural history) was better in the absence of these operative triggers: Symptoms (42% vs 3%, p<0.001); PHT (29% vs 9%, p=0.005) and Afib (44% vs 8%), p<0.001), in those without LV dysfunction, the survial is not significantly different (p=0.838). Similarly, postoperative survival was better in patients without all these triggers: Symptoms (84% vs 55%, p<0.001); PHT (75% vs 55%, p=0.001); Afib (80% vs 54%, p<0.001) and LV dysfunction, (74% vs 60%, p<0.0357).
Conclusion: In patients with severe degenerative MR, long-term survival is less in patients presenting with guidelines triggers for surgery. This suggests that current guidelines criteria are not appropriate to decide on the optimal timing of surgery and that correction of MR should be proposed before the onset of these triggers.

5213 | BEDSIDE
Evolution of functional mitral regurgitation and prognosis in medically managed heart failure patients with reduced ejection fraction

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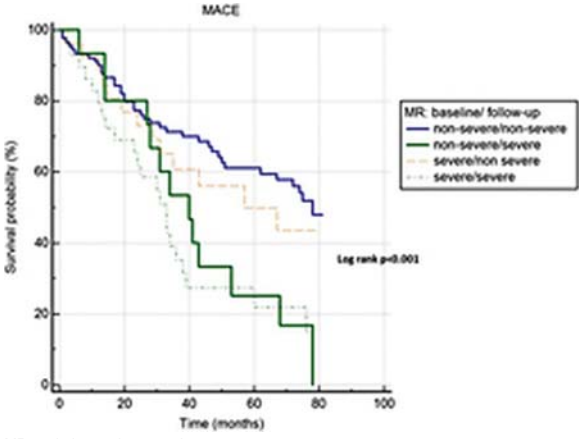
Background: Functional mitral regurgitation (FMR) in heart failure patients (pts) with reduced ejection fraction (HFrEF) is associated with a worse prognosis. It is uncertain to what extent medical management may alter the severity of FMR and its prognosis.
Methods: The extent of FMR was assessed at baseline and during an average follow-up of 43±25 months in 164 consecutive HFrEF pts (LVEF<40%) from the HF outpatient clinic between 2007 and 2014. Severe FMR was defined as MR grade 3–4 based on a validated integrative method. All patients received maximal tolerable HF medication. Major adverse cardiac event (MACE) was defined as a composite of cardiac death, need for heart transplantation or hospitalisation for heart failure and/or malignant arrhythmia's.
Results: A total of 57 (35%) pts showed severe MR and had a baseline risk profile comparable to HF pts without severe MR except for slightly worse EF (27% vs 30%,p=0.05). During follow-up, 46% of the severe FMR pts showed improvement to non-severe FMR (MR grade<3) whereas 14% of non-severe FMR pts developed severe FMR despite optimal HF treatment. Deterioration of FMR was associated with a poor outcome comparable with the outcome of pts with sustained severe FMR (MACE 86% vs 77%, adjusted HR 1.2 (95% CI 0.6–2.7)) whereas outcome of improved FMR was as good as with sustained non-severe FMR. (50% vs 45%, adjusted HR 1.4 (95% CI 0.7–2.7)) (see figure)



MR evolution and prognosis

Conclusion: Severe FMR is present in more than one third of patients with HFrEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.

5214 | BEDSIDE
Differential impact of mitral valve surgery on outcome of coronary artery bypass grafting with or without surgical ventricular reconstruction in the surgical treatment for ischemic heart failure trial

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Background: Mitral regurgitation (MR) increases mortality in patients with ischaemic heart disease, yet the benefit of adding mitral valve surgery (MVS) in those with significant MR undergoing surgical revascularisation remains unclear.
Purpose: We examined the impact of MVS on survival of patients with moderate or greater MR at baseline randomised to coronary artery bypass grafting (CABG) versus CABG+surgical ventricular reconstruction (SVR) in the STICH trial.
Methods and results: Among 867 patients with echocardiography core lab assessment of baseline MR severity, 211 had moderate or greater MR. Within this group, 50, 50, 62, and 49 patients underwent CABG, CABG+MVS, CABG+SVR, and CABG+SVR+MVS respectively. MR severity was numerically graded (0=≤trivial MR, 1=mild, 2=moderate, 3=moderate-severe, 4=severe). Cox model survival analyses were performed to assess the impact of MVS, adjusted for prognostic clinical variables and factors related to whether MVS was performed. Patients who underwent only CABG had a higher 4-year mortality rate of 46%, compared with 23% in CABG+MVS patients (adjusted hazard ratio [HR] 0.48, 95% confidence interval [CI] 0.15–1.58). In contrast, both the CABG+SVR and the CABG+SVR+MVS groups had a 4-year mortality of 40% (adjusted HR 0.84, 95% CI 0.39–1.80), similar to that of CABG alone. A significant interaction between MVS and randomised treatment arms was found, as MVS had a more favourable effect on survival in CABG patients than those receiving CABG+SVR (p=0.007). Baseline MR severity was similar between CABG+MVS and CABG+SVR+MVS patients (mean MR grade 2.8±0.8 vs. 2.7±0.8, p=0.435). At 4-month follow-up, there was no difference in MR grade between the 2 groups (1.1±0.9 vs. 1.1±0.8, p=0.887). At 2-year follow-up, however, CABG+MVS patients had significantly less MR than those who underwent CABG+SVR+MVS (0.7±1.0 vs. 1.2±1.0, p=0.045), with a larger reduction in MR grade between 4-month and 2-year follow-up among patients who received CABG+MVS (0.5±0.7 vs. 0.0±1.3, p=0.0308 after adjusting for the 4-month MR grade).
Conclusion: In patients with moderate or greater MR requiring surgical revascularisation, MVS had a more favourable effect on survival in patients undergoing CABG than those who received CABG+SVR, suggesting that the addition of SVR may potentially negate the anticipated benefit of MVS. This may be related to a different pattern of changes in MR over time after MVS between patients in the CABG and CABG+SVR treatment arms.
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5215 | BEDSIDE
The EVEREST II REALISM Continued Access study - 1 year outcomes in patients with primary mitral regurgitation

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Background and introduction: The EVEREST II REALISM Continued Access study (REALISM) is a prospective, multi-center, continued access study to collect data on the real-world use of the MitraClip device in both high risk (HR) and non-high surgical risk (NHR) patients.
Purpose: To describe the complete 1-year safety and effectiveness results in both HR and NHR patients with primary (degenerative) mitral regurgitation (MR).
Methods: REALISM patients had 3+ or 4+ degenerative mitral regurgitation. HR was defined as predicted by a STS risk calculator operative mortality of ≥12%, or surgeon assessment based on pre-specified HR factors. Outcome measures included NYHA functional class, quality of life measures (SF-36), and echocardiographic measurements by an independent core lab.
Results: A total of 374 primary MR patients (HR n=189; NHR n=185) were treated with the MitraClip device in the REALISM study. HR patients were older (HR 83±9 years; NHR 75±12 years) and had a higher incidence of baseline comorbidities compared to NHR patients, including coronary artery disease, congestive heart failure, moderate to severe renal disease, diabetes, prior myocardial infarction and prior cardiovascular surgery. HR patients were more symptomatic with 79% of patients being in NYHA functional class III/IV at baseline compared to 50% of NHR patients.
Despite these baseline differences, a large proportion of HR (82%) and NHR (78%) patients achieved and maintained MR reduction to ≤2+ at 1 year, accompanied by reductions in left ventricular end diastolic volumes (HR –19±25 ml; NHR

–15±24 ml). The proportion of patients in NYHA Class I/II at 1 year improved significantly regardless of risk status (HR 90%; NHR 92%). Scores for the physical and mental components of the SF-36 improved in both groups between baseline and 1 year. The overall rates of major adverse events at 1 year were comparable between the two risk groups (HR 28%; NHR 24%) while survival at 1 year was higher in NHR patients (HR 80%; NHR 92%).
Conclusions: One-year results from the REALISM study in a real-world patient population demonstrate that despite significant differences in baseline surgical risk status due to co-morbidities and age, primary MR patients achieve a significant reduction in MR and derive clinical benefit following percutaneous treatment with the MitraClip device, demonstrating the importance of this therapeutic option for select primary MR patients.
Acknowledgement/Funding: Study sponsored by Abbott Vascular

5216 | BEDSIDE
Successful MitraClip implantation beyond EVEREST II criteria and German consensus recommendations

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Aims: MitraClip (MC) implantation has been established as a therapeutic option for patients with severe mitral regurgitation and high surgical risk. Regarding patient selection actual recommendations are guided by the implantation criteria of the EVEREST II trial or the newer consensus recommendations of the focus group of the German Society of Cardiology (DGK recommendations). This study aimed to investigate the appropriability of these criteria in a real world scenario to predict the acute implantation success and the long-term outcome in order to select patients more precise for MC procedure.
Methods and results: Consecutive 251 symptomatic patients with moderate to severe or severe mitral regurgitation (MR) and high surgical risk received MC implantation in our heart center. Mitral valve morphology was evaluated by transthoracic and transesophageal echocardiography based on the EVEREST II criteria and DGK recommendations. At least one exclusion criteria of EVEREST II was met in 86% of patients: mostly LVEF $<$25% and/or LVESD $>$55 mm. According to DGK recommendations, in 28% of patients unsuitable valve morphology was considered. Carpentier IIIa morphology was the main reason for unfavorable structure in 20% of all patients. Nevertheless, implantation success rate was high (98%, 245 of 251 patients) and procedure success (residual MR-grade $\leq$2+ with successful clip implantation) was 90% (227 patients). The EVEREST II criterion, mitral valve orifice area (MVOA) $\leq$4.0cm^2 (11.6%, 29/251 patients) was the significant predictor of post-procedural mitral stenosis (transmitral mean pressure gradient $\geq$5mmHg) (OR 3.41, 95% confidence interval 1.53–7.57, P=0.003). In DGK recommendations, severe calcification in the grasping area (8.4%, 21/251) was the significant predictor of residual MR-grade $>$2+ (OR 3.47, 95% confidence interval 1.15–10.5, P=0.028) and had a predictive power of worse 2-year-outcome (HR 2.90, 95% confidence interval 1.55–5.42, P=0.001).
Conclusion: Beside exclusion criteria in the EVEREST II criteria or unsuitable valve morphology in DGK recommendations, MC was successfully implanted in 98% of patients and 90% of patients were successfully treated. We have to pay special attention to patients with MVOA $\leq$4.0cm^2 or severe calcification in the grasping area to avoid MS or residual MR after procedure. We believe that this report may help people to select the eligible patients beyond the criteria or recommendations.

5217 | BEDSIDE
Transcatheter mitral valve implantation in high-risk patients

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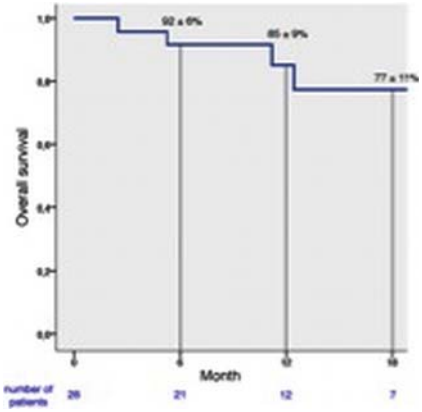
Background: Redo mitral surgery may be high risk or contraindicated. We evaluated mid-term results of transfemoral transcatheter mitral valve implantation (TMVI) in failed bioprostheses (BP) and ring annuloplasties (RA).
Methods: Transfemoral implantation of Edwards Sapien XT prosthesis was performed in 31 patients for degenerated mitral BP (n=13) or previous RA (n=18) between 2011 and 2015. Mean age was 61±24 years, all patients were in NYHA class $\geq$III, with a high surgical risk (EuroSCORE 38±26%). The cause of mitral failure was regurgitation in 14 patients, stenosis in 14 and both in 3.
Results: Procedure was unsuccessful in 5 patients (16%): 1 procedural death and 1 THV migration during rescue procedures on patients with ECMO, 1 conversion to surgery, 1 need for a second prosthesis and 1 moderate paraprosthetic regurgitation.
In the 17 patients with stenotic BP or RA, mean gradient decreased from 14±5mmHg to 8±3mmHg (p$<$0.0001), whereas all but 1 patient had mitral regurgitation $\leq$2/4 after the procedure.
During hospitalization, 3 patients died (1 rupture of inferior vena cava, 1 infective endocarditis and 1 urgent surgery for perforation of the aorta). Among the 28 patients discharged alive, 6 died during a mean FU of 13 months, mostly from cardiac cause (3 sudden death, 2 heart failure). The 18-months survival rate in these patients was 77±11% (Figure).
At last FU among survivors, 21 patients were in NYHA I-II, and only 1 in NYHA III due to a periprosthetic MR 3/4. This inoperable patient benefited from a successful valve-in-valve-in-valve 38 months after the first THV implantation.



Survival after TMVI

Conclusions: Transfemoral TMVI for deterioration of BP or surgical repair may be performed in high-risk patients and provides good mid-term results.

5218 | BEDSIDE
Initial results of fully percutaneous transcatheter mitral valve implantation for native mitral valve disease in patients with extensive annular calcification

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Background: Extensive mitral annular calcification (MAC) remains a technical challenge and may be associated with complications during mitral valve surgery. Very few cases have been reported showing the feasibility of transcatheter mitral valve implantation (TVMI) in these patients and little evidence exists on TVMI using a fully percutaneous procedure.
Objectives: We aimed to evaluate the acute clinical and hemodynamic results of fully percutaneous TVMI for native mitral valve disease in patients with extensive MAC.
Methods: From 2013 to 2015, 6 patients considered inoperable by the heart team underwent TMVI in our institution. Procedures were performed by venous transseptal approach using the Edwards Sapien XT or Sapien 3 valve. Clinical outcomes were defined according to the VARC-2 criteria.
Results: The mean age was 66±13 years. Patients had severe comorbidities leading to a mean EuroSCORE II of 7.8±4.6. All patients were in NYHA functional class III (2) or IV (4). An Edwards Sapien XT and Sapien 3 valve were used in 5 (83%) and 1 patient (17%), respectively and one-half of patients received a 26-mm and the other-half, a 29-mm valve. One prosthesis was implanted in good position in all patients. Two patients required a second prosthesis implantation due to a malpositioning of the first one. At 30-day, one patient had died due to acute infectious endocarditis and another one required percutaneous closure of a residual atrial septal defect. There was no other intra-hospital complication. The mean transmitral gradient after TVMI was 4.2±0.7mmHg and mild mitral regurgitation occurred in 2 patients (33.3%) and was related to the presence of paravalvular leaks. No patient had moderate or severe mitral regurgitation. TMVI was associated with a significant decrease in pulmonary artery systolic pressures (61±15 vs 50±11mmHg, p=0.026). One patient with severely calcified mitral valve and subvalvular apparatus had a significant obstruction of left ventricular outflow tract with a mean gradient of 45 mmHg.
Conclusions: Fully percutaneous TMVI is feasible in inoperable patients with severe mitral valve disease and MAC and may provide clinical benefits and hemodynamic improvement. However, the risk of peri-procedural complications remains a concern.

5219 | BEDSIDE
Should we reconsider the role of anticoagulation in moderate mitral stenosis?

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Background: According to current guidelines, anticoagulation is indicated in mitral stenosis (MS) patients with atrial fibrillation (AF), a history of embolism or a left atrial thrombus, and should be considered in MS patients with sinus rhythm when dense spontaneous echo contrast or enlarged left atrium (LA) is detected. Routine anticoagulation therapy is still controversial.
Purpose: We determined the natural history of moderate MS, focused on embolic events and all-cause death, and analyzed the association among patient's characteristics.
Methods: We conducted a retrospective study by screening for isolated moderate

MS patients (mitral valve area 1.0–1.5 cm^2 by planimetry and pressure half-time method), who were initially decided not to undergo intervention, from the medical records of ou hospital between the years 1998 and 2010. Patients with severe disability or end-stage disease were excluded.
Results: Among 367 isolated MS patients, 120 patients were eligible. The mean age of all patients was 53.8±11.2 years. The ratio of men to women was about 1:2. 30% of patients presented with or had a history of stroke. 43.3% of patients had sinus rhythm. The mean mitral valve area was not different between patients with sinus rhythm and those with AF (1.21 vs. 1.22 cm^2, p=0.84). Patients with sinus rhythm were younger (49.2 vs. 57.3 years, p<0.01) and had smaller LA (M-mode diameter 44.7 vs. 49.6 mm, p<0.01) than patients with AF. Among patients with sinus rhythm, one third of patients used warfarin and had higher history of stroke (37.5% vs. 4.3%, p<0.01). Two third of patients with sinus rhythm developed AF during follow-up (median duration 3.4 year, IQR 1.8–6.4) and AF development was strongly associated with embolic events (p<0.01). The mean LA diameter by M-mode was not different between patients with sinus rhythm who developed AF and those who did not (45.2 vs. 44.1 cm, p=0.69). The incidence of embolic events and all-cause death was similar between patients with AF with warfarin and patients with sinus rhythm and no warfarin use, while patients with sinus and warfarin use tended to have lower incidence (HR 0.56, 95% CI 0.2–1.3; p=0.06). Embolic events were associated with mortality (HR 2.3, 95% CI 1.2–4.6; p=0.03).
Conclusions: In moderate MS, systemic embolism occurred commonly and was associated with mortality. Patients with sinus rhythm and no warfarin use had a similar prognosis as those with AF and warfarin use had. Regardless of LA diameter, warfarin use in moderate MS with sinus rhythm may be beneficial. Further studies are needed.

BEST POSTERS SESSION 6

BEST POSTERS IN RESYNCHRONISATION THERAPY

P5221 | BEDSIDE
Differentiating the electromechanical substrate responsive to cardiac resynchronisation therapy from non-electrical dyssynchrony substrates by computer-assisted regional strain analysis

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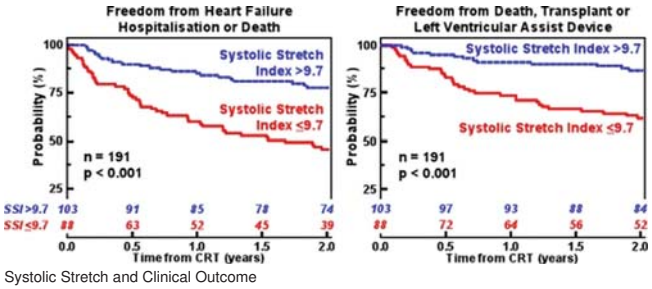
Background: Heterogeneous regional timing of left ventricular (LV) deformation, or mechanical dyssynchrony, is often observed in heart failure (HF) patients regardless of QRS duration.
Purpose: We hypothesized that myocardial substrates for contraction heterogeneity may exist due to electromechanical activation delay, regional differences in contractility, or regional scar, and that we could differentiate the electromechanical dyssynchrony substrates that are responsive to cardiac resynchronization therapy (CRT) from non-electrical substrates unresponsive to CRT.
Methods: We first used CircAdapt computer simulations of LV radial strain to differentiate electromechanical from non-electrical hypocontractility and scar substrates of mechanical dyssynchrony. This analysis led to definition of the novel systolic stretch index (SSI), as the sum of posterolateral systolic pre-stretch and septal systolic rebound stretch. SSI was prospectively quantified by automated echocardiographic radial strain analysis in 191 HF patients (QRS>120ms) treated with CRT.
Results: Patients with baseline SSI>9.7% had significantly fewer HF hospitalizations or deaths over 2 years (figure) (p<0.001, hazard ratio (HR)=3.15, 95% confidence interval (CI)=1.90–5.23), and fewer deaths, transplants or LVADs (p<0.001, HR=3.48, CI: 1.83–6.62), even after adjustment for potential covariates of age, gender and ischemic disease (p<0.05 for both endpoints). SSI was more closely associated with clinical outcome than peak-to-peak radial strain delay or interventricular mechanical delay.



Systolic Stretch and Clinical Outcome

Conclusions: SSI specifically characterized electromechanical substrates responsive to CRT. SSI performed better than currently used dyssynchrony indices at identifying patients with electromechanical substrates who benefitted more favourably from CRT.

P5222 | BEDSIDE
Anatomical and electrical interlead distance predict outcome in cardiac resynchronization therapy patients

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Introduction: Approximately one third of CRT recipients do not respond to the therapy. Procedural strategy may play a pivotal role in obtaining CRT response.
Methods: From the CRT MORE, 216 patients with left bundle branch block and sinus rhythm who received CRT, were included in analysis. At implantation the electrical inter-lead distance (EID), defined as the time interval between spontaneous peak R-waves of the same QRS complex detected at the RV and LV pacing sites, was measured. The anatomical distance between the RV and LV lead was determined on chest X-rays in postero-anterior and lateral views. A positive clinical response was defined as "Improved" Clinical Composite Score at the 6-month follow-up. A positive echocardiographic response was defined as a decrease of at least 15% in left ventricular end-systolic volume (LVESV) at the 6-month follow-up visit in comparison with the baseline visit.
Results: The mean EID was 74±41ms and the mean horizontal corrected interlead distance (HCID) was 125±73mm. After 12 months, 138 (64%) patients were classified as responders according to the echocardiographic criteria and 87 (40%) patients were clinical responders. To investigate the ability of EID and HCID to predict clinical response, receiving operating characteristic curves analysis was performed. Optimal sensitivity and specificity were obtained at a cut off level of 84ms for EID (53% and 67%, respectively) and 90mm for HCID (80% and 48%, respectively). In a multivariable model, only baseline IED and HCID above best cut-off values were independently associated with the occurrence of cardiovascular hospitalization or death (HR [CI] 0.2628 [0.1106, 0.6244], p<0.05 for EID >84ms, HR [CI] 0.3289 [0.1731, 0.6252], p<0.05 for HCID>90mm). At 24 months, the rate of freedom from events was 94% in patients fulfilling both conditions, 88% in patients fulfilling one condition and 71% in patients with both variables below the stated cut off values.
Conclusions: Both anatomical and electrical RV-LV interlead distance are predictors of CRT response. Positioning the LV lead at a site that results in EID>84ms and HCID>90mm seems associated with a very good outcome.

P5223 | BEDSIDE
Good relation between left ventricular electrical activation and contraction in patients undergoing cardiac resynchronization therapy

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Background: Placing the left ventricular (LV) lead in the region of latest electrical activation or the region of latest peak contraction by speckle tracking echocardiography has both been shown to improve response to cardiac resynchronization therapy (CRT). Whether these regions correspond within CRT patients is uncertain. We compared the timing of LV electrical activation and peak contraction in CRT candidates.
Methods: Twenty-eight consecutive CRT candidates underwent standard echocardiographic evaluation before implantation and intra-procedural coronary venous electro-anatomic mapping (EAM) using EnSite NavX. Coronary venous anatomy was classified according to the American Heart Association 17-segment heart model by detailed evaluation of biplane coronary venograms. The electrical activation time of each myocardial segment was calculated as the average of all electrical activation times measured within a segment. The peak contraction time corresponding to each mapped myocardial segment was determined as the time to peak longitudinal strain by speckle tracking analysis. Pearson's correlation coefficient was computed between the electrical activation and peak contraction times observed for each patient. The segments of latest electrical activation and latest peak contraction were determined in each patient.
Results: Successful measurements by both coronary venous EAM and speckle tracking echocardiography allowed analysis in 23 of 28 patients. There was a strong correlation between electrical activation and peak contraction times within each patient (R2 = 0.85±0.09). The slope of the trend line was positive in all patients, indicating that increasing electrical activation time results in increased peak contraction time. However, the slope and hence the magnitude of this relationship varied greatly between patients. The regions of latest electrical activation and latest peak contraction corresponded in 19 of 23 patients (83%) and were adjacent in the other 4 patients.
Conclusion: This study demonstrates that there is a strong positive correlation between the timing of LV electrical activation and peak contraction in patients undergoing CRT. This suggests that a strategy of LV lead placement guided by electrical measurements is equivalent to that guided by speckle tracking echocardiography.

P5224 | BEDSIDE

Metabolic scintigraphy with radiolabeled fatty acid in prognosis of cardiac resynchronization therapy in patients with dilated cardiomyopathy

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Purpose: of the study was to study perfusion and metabolism of the left ventricular (LV) myocardium in patients with idiopathic dilated cardiomyopathy (DCMP) and to identify the scintigraphic predictors of the efficacy of cardiac resynchronization therapy (CRT).
Methods: The study comprised 63 patients with DCMP and NYHA class III-IV chronic heart failure. Before CRT, all patients received scintigraphy with 99mTc-MIBI and with 123I-BMIPP for evaluation of myocardial perfusion and metabolism, respectively. Before CRT and twelve months after, all patients underwent echocardiography study to estimate intracardiac hemodynamics.
Results: Patients were divided into two groups 6 months after CRT: (1) responders - LV ESV decreased by ≥15% (n=39);(2) non-responders - LV ESV decreased by <15% (n=24). Before CRT, LV pumping function didn't significantly differ between groups. Significant differences were found in the following preoperative scintigraphic parameters: myocardial perfusion defect size (9,22±5,06% and 12,5±4,22%, p<0,01) and metabolic defect size (9,21±5,42% and 11,27±5,39%, p<0,01). Correlation analysis demonstrated the presence of significant association (r=0.37, p<0.5) between the sizes of metabolic defect and changes in the values of LV ESV after 12 months the implantation of CRT device. Metabolic scintigraphy showed higher diagnostic efficacy in determination of indications for CRT compared with perfusion scintigraphy (AUC 0.722 and AUC 0.612, respectively). The best metabolic defect size threshold value of 7.35% predicted CRT efficacy with the sensitivity and specificity of 77.8% and 66.7%, respectively. We also made an analytical review of methods for obtaining of radiopharmaceuticals that are based on 99mTc -labeled fatty acids and their use in cardiology. We make conclusion about efficiency of application and investigation of 99mTc fatty acids radiopharmaceuticals that contain chelate groups EDTA or DTPA. In this study, quantum-chemical modeling of one of such conjugate is conducted and its bioavailability is thus confirmed.
Conclusions: The results of myocardial metabolic scintigraphy with 123I-BMIPP may be used as the secondary criteria for selection of patients for CRT and for prediction of the efficacy of this interventional treatment modality in patients with DCMP. 99mTc fatty acids based on chelate groups EDTA or DTPA are the perspective tracers for myocardial metabolism imaging.

BEST POSTERS IN ACUTE CORONARY SYNDROMES

P5226 | BEDSIDE

Troponin positive acute coronary syndrome with unobstructed coronary arteries: improved diagnostic accuracy of early cardiovascular magnetic resonance investigation, and implication for patients

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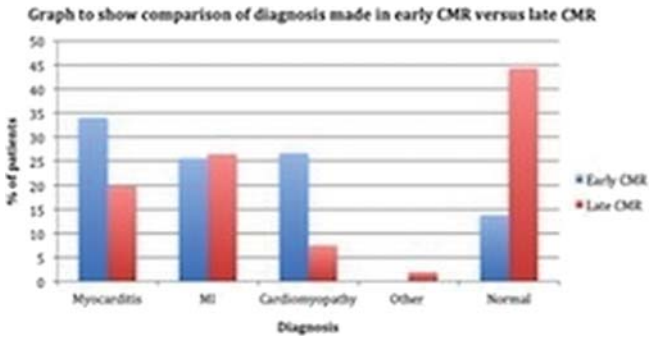
Background: 7–15% of patients with ACS have non-obstructive coronary artery. In these patients Cardiac MRI (CMR) can identify different underlying etiologies, such as myocarditis, myocardial infarction (MI) with spontaneous recanalization/embolus or Tako-Tsubo cardiomyopathy. However the diagnostic pick-up rate of these aetiologies by CMR is highly variable in the literature.
Aim: To improve CMR diagnostic accuracy in patients with troponin positive ACS and unobstructed coronaries by imaging patients early after presentation.
Methods: Registry data on consecutive patients with troponin positive ACS and unobstructed coronaries, referred for a CMR (Sept 2011-Jul 2014). Comprehensive CMR protocol was used.
Results: 204 consecutive patients (mean age 55yrs) were included (51% males).



An "early" CMR (<2weeks from presentation) was performed in 96 patients (median 4 days) and 108 patients underwent a "late" (>2weeks from presentation) CMR scan (median 49 days). Overall, a cause for the troponin rise was found in 70% of patients. The diagnostic pick up rate significantly improved when the scan was done early: 82% vs 54% when CMR performed "late" (p<0.0001). Myocarditis was the most common diagnosis in the early arm (34%) whereas reperfused MI in the late group (26%). Further subgroup analysis revealed a diagnostic pick rate of 87% when the CMR scan done <1week (n=78) from admission (vs 82% when done <2weeks, p=0.40).
Conclusion: In a large cohort of patients with troponin positive ACS and unobstructed coronary arteries CMR was able to establish a final diagnosis in overall 70%. However, the diagnostic value of CMR improves significantly (up to 87%) when carried out within 2 weeks from presentation, with no difference between 1 week and 2 weeks. Accurate diagnosis have a clinical impact on management.

P5227 | BEDSIDE

Dynamic enhancement pattern of unstable coronary plaque: analysis by 320-row area detector computed tomography

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Background: Intraplaque neovascularization is a marker of unstable coronary plaque. We investigated a difference in dynamic enhancement pattern of coronary plaque between stable and unstable angina pectoris, using 320-row area detector computed tomography (CT), which enables whole-heart volumetric acquisition in a single gantry rotation.
Methods: We analysed 106 coronary plaque segments in 33 patients (mean age 69.8±8.3 years, 32 male) with angina pectoris (13 stable, 25 unstable) who underwent coronary CT and percutaneous coronary intervention (PCI). Coronary plaques were evaluated using 320-row area detector CT with and without contrast enhancement. Culprit plaques (PCI target) of unstable patients were defined as unstable plaque, whereas culprit plaques of stable patients and non-culprit plaque were defined as stable plaque. Coronary plaque without contrast enhancement, corresponding to the plaque detected by contrast enhanced CT, was identified using unique calcification as a landmark. The mean Hounsfield unit (HU) in the coronary plaque was measured, and the presence of positive vascular remodeling was evaluated. Coronary artery stenosis was quantified by coronary angiography.
Results: Unstable patients were younger than stable patients (66.6±7.2 vs 76.1±6.7 years, p<0.01). Positive vascular remodeling was more frequently observed in unstable than stable patients (68.0% vs 15.4%, p<0.01). Coronary artery stenosis was not different between the 2 groups. In CT without contrast enhancement, plaque HU was not different between the 2 groups (unstable: 25.0±32.4 vs stable: 24.9±33.1). With contrast enhancement, plaque HU was significantly elevated in both groups from those without contrast enhancement to 53.9±24.1 (unstable: p<0.01) and to 42.6±33.5 (stable: p<0.01). Unstable plaque showed higher enhancement (delta HU) than stable plaque (28.9±23.5 vs 17.7±25.5, p=0.024).
Conclusions: Dynamic enhancement pattern is different between unstable and stable coronary plaque. Compared to stable plaque, unstable plaque shows higher contrast enhancement, suggesting the increased neovascularization in the plaque.

P5228 | BEDSIDE

Age dependent association of body mass index with coronary artery calcification: true or false?

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Background and introduction: Obesity is an increasing problem worldwide and recognized as a major risk factor for cardiovascular disease. On the other hand, a paradoxical protective effect of obesity, known as the "obesity paradox", has been previously reported.
Purpose: The aim of the present study was to investigate whether there is an age dependent association between body mass index (BMI) and coronary calcium score (CCS) in a large outpatient population.
Methods: We included 4.079 consecutive patients, referred for coronary CT-angiography as part of diagnostic work-up. Patients who underwent a CCS scan to determine amount of calcification using the Agatston method and whereby data regarding BMI were available, were included. Patients with known history of prior revascularization, pacemaker or implantable cardioverter-defibrillator, were excluded. Scans were performed between December 2007-May 2014, using 64-slice multidetector CT-scanner (Philips Healthcare; n=1.735) or dual-source CT-scanner (Siemens Definition Flash; n=2.344). Data regarding clinical risk factors: current smoking, diabetes mellitus type 2, positive family history, systolic blood pressure and lipid spectrum were assessed. Missing values according to risk factors were imputed using multiple imputation. Univariable and multivariable

analyses were performed using linear regression. 95% confidence intervals (CI) and two-tailed p-values <0.05 were used to evaluate statistical significance. This study complies with the ethical principles of the Declaration of Helsinki of the World Medical Association.
Results: Univariate regression analysis demonstrated a significant association between age-BMI interaction (B 0.26; 95% CI: 0.22–0.30; p-value <0.001); no association was observed between BMI and CCS (B 0.92; 95% CI: –2.2–4; p-value <0.57). Within multivariate regression analysis, including age, BMI and the age-BMI interaction, only age showed a significant independent association with CCS (B 9.2; 95% CI: 2.3–16.2; p-value <0.009). Including also risk factors, the significant independent predictors for CCS were age, smoking, diabetes mellitus type 2, family history and total cholesterol (p-value <0.011).
Conclusion: Within the present study, age and clinical risk factors show a significant independent association with CCS. No age dependent association was observed between BMI and CCS. These data do not confirm the so called "obesity paradox".

P5229 | BEDSIDE
Association of big endothelin-1 with coronary artery calcification

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Background: The coronary artery calcification (CAC) is clinically considered as one of the important predictors of atherosclerosis. Several studies have confirmed that endothelin-1 (ET-1) plays an important role in the process of atherosclerosis formation. However the relationship of ET-1 and CAC remains uncertain. The aim of this study was to investigate whether big ET-1 is associated with CAC.
Methods: A total of 510 consecutively admitted patients from February 2011 to May 2012 in our hospital were analyzed. All patients had received coronary computed tomography angiography (CCTA) and then divided into the two groups based on the results of coronary artery calcium score (CACS). The clinical characteristics including traditional and calcification-related risk factors were collected and the plasma big ET-1 level was measured by ELISA. The association of ET-1 with CAC was evaluated.
Results: Patients with CAC had significantly elevated big ET-1 levels compared with those without CAC (0.7±0.5 vs. 0.5±0.4 pmol/L,P<0.001). Patients in higher big ET-1 tertile had elevated CACS (P<0.001). In the multivariate analysis, big ET-1 (OR=101.83, 95% CI: 19.95–519.92, P<0.001)appeared as independent factors predictive of the presence of CAC. There was a positive correlation of the big ET-1 level with CACS (r=0.567, p<0.001). The 10-year Framingham risk (%) was higher in the group with CACS >0 and the highest tertile of big ET-1 (P<0.001). The area under the receiver operating characteristic curve (AUC) for the big ET-1 level in predicting CAC was 0.83 (95% CI 0.79–0.87, p<0.001), and the optimal cutoff value for the plasma big ET-1 level for predicting CAC was 0.30 pmol/L, with a sensitivity of 70.6% and specificity of 87.7%.
Conclusion: The data, for the first time, demonstrated that the plasma big ET-1 level was a valuable independent predictor for CAC in our study.

BEST POSTERS IN CARDIAC COMPUTED TOMOGRAPHY

P5231 | BEDSIDE
Association of quantitative global plaque volume and Agatston score with major cardiovascular events on long-term follow-up of patients referred for coronary CT angiography

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Background: Coronary artery calcification quantified by the Agatston score is considered an established surrogate marker for the global atherosclerotic plaque burden. Nevertheless, little is known about the relationship between calcification, non-calcfied plaque in coronary CTA and their respective predictive value regarding major cardiovascular adverse events (MACE) on long term follow-up.
Methods: 1034 consecutive patients in whom coronary CT angiography (CTA) was performed between 2005 and 2007 were systematically followed-up by structured telephone interview. The volume of calcified and non-calcified plaque in all coronary segments was quantified by manual planiemtry to obtain the global plaque burden. Major adverse cardiovascular events "MACE" was defined as a combined endpoint of cardiac death resuscitated cardiac arrest, myocardial infarction and/or stroke.
Results: 449 patients lost to follow-up were excluded from the analysis. 585 patients (mean age 59±11 years, 59% males) were included. The median follow-up period was 95 months (range 82–109 months). All-cause mortality was 5% on follow-up (31/585). MACE occurred in 45 (7.7%) patients: 2 cardiac deaths, 14 myocardial infarctions, 5 resuscitated cardiac arrests and 26 strokes. The total Agatston score as well as the global plaque volume were significantly higher in patients who suffered MACE on follow up (mean Agatston score 191±378 vs. 140±336, respectively, p=0.03 and mean global plaque volume 2.9±5.5 mm^3 vs. 1.8±3.4 mm^3, respectively, p=0.009). Agatston score as well as global plaque volume were not significantly different in patients with and without stroke on follow-up (p>0.5). However, the mean global plaque volume was significantly higher in patients who developed myocardial infarction compared to patients without (5.2±8 mm^3 vs. 1.8±3.4 mm^3, respectively, p=0.006) whereas the mean Agatston score in patients with and without myocardial infarction was not significantly different (247±356 vs. 137±319, respectively, p=0.07). ROC-curve analysis showed an area under the curve (AUC) of 0.7 (p=0.008) for global plaque volume as a predictor for myocardial infarction versus 0.63 (p=0.63) for Agatston score.
Conclusions: In a large patient cohort, total calcified plaque burden and global plaque burden are significantly higher in patients who develop MACE on follow-up. Global plaque burden is a better predictor of future myocardial infarction than the Agatston score. These data indirectly point to a potential causative role of the non-calcified plaque burden in causing future myocardial infarctions on long-term follow-up.

P5232 | BEDSIDE
Independent prognostic value of coronary artery calcium score and coronary computed tomography angiography in an outpatient cohort of low to intermediate risk chest patients

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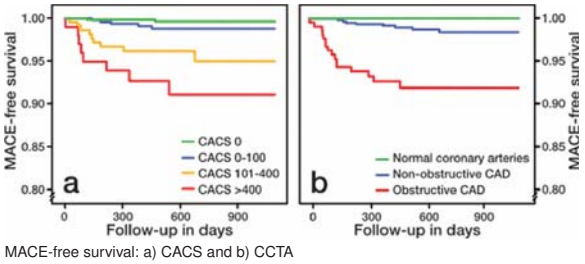
Background: Limited studies report on the additional prognostic value of coronary computed tomography angiography (CCTA) to the coronary artery calcium score (CACS).
Purpose: This study aimed to evaluate the prognostic value of CCTA independent of clinical risk factors and CACS in a routine clinical cohort of symptomatic patients with low or intermediate pre-test probability (PTP) of obstructive coronary artery disease (CAD).
Methods: For a median of 637 days, 1551 chest pain patients from the out-patient clinic with no history of CAD and low or intermediate PTP of CAD were followed for major adverse cardiac events (MACE), defined as death, myocardial infarction or late revascularization. Cox proportional hazard regression was used to evaluate the prognostic value of CCTA, independent of risk factors and CACS.
Results: MACE occurred in 23 patients (1.5%): 3 (0.2%) death, 4 (0.3%) myocardial infarctions and 16 (1.3%) late revascularizations. Both increase in CACS and presence of CAD at CCTA were associated with decreased MACE-free survival (log-rank p<0.01, figure 1). Multivariate analysis, adjusting for risk factors and CACS, showed independent prognostic value of CCTA (p<0.001). CCTA showed obstructive CAD in 3.1% of patients with CACS of zero. No events occurred in patients with CACS of zero without obstructive CAD at CCTA, whereas 2/23 patients (9%) with CACS of zero with obstructive CAD at CCTA had a MACE.



MACE-free survival: a) CACS and b) CCTA

Conclusions: This is the first study to show the prognostic value of CCTA, independent of CACS and risk factors in chest pain patients with low to intermediate PTP of obstructive CAD, in which CCTA is appropriate. Furthermore a non-negligible amount of patients with CACS of zero have obstructive CAD at CCTA. CCTA can be used to identify those patients with CACS of zero at risk for MACE.

P5233 | BEDSIDE
Characteristics of atherosclerotic plaques evaluated at coronary computed tomography angiography associated with higher risk of future acute coronary syndrome: a long-term follow-up study

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Background: Obstructive coronary artery disease (CAD) is associated with higher cardiovascular events rate. Recent studies suggested that even non-obstructive plaques increase cardiovascular events rate at long-term follow-up. However, how to discriminate patients at higher risk for acute coronary syndrome (ACS) among patients with non-obstructive CAD is still unclear.
Purpose: Aim of our study is to identify plaque characteristics at coronary computed tomography angiography (CCTA) evaluation associated with high risk of ACS at long-term follow-up in a population of patients with non-obstructive CAD.
Methods: We enrolled 198 patients who underwent CCTA for suspected CAD in our center between April 2005 and December 2008 and who were found to have non-obstructive CAD. We evaluated coronary arterial remodeling index (RI)

by using vessel diameter (RIdiam = lesion diameter/reference diameter) and vessel area (RIarea = lesion area/reference area), attenuation value of plaque (HU), stenosis severity (lesion lumen area/reference lumen area) and plaque burden (PB = lesion area/lesion lumen area) for each coronary plaque detected. Outcome measure was a composite of hard cardiac events (cardiac deaths, nonfatal myocardial infarctions and unstable angina).
Results: A long follow-up (mean 95±17 months) was obtained in 186 patients (93,3%). A total of 9 events were recorded (2 STEMI, 2 NSTEMI, 5 UA) in 9 different patients. Patients with and without events had similar HeartScore (median: 2,5% vs 2,4%, respectively; p=0.2855) and medications use (of particular interest ASA 55% vs 30% respectively, p=0.3252 and statin 33% vs 24% respectively, p=0.8321). Patients with ACS had higher degree of coronary artery stenosis (mean 38,5% vs 31,9%, respectively; p=0.0258), higher PB (median 0.52 vs 0.43, respectively; p=0.0120), higher RIarea (mean 1.58 vs 1.28; p=0.0006), higher RIdiam (median 1.45 vs 1.25 p=0.0001) and lower HU (median 163 vs 501 p=0.0368). At multivariate analysis only the presence of at least 2 segments with positive RIarea has been found to be significantly associated with ACS occurrence (HR 17.2 CI 95% 1.06–179; p=0.0178). Cumulative ACS-free survival was 98% for patient without positive RIarea plaque, 93% for those with one positive RIarea plaque and 79% for those with more than 2 positive RIarea plaque (log-rank p=0.0012).
Conclusions: CCTA plaque evaluation appears to have prognostic significance and positive remodeling index seems to be the most promising tool for risk stratification in patients with non-obstructive CAD, beyond coronary stenosis and traditional risk factors.

P5234 | BEDSIDE
Coronary CT angiography anatomic assessment and lesion-specific ischemia: impact of integrating coronary plaque volume and CT derived fractional flow reserve

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Background and introduction: The correlation of stenosis assessment by coronary CT angiography (CTA) and downstream ischemia is low. Consequently, coronary CTA is a poor gatekeeper to the cath lab. Both plaque assessment and non-invasive fractional flow reserve (FFR) derived from CTA (FFRct) hold superior and additive diagnostic performance when compared to coronary CTA anatomic assessment in identifying lesion-specific ischemia.
Purpose: The aim of the present study was to evaluate the diagnostic performance of a multi-imaging strategy combining coronary CTA stenosis, plaque assessment, and FFRct.
Methods: As part of a prospective multicentre trial, we performed coronary CTA, FFR, and FFRct in 254 patients suspected of coronary artery disease. A site-read CTA stenosis >50% was considered obstructive. We quantified low-density non-calcified plaque (LD-NCP) volume by semi-automated software (AutoPlaq) from standard CTA images. LD-NCP volume was dichotomized using ROC analysis to define the optimal threshold. Ischemia was defined by FFRct or FFR ≤0.80.
Results: Mean FFR in 484 vessels was 0.87 (±0.13). FFR was ≤0.80 in 100 (21%) vessels. Overall, addition of LD-NCP (≥30 mm^3) to coronary CTA anatomic interpretation improved the diagnostic accuracy and specificity for detection of lesion-specific ischemia by FFR (Table). Adding FFRct to LD-NCP and coronary CTA assessment further improved accuracy, specificity and PPV with no sacrifice in sensitivity or NPV (Table).

Diagnostic performance

	Coronary CTA stenosis	CTA stenosis & LD-NCP ≥30 mm^3	CTA stenosis & LD-NCP ≥30 mm^3 & FFRct ≤0.80
Accuracy	64% (60–69%)	78% (75–82%)	86% (83–89%)
Sensitivity	83% (74–90%)	63% (53–73%)	57% (47–67%)
Specificity	59% (54–64%)	83% (79–86%)	94% (91–96%)
PPV	35% (29–41%)	49% (40–57%)	70% (59–80%)
NPV	93% (89–96%)	90% (86–93%)	89% (86–92%)

NPV, negative predictive value; PPV, positive predictive value.

Conclusions: Quantification of LD-NCP improves diagnostic performance of coronary CTA and may optimize selection of patients for FFRct analysis. Adding FFRct computation to patients with stenosis and a LD-NCP plaque volume ≥30 mm^3 may optimize selection of patients to the cath lab.

BEST POSTERS IN VASCULAR BIOLOGY

P5236 | BENCH
Nicotinamide-streptozotocin-induced type 2 diabetes in uninephrectomized high-fat-fed rats: a novel non-genetic rat model of diabetic nephropathy

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Background: The prevalence of diabetic nephropathy in type 2 diabetes (DM2) rises dramatically, with concomitant increase in associated cardiovascular morbidity and mortality. One of the optimal strategies for investigation of methods and mechanisms of nephroprotection in DM2 is using an animal model of DN without genetic alteration which mimics natural history of diabetic kidney disease in humans as close as possible, both clinically and morphologically.
Purpose: To develop relatively easy reproducible non-genetic rat model that consequentially mimics all stages of DN observed in DM2.
Methods: 3 weeks after unilateral nephrectomy, twenty 9-weeks old male Wistar rats were fed high-fat diet with beef tallow for 5 weeks and then successively received doses of nicotinamide (NA, 230 mg/kg) and streptozotocin (STZ, 65 mg/kg) intraperitoneally in 15-min interval. One week later, glucose tolerance test was performed,and 17 rats with glucose levels between 8,0 and 14,0 mmol/l were selected. Control uninephrectomized rats received vehicle instead of NA and STZ, and fed normal chow. After 10, 20 weeks, and at the end of the experiment (at week 30), urine and blood samples were collected. Histological examination (PAS and Masson's trichrome stainings) and electronic microscopy were also performed.
Results: HbA1c in diabetic group was considerably higher compared to control rats throughout the experiment, with a significant decrease of serum insulin level by week 20. At week 10, routine blood biochemical markers of kidney dysfunction did not statistically differ between groups with tendency to hyperfiltration, and albuminuria was only slightly but not significantly different between groups. In contrast, early markers of tubular dysfunction (KIM-1 and NGAL) were highly increased in diabetic animals (205±18 ng/ml and 565±50,4 pg/ml, respectively) with p-value <0.05 compared to non-diabetic rats (108±10,2 and 197±30,6, respectively) indicating early stage of DN confirmed by early electronic glomerular changes. Significant microalbuminuria (MAU) was detected at week 20 (65±3,6 mg/24h), followed by overt proteinuria at week 30 (MAU 336±28,4 mg/24h), both of which were absent in control group (6,5±1,1 and 16,6±2,5, respectively), p<0.05 each. Also the creatinine clearance gradually decreased from week 20 (2,3±0,21 ml/min/kg) until the end of the study (1,8±0,35 ml/min/kg), and was histologically confirmed by mesangial expansion and diffuse glomerular sclerosis, respectively.
Conclusion: Uninephrectomized high-fat-fed rats with NA-STZ-induced diabetes develop all features of DN in DM2.

P5237 | BENCH
Characterization of hemodynamics in great arteries of wild-type mouse using CFD based on ultrasound images

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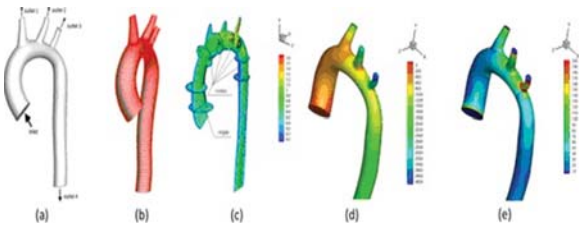
Objective: Hemodynamic factors in cardiovascular system are hypothesized to play a significant role in causing structural heart development. It is thus important to improve our understanding of velocity characteristics and parameters. We present such a study on wild-type mouse to characterize the vessel geometry, flow pattern and wall shear stress (WSS) in great arteries.
Methods: Micro-ultrasound imaging for small animals was used to measure blood boundary and velocity of the great arteries. Subsequently, specimens flow boundary conditions were used for 3D reconstructions of great artery and aortic arch dimensions and blood flow velocity data were input into subject-specific computational fluid dynamics (CFD) for modeling hemodynamics.
Results: Measurement by Micro-ultrasound imaging showed blood velocities in great artery and aortic arch had strong correlations with vascular sizes, while blood pressure had a weak trend in relation to vascular size. Wall shear stress magnitude increased when closer to arterial branches and reduced proximal to the root aorta and descending aorta, and the parameters were related to the fluid mechanics in branches in some degree.



CFD simulation of mice aortic vessels

Conclusion: We developed a method to investigate fluid mechanics in mouse arteries, using a combination of micro-ultrsound and CFD, and demonstrated its ability to reveal detailed geometric, kinematic and fluid mechanics parameters.

P5238 | BENCH
Modeling Marfan syndrome with induced pluripotent stem cell-derived vascular smooth muscle cells

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Background: Marfan syndrome (MFS) manifests aneurysm and dissection in the ascending aorta which are often fetal. Drug therapy is not always sufficient to suppress the manifestations. Previously, it has been reported that transforming growth factor β (TGF-β) signaling is enhanced in tissues and vascular smooth muscle cells (VSMCs) from aortic aneurysms in MFS patients.
Purpose: The objective of this study is to establish a patient-specific induced pluripotent stem cell-derived vascular smooth muscle cells (iPSC-SMCs) as a model of MFS.
Methods: Dermal fibroblasts obtained from a MFS patient were reprogrammed into induced pluripotent stem cells (iPSCs) using retroviral vectors expressing OCT4, SOX2, c-MYC and KLF4. The MFS iPSCs were coaxed to differentiate into vascular smooth muscle cells (VSMCs) via neuroectodermal lineage from which ascending aorta originates and compared with healthy control iPSC-VSMCs.
Results: Both of MFS and control iPSCs could be differentiated into neuroectodermal lineage in which SOX2, PAX6 and NESTIN expression detected by reverse transcription polymerase chain reaction (RT–PCR). Addition of TGF-β1 and PDGF-BB could differentiate both neuroectodermal cells into VSMCs. Quantitative PCR showed that myosin heavy chain 11 (MYH11), myocardin (MYCD) and serum response factor (SRF) expressed at higher levels in MFS iPSC-VSMCs than in control iPSC-VSMCs. Addition of TGF-β1 increased matrix metalloproteinase-2 (MMP-2) mRNA level. Immunostaining for smoothelin (SMTN) and MYH11 were more intense and enhanced nuclear accumulation of SMAD2/3 was found in MFS iPSC-VSMCs than in control iPSC-VSMCs.
Conclusion: MFS iPSC-VSMCs expressed more mature contractile proteins and transcription regulator of smooth muscle genes than normal iPSC-VSMCs and showed enhanced TGF-β signaling. The characteristics were similar to reported characteristics of VSMCs explanted from MFS patients' aneurysms and iPSC-VSMCs could be a model of MFS.

P5239 | BENCH
Resveratrol inhibits aortic root dilatation in marfan mice

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Background and purpose: Marfan syndrome (MFS) is an autosomal connective tissue disorder caused by mutations in the fibrillin-1 gene. MFS patients are at risk for lethal aortic aneurysm development and dissection. β-blockers and losartan are medication options, however, more treatment possibilities are needed, since losartan is less effective in 67% of the MFS patients. Aneurysm formation can be studied in various mouse models. Spontaneous aneurysm formation occurred in smooth muscle cell-specific sirtuin-1 (SIRT-1)-deficient mice. SIRT1 is an NAD+-dependent deacetylase, which can prevent cellular senescence. Since resveratrol is known to induce SIRT1 and reduce senescence, we investigated resveratrol treatment in a MFS mouse model.
Methods: We studied vascular senescence, aortic root dilatation and the effect of resveratrol in Marfan mice.
Results: Senescence was observed in the ascending aorta of MFS mice and correlated positively with aortic root dilatation rate. Resveratrol significantly inhibited dilatation, even more efficiently than losartan. Resveratrol treatment did not decrease activation of SMAD2 and ERK1/2, which are downstream pathways of the angiotensin-II receptor-1, and blocked by losartan. However, the aortic root of resveratrol-treated mice showed significantly increased nuclear SIRT1, decreased medial area, less elastic lamina breaks and decreased matrix metalloproteinases MMP2, MMP1 and MMP13 expression.
Conclusion: Resveratrol inhibits aortic root dilatation in MFS mice via a different mechanism of action than is considered for losartan and seemingly via modulation of the extracellular matrix. Resveratrol may hold promise as a novel therapeutic for MFS patients, especially for patients with a dominant negative fibrillin-1 mutation who do not respond to losartan effectively.

BEST POSTERS IN TRICUSPID DISEASE

P5241 | BEDSIDE
Outcomes of tricuspid valve replacement: a meta-analysis

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Background: Tricuspid valve replacement (TVR) is a quite uncommon intervention historically associated with high mortality and morbidity. Due to its low prevalence among cardiac surgical procedures, current knowledge of long-term results of TVR is limited.
Purpose: Aim of the present meta-analysis was to assess rates of mortality and reoperation after TVR, and to investigate factors influencing these outcomes.
Methods: On December 5th 2014, PubMed, Embase, and Cochrane library were searched for studies reporting on mortality and need for reoperation after TVR; and a total of 204 papers were identified. After careful screening, a total of 35 studies were included in the analysis, heterogeneity was investigated with Cochrane-Q-statistic, and the Egger's test was used to assess publication bias for the outcomes investigated.
Results: Finally, a total of 3095 patients receiving TVR with a mean follow-up of 6.7 years were included; of those 1654/3095 (53%) received a biological prosthesis. Pooled analysis showed a rate of 16.9% (95% CI 14.7–19.3,I260.6) for 30-day mortality; which was not influenced by prostheses used (Qmodel 1.03,p=0.85, for biological prostheses). At follow-up, cumulative mortality was 41.5% (95% CI 35.4–47.7,I2 89.2), and was not influenced by type of prostheses used (Qmodel 1.98,p=0.16, for biological prostheses). Rate of reoperation on the tricuspid valve was 9.4% (95% CI 6.8–12.8, I277.2), it was more likely to occur in smaller series (Egger's p=0.05), and was not influenced by type of prostheses implanted (Qmodel 1.6, p=0.26).
Conclusions: Despite scientific progresses, TVR is still burdened by considerable mortality rates, both early and late after surgery. Type of prostheses implanted (biological vs. mechanical) does not influence any of the outcomes investigated, whilst incidence of reoperation is increased in small volume centres.

P5242 | BEDSIDE
Rigid annuloplasty ring or flexible band for treating functional tricuspid regurgitation? Insights from a clinical and echocardiographic study

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Background: The use of annuloplasty rings or bands to treat functional tricuspid regurgitation (TR) is becoming common practice in cardiac surgery. However, what is the ideal annuloplasty device remains an open question.
Purpose: In the present study, we compared rigid annuloplasty rings vs. flexible bands for the treatment of functional TR.
Methods: From March 1999 throughout June 2014, a total of 444 consecutive patients with grade ≥2+ functional TR (graded from 0 to 3+) underwent tricuspid valve repair by using an annuloplasty device. Three different models (Carpentier-Edwards Classic, Edwards MC3, and Carpentier-Edwards Physio) of rigid ring and three different models (Medtronic-Duran, Koehler mrs, and Carbomedics Annuloflex) of flexible bands were used in 95 (21.4%, R-group) and 349 (78.6%, B-group) patients, respectively. Immediate outcomes and late clinical and echocardiographic results were compared in the two groups.
Results: Between the two groups, there were no significant differences in preoperative clinical and echocardiographic characteristics, 30-day mortality (R-group = 8.4% vs. B-group = 6.6%, P=0.54) and perioperative complications. Follow-up (mean: 4.6±3.7 years) was 98.4% complete. New York Heart Association class and symptoms of right heart failure were significantly improved (P<0.001). The 7-year nonparametric estimates of overall survival (including hospital mortality) – R-group = 61.2% [95% confidence interval (CI): 52.4–70] vs. B-group = 65.8% (95% CI: 62.8–68.8) – and freedom from cardiac death (including hospital mortality) – R-group = 74.9% (95% CI: 67.3–82.5) vs. B-group = 78.5% (95% CI: 75.9–81) – were comparable (P=0.16 and 0.47, respectively). TR of grade ≥2+ at follow-up was found in 29/396 (7.3%) patients, and the 7-year nonparametric estimate of freedom from significant TR was 93.6% (95% CI: 90–97.2) for R-group and 92.4% (95% CI: 90.3–94.5) for B-group (P=0.66). In both groups there was a significant tricuspid annular and right ventricular (RV) reverse remodeling but only in B-group there was a significant improvement in RV fractional area change (P=0.0044) and tricuspid annular plane systolic excursion (P=0.043).
Conclusions: Cardiac operations in patients with functional TR are performed with high early mortality. On a long-term basis, rigid rings and flexible bands are equally effective in controlling TR within grade 1+. Flexible bands may help RV function recovery.

P5243 | BEDSIDE
Is two-dimensional measurement of tricuspid annulus the most appropriate criteria for selecting candidates for surgery? Insights from 3D echocardiography

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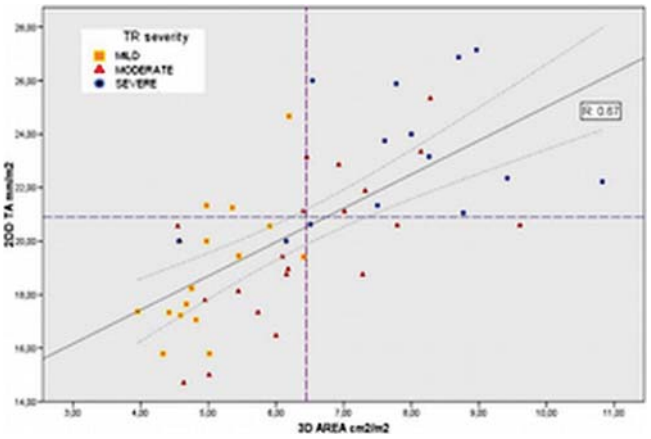
Background: Current guidelines recommend tricuspid valve (TV) surgery in patients with non-severe functional tricuspid regurgitation (FTR) when tricuspid annulus (TA) is dilated >21 mm/m^2 by 2D echocardiography (2DE). Significant FTR leads progressively to a circular TA shape. This dilatation might be underestimated with single linear measurements and on the contrary, may generate unnecessary interventions in slight degrees of FTR. Assessment of diastolic TA area by 3D transthoracic echocardiography (3DTE) could provide a more objective measure of TA dilatation, however to date, no 3DTE area value has been described for this purpose.

Objectives: To evaluate the diagnostic performance of 3D Area (3DA) in comparison to classic 2D diameter (2DD) for selecting candidates to TV surgery.
Methods: 2DE and 3DTE data sets of the TV were prospectively acquired in 50 patients (Age: 69±9, 82% women) with rheumatic left-side valve disease. FTR was divided in three groups: mild (N: 15), moderate (N: 21) and severe (N: 14). Diastolic 3DA was measured in addition to conventional 2D diameter (2DD).
Results: Optimal cut-off points for severe FTR detection using both 3DA (6.5 cm^2/m^2) and 2DD (21 mm/m^2, identical to the described in the literature), were identified by ROC analysis: 2DD: AUC 0.85, Se: 86%, Sp: 72%; 3DA: AUC 0.84, Se: 86%, Sp: 78%. Potential selection of candidates for TV surgery, based on the combination of 2DD and 3DA is shown in Figure. Better specificity of 3DA helped to reclassify surgical indication in mild and moderate degrees of TFR.



Conclusions: Although 2DD >21 mm/m^2 seems to be a reasonable criterion of marked dilatation of TA in FTR, the combination with diastolic 3DA assessment, cut-off value of 6.5 cm^2/m^2, might improve selection of candidates for TV surgery.

P5244 | BEDSIDE
Tricuspid valve annuloplasty for functional tricuspid regurgitation: immediate outcomes and risk factors for late failure

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Background: Risk factors for recurrent regurgitation after tricuspid valve annuloplasty (TVA) for tricuspid regurgitation (TR) secondary to left-sided heart valve disease (functional TR) remain uncertain.
Purpose: To investigate immediate outcomes and late failure of repair (TVA) for functional TR.
Methods: 524 (mean age: 69.9±9.6 years) consecutive patients with grade ≥2+ TR (graded from 0 to 3+) underwent TVA at the present authors' institution from March 1999 throughout June 2014. All patients suffered from left-sided heart valve disease needing surgical treatment. The mean expected operative risk according to EuroSCORE II was 10.4±12.2%. Clinical data and echocardiographic studies were retrospectively reviewed during a mean follow-up of 4.9±3.7 years. Risk factors for late failure of repair were identified by multivariable analysis.
Results: The DeVega suture annuloplasty (SA), rigid rings or flexible bands were used in 15.3, 18.1 and 66.6% of patients, respectively. Thirty-day mortality was 7.1%, and age >70 years (P=0.002), left ventricular (LV) dysfunction (defined as LV ejection fraction ≤35%, P=0.015), right ventricular (RV) dysfunction [defined as tricuspid annular plane systolic excursion ≤16 mm (P=0.0023) and RV fractional area change <35% (P=0.003)] and prolonged (>5 h) duration of surgery (P<0.0001) were independent risk factors. Prolonged (>48 h) invasive ventilation (16.3%), low cardiac output (10.2%), acute kidney injury (18%) and mediastinal re-exploration (20%) were the most frequent major postoperative complications. The 10-year non-parametric estimates of overall survival and freedom from cardiac death (including hospital mortality) were 51.7 [95% confidence interval (CI): 48.4–55] and 71.5% (95% CI: 68.7–74.3), respectively. TR of grade ≥2+ at follow-up was found in 35/467 (7.5%) patients, and the 10-year non-parametric estimate of freedom from significant TR was 81.5% (95% CI: 78–85.2). Predictors of recurrent TR were the use of suture annuloplasty (P=0.023), LV dysfunction (P=0.0022) and RV dysfunction (P<0.0001). At follow-up, significant TR combined with recurrent left-sided heart valve disease (P=0.038) and RV dysfunction (P<0.0001).
Conclusions: Cardiac operations in patients with functional TR are performed with high early mortality and frequent postoperative complications. On a long-term basis, TR is generally controlled within grade 1+ in patients without preoperative biventricular dysfunction. Late failure of repair is linked to the fate of left-sided heart valve repair and RV function. The use of SA should be discouraged.

BEST POSTERS IN ELDERLY AND CARDIOVASCULAR DISEASES

P5246 | BEDSIDE
Hypertensive target organ damage and longitudinal changes in brain structure and function in older patients with manifest cardiovascular disease: The SMART-MR study

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Background: High blood pressure has been related to structural and functional changes of the brain. In populations with high cardiovascular risk, hypertensive target organ damage might better represent exposure to high blood pressure than the blood pressure measurement itself.
Methods: To examine the association of hypertensive target organ damage with changes in brain structure and function, data was used from the prospective SMART-MR Study. Renal function, albuminuria, and left ventricular hypertrophy on electrocardiography were measured in 663 patients with manifest cardiovascular disease (mean [SD] age 57 [9] years, 81% men). At baseline and after a mean of 3.9 years of follow-up, 1.5 T brain MRI was performed to quantify progression of global brain atrophy (decrease in brain parenchymal fraction as % of intracranial volume (ICV)) and progression of cerebral small-vessel disease (increase in white matter lesion volume or new lacunar infarcts). Memory and executive functioning were assessed with neuropsychological tests.
Results: Regression analyses showed that an increasing number of signs of target organ damage was associated to more progression of global brain atrophy and more rapid decline in memory performance (Figure). Compared to no target organ damage, mean differences in change in brain parenchymal fraction (95% CI) for 1 and ≥2 signs of organ damage were −0.12 (−0.30; 0.06) and −0.41 (−0.77; −0.05) %ICV and mean (95% CI) differences in change in memory performance (z-score) were −0.15 (−0.29; −0.00) and −0.27 (−0.54; −0.01). These results were independent of blood pressure, antihypertensive treatment, and other confounders. Target organ damage was not associated with progression of cerebral small-vessel disease or change in executive functioning.
Conclusions and relevance: In this high-risk cardiovascular population, more extensive hypertensive target organ damage was associated with progression of global brain atrophy and greater decline in memory performance. Routinely assessed signs of target organ damage could identify those patients at the highest risk of cognitive decline.

P5247 | BEDSIDE
Results of the cardiac surgery in octogenarians

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Introduction: Cardiac surgery in octogenarians with severely decreased functional status is increasingly common, but outcome data are still limited.
Purpose: The aim of this study was to compare postoperative outcome, medium-term survival and quality of life of low, medium and high risk octogenarians undergoing cardiac surgery.
Methods: 285 octogenarians were included who underwent any cardiac surgical procedure between January 2011 and December 2012. Five out of all twelve national adult cardiac surgical centres participated in the study, representing almost half of all octogenarians operated in our country in that period. Patients were divided into low, medium and high-risk groups according to the operative risk calculated using EuroSCORE II. Preoperative, operative and postoperative data of the patients were collected retrospectively. Follow-up was performed in May 2014 by interviewing the patients by telephone. All patients also completed a questionnaire assessing quality of life by objective and subjective means.
Results: There was a higher 30-day mortality (20% vs. 6.4% vs. 5.2% respectively, p<0.001), long-term mortality (20% vs. 8.5% vs. 8.3% respectively, p<0.05) and higher incidence of low cardiac output syndrome (16.8% vs. 1.1% vs. 4.2% respectively, p<0.05) in the high-risk group compared with the medium- and low-risk groups, respectively. The actual mortality in all groups was significantly higher than predicted using EuroSCORE II. There was also a lower quality of life as measured using the Karnofsky score in the high risk group compared with the medium- and low-risk groups (44.4 vs. 70.1 vs. 70.6 respectively, p<0.001). Greater improvement in NYHA status was noted in the high- and medium-risk groups compared with the low-risk group (51% vs. 45% vs. 24% respectively, p<0.05).
Conclusions: Our study has shown that high-risk octogenarians undergoing car-

diac surgery still represent a significant challenge for medical practitioners. Before referring for cardiac surgery, the potential for a higher than expected mortality rate and decreased functional status should be taken into account. Additionally, our study reveals that Euroscore II significantly underestimates real operative risk in octogenarians undergoing cardiac surgery.

P5248 | BEDSIDE
Transcatheter aortic valve implantation in very elderly patients: immediate results and medium term follow-up

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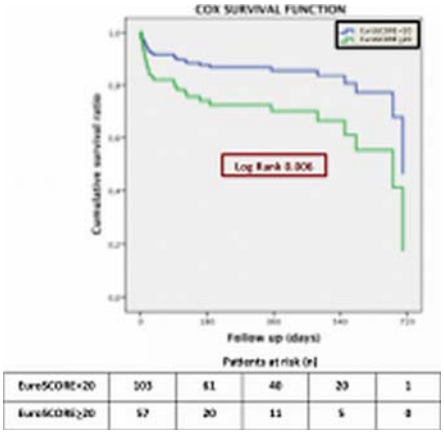
Objective: Our aim was to evaluate immediate transcatheter aortic valve implantation (TAVI) results and medium-term follow-up in very elderly patients with severe and symptomatic aortic stenosis (AS).
Methods: Multicenter, observational and prospective study carried out in 3 hospitals. We included consecutive very elderly (>85 years) patients with severe (AS) treated with TAVI. The primary endpoint was to evaluate death from any cause at 2 years.
Results: The study included 160 consecutive patients with a mean age of 87±2.1 years [range, 85–94] and a mean logistic EuroSCORE of 18.8% ± 11.2%, with 57 (35,6%) patients scoring ≥20%. Procedural success rate was 97.5%. 25 (15.6%) patients had acute complications, being mayor bleeding the most frequent. No procedure needed conversion to surgery. Global mortality rate during hospitalization was 8.8% (n=14) and 30-day mortality rate was 10% (n=16). Median follow up period was 252.24±232.17 days. During the follow-up period, 28 (17.5%) patients died, 17 of them due to cardiac cause. Two year overall and cardiac survival estimated rates using the Kaplan-Meier method were 71% and 86.4% respectively. Cox proportional hazard regression showed that the variable EuroSCORE ≥20 was the unique variable associated with overall mortality.



EuroSCORE<20	103	61	40	23	1
EuroSCORE≥20	57	20	11	5	0

Cox survival curves by EuroSCORE

Conclusions: TAVI is safe and effective in a selected population of very elderly patients. Our findings support the adoption of this new procedure in this complex group of patients.

P5249 | BEDSIDE
Impact of low diastolic blood pressure on risk of cardiovascular death in elderly and late-elderly patients with coronary artery disease after coronary revascularization: the CREDO-Kyoto Registry

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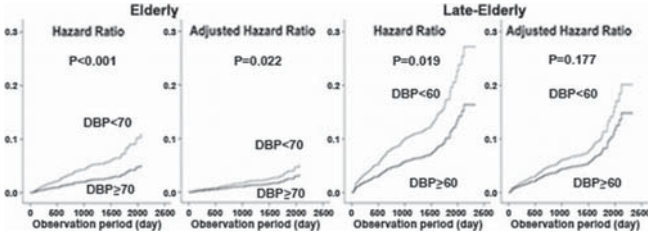
Background: It remains controversial whether low diastolic blood pressure (DBP) is a risk for cardiovascular (CV) events in patients with coronary artery disease (CAD), especially in the elderly.
Purpose: We investigated the impacts of age and low DBP on CV death in CAD patients after coronary revascularization.
Methods and results: We examined 2619 Young/Middle-aged (–64 years), 2932 Elderly (65–74 years), and 1629 Late-Elderly (75 years-) CAD patients who underwent first coronary bypass graft or percutaneous coronary intervention in the CREDO-Kyoto study. Cumulative hazard ratio (HR) for CV death was higher in patients with DBP<70mmHg in Elderly group and in patients with DBP<60mmHg, but not <70mmHg, in Late-Elderly group, compared with each counterpart (Figure), whereas low DBP was not associated with increased CV death in Young/Middle-aged group. Step-wise logistic regression analysis showed that independent risk factors for CV death in low DBP patients were creatinine clearance (inversely), prior cerebrovascular disease, and hemoglobin (inversely) in Elderly group and creatinine clearance (inversely), prior heart failure, and malignancy in Late-Elderly group. After adjustments with the independent risk factors, cumulative HRs were similar in patients with DBP<60 and with DBP≥60mmHg in Late-Elderly group and only small difference of HR was shown between patients with DBP<70 and with DBP≥70mmHg in Elderly group.



Conclusion: In elderly and late-elderly revascularized CAD patients with low DBP, renal dysfunction, co-existing CV disease, and poor general condition were independent risks of CV death, whereas low DBP itself may be a risk marker but not a major causal factor. In elderly and late-elderly CAD patients with low DBP, attention should be paid upon CV and non-CV comorbidity.

BEST POSTERS IN KNOWN AND EMERGING RISK FACTORS AFTER CARDIAC SURGERY

P5251 | BEDSIDE
Blood transfusion and increased hospital morbidity and mortality in patients undergoing coronary artery bypass grafting

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Background: The transfusion of blood components has played an important role in hemodynamic management during the perioperative period. Despite its proven benefits, unnecessary transfusions are likely to be associated with unnecessary morbidity and mortality.
Objective: The aim of this study was to evaluate the impact of the transfusion of hemoderivates on clinical outcomes during post-operative period and 30-day mortality.
Methods: A total of 1378 patients who underwent isolated or combined CABG surgery between January 2011 and December 2012 had their transfusional, clinical and hematological data reviewed. The effect of transfusion of blood components was tested in a multivariate analysis for the prediction of three prespecified coprimary end points: ischemic, infectious and hospital mortality. Hospital mortality outcome was tested in a stratum of low-risk patients, in order to isolate the effect of pre-operative risk on the outcomes, through the logistic EuroSCORE calculation.
Results: The overall transfusion rate was 63.9%. The transfusion of blood components was associated with greater likelihood of occurrences of the three coprimary end points: infectious composite (OR 2.67; CI 95% 1.70 to 4.19; P<0.001), ischemic composite (OR 2.42; CI 95% 1.70 to 3,46; P<0.001); and hospital mortality (OR 3.07; CI 95% 1.53 to 6.13; P<0.001). When assessing only patients with logistic EuroSCORE ≤2% in both groups, the mortality rate was greater among the ones who underwent blood transfusions [6% versus 0.4% (P<0.001)], contradicting the view that the greatest mortality in the group of transfused patients would result from the most severe condition of the patient.
Conclusion: The blood transfusion in patients who underwent CABG surgery is strongly associated with ischemic events, infectious complications and hospital mortality. This result reinforces the notion that this practice without clear specified critera should be discouraged due to these risks.

P5252 | BEDSIDE
Smokers undergoing coronary surgery are at a greater risk for perioperative complications

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Introduction: Smoking is a known risk factor for cardiovascular diseases, but its effect on operative outcomes is still debated.
Purpose: To analyse patients submitted to CABG, comparing active smokers with past smokers and non-smokers in terms of disease severity, risk factors, surgical indications, surgical outcomes and complications.
Methods: Search the Center's database for patients submitted to CABG from January 1st 1990 to December 31st 2013.
Results: 10,791 patients were submitted to CABG (9327 male/1464 female), 1208 active smokers, 4,013 past smokers and 5,570 non-smokers. 96.6% of active or past smokers were male, compared to 76.8% in non-smokers (p<0.001). Also significant was the incidence of COPD (4.0% vs. 2.5%, p<0.001), obesity

(69.6% vs. 66.2%, p<0.001) and peripheral vascular disease (11.6% vs 6.3% p<0.001). Active smokers had had acute coronary syndromes in 60.3%, compared to 58% in past-smokers and 45.3% in non-smokers.(p<0.001) Patients with a history of smoking more often had moderate to severe LV dysfunction (14.5% vs. 9.4%, p<0.001).
Need for postoperative mechanical assistance was not different (p=0.7), but the use of inotropes was greater in active smokers (p=0.012). Although the incidence of respiratory failure was not different (0.7% vs. 0.5%, p=0.066), pulmonary infections were significantly greater in active smokers (2.0% vs. 1.3%, p<0.001). The incidence of cardiac arrest and significant arrhythmias was greater in non-smokers (0.5% vs. 0.36%, p<0.001; and 26% vs. 22.8%, p<0.001, respectively), but in-hospital mortality was similar (p=0.799). The average length of stay was higher in active smokers (7.96, SD: 6.86 vs. 7.46, SD: 6.4, p=0.003).
Conclusions: Active smokers presented with worse CAD, more comorbidities and complications. Past smokers were found to be an intermediate group between active and non smokers. Smoking cessation before surgery may reduce complications. A longer follow-up is required to assess longterm consequences.

P5253 | BEDSIDE
Genetic variant in glycoprotein receptor Ia is associated with major adverse cardiac and cerebrovascular events after coronary artery bypass graft surgery

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Genetic variant in glycoprotein receptor Ia is associated with major adverse cardiac and cerebrovascular events after coronary artery bypass graft surgery
Background: A high occurrence of major adverse cardiac and cerebrovascular events (MACCE) after coronary artery bypass graft (CABG) surgery still exists. It has been suggested that variations in genes related to platelet function are independently associated with MACCE after CABG.
Methods: Two separate cohorts of patients undergoing CABG surgery were examined, and MACCE after the index CABG was recorded. In a discovery cohort of 1576 patients, 44 single-nucleotide polymorphisms (SNPs) related to platelet function were tested. Cox proportional hazard models were used to identify clinical and genomic multivariate predictors of MACCE. The positive SNPs were verified in a replication cohort with 646 patients. We have complied with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects and/or animals. All patients were provided written informed consent to be involved in the study.
Results: In discovery cohort, the average age of MACCE cases was significantly higher than that of patients without MACCE (P=0.010) and β-blocker users were significantly lower in MACCE cases as compared with patients without MACCE (P=0.0003). And for other clinical factors, there is no difference. Three SNPs (PTGS2 rs5277 C/G, HR=1.554, p=0.039; F13A1 rs5982 C/T, HR=1.402, p=0.017; GP Ia rs1126643 C/T, HR=1.429, p=0.014) were independently associated with significantly increased risk of MACCE. After adjusted by multiple clinical risk factors, they still showed positive to increase the risk of MACCE. In the replication cohort of 646 patients from a multi-center study, we verified that GP Ia rs1126643 C/T SNP (HR=1.733, p=0.020) was associated with a significantly increase of MACCE.
Conclusion: In 2 independent cardiac surgery cohorts, we firstly reported GP Ia rs1126643 C/T SNP was associated with increased risk of MACCE after CABG.

P5254 | BEDSIDE
Troponin T value and hospital mortality after cardiac surgery

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Introduction: The Third Universal Definition of Myocardial Infarction (MI) arbitrarily defines the MI diagnosis after coronary artery bypass grafting (CAGB) as the elevation of cardiac biomarker value greater than or equal to 10 times the 99th percentile of the upper reference limit (URL) in patients with normal baseline troponin values (≤99th percentile URL) in addition to either new pathological Q waves or new left bundle branch block, or angiographic documented new graft or new native coronary artery occlusion, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Objective: Due to the challenges in the diagnosis of myocardial injury and MI after CABG or cardiac valve surgery (CVS), the aim of this study was to determine the better troponin T (TnT) value (4th generation or ultrasensitive) cut-off after cardiac surgery (CABG or CVS) associated with increased hospital mortality (30 days).
Methods: We analyzed 479 patients undergoing cardiac surgery (CABG - 274; CV - 205) from February 2011 to November 2014. TnT value was measured immediately before surgery and on the morning of the 1st postoperative day. Area Under the Receiver Operating Characteristic Curve (ROC curve) and multiple Cox regression models were used to evaluate the TnT value as a predictor of hospital mortality.
Results: Area under the ROC curve with better sensitivity and specificity for death was 0.77. The cut-off found was the elevation of 47 times the TnT value above the reference value (99th percentile). Setting this value to 50 times did not change the area under the ROC curve and had a sensitivity of 69%, specificity of 74%, positive predictive value of 16% and negative predictive value of 97%. The patients were then divided into two groups: TnT <50x (99th) and TnT ≥50x (99th). Twenty-nine percent of the patients had ≥50x TnT (99th) in the 1st postoperative day with 30-day mortality of 16% compared to 2.9% of death in those with TnT <50x (99th) – P<0.001. Eleven variables were evaluated and three were identified as independent predictors of death after cardiac surgery: age (HR - 1.12; 95% CI - 1.08 to 1.17), cardiopulmonary bypass time (HR - 1.02; 95% CI - 1.01 to 1.03) and TnT ≥50x (99th) (HR - 4.20; 95% CI - 1.90 to 9.30).
Conclusion: Elevation of the TnT value greater than or equal to 50 times the reference level (99th percentile), regardless of the clinical, electrocardiographic and image findings, was an independent predictor of 30-day mortality after cardiac surgery.

BEST POSTERS IN BASIC CARDIO-ONCOLOGY RESEARCH

P5256 | BENCH
A selective angiotensin-II type 2 receptor agonist reduced cancer cachexia-induced cardiomyopathy

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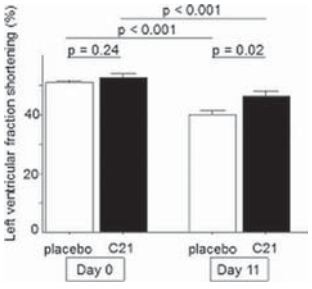
Background: Angiotensin-II has been shown to be up-regulated in cachexia. Angiotensin-II mediates its actions via AT1 and AT2 receptors, and AT2 receptor acts in anti-proliferative, anti-inflammatory, and anti-apoptotic ways. We sought to test the effects of compound21 (C21), a selective AT2 receptor agonist, on survival, body weight, and cardiac function in cancer cachexia model.
Methods: The Yoshida hepatoma AH-130 rats were treated with C21 at 0.2mg/kg (n=15) or placebo (n=44) per gavage daily for a maximum of 17 days. Cardiac function was analysed by M- and B-mode echocardiography on day 11. The proteasome/caspase activity as well as Western blotting for muscle-specific metabolic proteins in heart and gastrocnemius were analysed.
Results: C21 improved survival (hazard ratio: 0.45, p=0.03) and reduced weight loss by 44% (p<0.01) at the end of study. Left ventricular fraction shortening (FS), a measure of systolic function, was similar at the beginning among groups (52.7±1.1 in C21 vs. 50.9±0.7% in placebo, p=0.24) and decreased on day 11 in both groups (p<0.001). On day 11, however, FS was significantly greater in C21 group than placebo (46.3±1.8 vs. 39.9±1.3%, p=0.02). Heart rate (380±14 vs. 342±9bpm, p=0.04), left ventricular mass (488±27 vs. 436±12mg, p=0.06), and cardiac output (53.2±7.1 vs. 40.7±3.1ml/min, p=0.07) were higher in C21 group on day 11, suggesting an attenuated cardiac impairment in this model of cancer cachexia. Whereas proteasome/caspase activity was similar among groups in gastrocnemius, myostatin expression in heart was reduced by 32% in C21 group (p=0.03).



Conclusion: Selective AT2 receptor stimulation by C21 had beneficial effects on cardiac function in a rat model of cancer cachexia. This effect may have contributed to better outcome of animals treated by C21.

P5257 | BEDSIDE
Plasma levels of tumor necrosis factor in relation to intramuscular gene expression of TNF, metabolic related enzymes and skeletal muscle pathology in heart failure

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Background: In the syndrome of heart failure (HF) plasma levels of TNF are elevated, but the relationship between skeletal muscle abnormalities, skeletal muscle biosynthesis and the increased secretion of TNF has not been clarified. The pur-

pose of the current study was to assess the interactions between expression of TNF mRNA in skeletal muscle, plasma levels of TNF, changes in skeletal muscle pathology and intramuscular gene expression of enzymes related to skeletal muscle biosynthesis
Methods: Twenty patients with HF and left bundle branch block who were offered cardiac resynchronization therapy (CRT) were studied. Blood samples and skeletal muscle biopsies were harvested at baseline and after 6 months of CRT. Plasma levels of TNF were measured using a multiplex cytokine immunoassay. Measurements of fibre diameter, interstitial fibrosis, vascular density and inflammation were performed with light microscopy. Point-counting stereology on electron micrographs was used for morphometric registration. Total RNA was extracted from skeletal muscle and quantification of skeletal muscle gene expression of TNF, mitochondrial transcription factor A (TFAM) and nicotinamide phosphoribosyltransferase (NAMPT) was performed.
Results: Alterations in plasma levels of TNF correlated statistically significant with alterations in intramuscular gene expression of TNF ($R=0.56$, $p<0.05$) and were negatively correlated to mRNA levels of TFAM ($r=-0.81$, $p=0.001$) and NAMPT ($r=-0.81$, $p<0.001$) within the skeletal muscle. Alterations in skeletal muscle expression of mRNA levels of TNF were statistically significant correlated with changes in mitochondrial density ($r=-0.561$, $p=0.037$) and borderline statistical significant correlated with changes in capillary density ($r=0.564$, $p=0.036$ Pearson's, $r=0.475$, $p=0.086$ Spearman'rho)
Conclusions: Alterations in plasma levels of TNF co-varies with alterations in intramuscular gene expression of both TNF and skeletal muscle mitochondrial protein synthesizing enzymes. The alterations in intra muscular gene expression of TNF correlate with alterations in skeletal muscle ultrastructure.

P5258 | BENCH
Effects of late exercise on cardiac remodeling and myocardial calcium handling proteins in rats with moderate and large myocardial infarction size

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Purpose: Physical exercise is accepted as a non-pharmacological treatment to attenuate myocardial infarction (MI)-induced cardiac remodeling. However, it is unsettled whether late exercise modulates post-infarction cardiac remodeling differentially according to infarct size. We investigated the effects of a treadmill exercise protocol started at late stage heart failure on cardiac remodeling and myocardial calcium handling protein expression in rats with moderate and large sized MI.
Methods and results: Three months after inducing MI, rats were assigned into sedentary and exercise groups for three months. Exercise rats underwent treadmill at 16 m/min, 40 min/day, 5 days/week, for three months. Transthoracic echocardiography was performed before and after exercise protocol. After assessing infarct size by histological analysis, rats were subdivided into four groups: moderate-MI sedentary (Mod MI-Sed; n=7), Mod MI exercised (Mod MI-Ex; n=7), Large MI-Sed (n=11), and Large MI-Ex (n=10). Before exercise, cardiac changes in infarcted rats were demonstrated by comparing results to a Sham group; alterations were more intense in rats with large [>40% left ventricle (LV) area] than moderate (30–40% LV area) MI size. Systolic function, evaluated by the variation in LV fractional area change between after and before exercise, was statistically improved in exercise than sedentary groups. Protein expression was evaluated by Western blot. Phospholamban was higher in Large MI-Sed than Mod MI-Sed. Exercise attenuated phospholamban increase in Large MI-Ex group. Calsequestrin expression increased in both exercise compared to sedentary groups. L-type calcium channel was higher in Mod MI-Ex than Mod MI-Sed. SERCA2a and Na+/Ca2+ exchanger did not differ between groups.
Conclusion: Late aerobic exercise improves systolic function and modulates intracellular calcium signaling protein expression in rats with moderate and large myocardial infarction. This study is the first to show that treadmill exercise increases myocardial calsequestrin protein expression in rats with both moderate and large sized myocardial infarction.

P5259 | BENCH
Myofilament changes in doxorubicin-induced cardiotoxicity

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Introduction: Cardiomyopathies represent important cause of premature death from heart failure. Several studies demonstrate that administration of doxorubicin, results in cardiac toxicity. Alterations in titin have been reported in patients with this disease. The present work aims to evaluate the early myocardial changes of doxorubicin-induced cardiotoxicity.
Methods: Male New Zealand white rabbits were injected intravenously twice weekly for 8 weeks with doxorubicin (DOX-HF, 1mg/kg, n=17) or with an equivolumetric dose of saline (Control, n=18). Echocardiographic evaluation was performed 1 week before the end of protocol. Myocardial samples were collected to evaluate functional properties of isolated skinned cardiomyocytes in terms of myofilaments active and passive tension and calcium sensitivity (pCa50 and nHill). Sirius-red, hematoxylin-eosin and TUNNEL stained samples were used to quantify myocardial fibrosis, cardiomyocytes area and apoptotic nucleus, respectively. BAX, BCL-2, NF-KB, BECLIN and PINK-1 expression were measured. Titin isoform expression, phosphorylation and degradation were quantified.
Results: DOX-HF group presented cardiac hypertrophy as evidenced by an increase in heart to body weight (2.38±0.09 vs 2.17±0.06mg/g) and by the increased right ventricle (RV) and left ventricle (LV) cardiomyocyte area (RV: 268±12 vs 235±16μm^2 and LV: 380±20 vs 331±27μm^2). Concerning cardiomyocytes function, DOX-HF group presented increased active tension (21.4±1.9 vs 16.5±1.1mN/mm^2) without significant differences in passive tension or myofilaments sensitivity to Ca2+. DOX-HF group showed a decrease in total titin phosphorylation (49.0±6.1 vs 85.2±9.9%), more pronounced in N2B isoform (62.6±9.1 vs 31.0±4.4%), as well as an increase in the ratio between the compliant isoform and the stiffer isoform (N2BA:N2B: 0.5±0.1 vs 0.3±0.1%). Despite similar percentage of apoptotic nuclei DOX-HF presented a significant increase in Bax/Bcl-2 ratio (2.5±0.4 vs 1.3±0.2AU). The extracellular matrix showed marked alterations as confirmed by the significant increase in myocardial interstitial fibrosis in LV from DOX-HF group (12.1±1.4 vs 7.8±1.2%).
Conclusions: This work describes novel and early myocardial effects of doxorubicin-induced cardiotoxicity, including changes at the level of myofilaments (titin), apoptotic-gene expression and extracellular matrix. These early changes precede the initial echocardiographic diagnosis of cardiomyopathy, emphasizing the need for an early detection of cardiac damages associated to cancer treatments in order to allow for therapeutic adjustments and prevent the progression of cardiomyopathy.

BEST POSTERS IN HYPERTENSION IN SPECIFIC POPULATIONS

P5261 | BENCH
Nationwide prevalence, awareness, treatment and control of hypertension among the adult population in Bangladesh

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Objective: To evaluate the prevalence, awareness, treatment and control of hypertension among elderly individuals in Bangladesh.
Methods: Socio demographic and anthropometric data and data on blood pressure were obtained for 7839 adults aged 35 years or more from the biomarker sample of the 2011 Bangladesh Demographic and Health Survey (DHS), which was a nationally representative survey with a stratified, multistage, cluster sampling design. Blood pressure values considered normal are less than 120 mmHg for SBP and less than 80 mmHg for DBP. An SBP value of 120–139 mmHg or a DBP value of 80–89 mmHg is classified as pre hypertension.
Results: Overall, 73 percent of men and women age 35 and older had their blood pressure measured prior to the survey, and 27 percent had never had their blood pressure measured in their life. Overall prevalence of hypertension – defined by systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 or reporting history of hypertension – was found to be 32% in Bangladeshi adult women and 19% in adult men. An additional around 28 percent of women and men are prehypertensive. Higher rate of hypertension is seen in urban population than in rural population. 15.9% of survey participant were told by a doctor having high blood pressure. Hypertension has significant association with age, BMI, educational level, working status, geographical region, wealth status, presence of diabetes. Forty-five percent of women and 57 percent of men are not aware that they have elevated blood pressure. Eleven percent of women and 8 percent of men are aware of their hypertension, but are not treating it. Forty-five percent of women and 36 percent of men with hypertension are taking medication for their condition, but over half of them have not controlled their blood pressure to normal levels. Only 20 percent of women and 16 percent of men with hypertension are taking medication and have their blood pressure under control. Among hypertensive subjects, 25% women and 20% men are aware of their condition, are taking medication to lower the blood pressure, but are unsuccessful in controlling the elevated blood pressure.
Conclusion: Our findings emphasize the need to implement effective and low cost management regimens based on absolute levels of cardiovascular risk appropriate for the economic context. From a public health perspective, the only sustainable approach to the high prevalence of hypertension in Bangladesh is through a strategy to reduce the average blood pressure in the population.

P5262 | BEDSIDE

Age-related change of blood pressure and brachial-ankle pulse wave velocity in native Papuan populations

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Background: Systolic blood pressure (SBP) and arterial stiffness (AS) are closely related and may behave reciprocally as cause or effect and interact in a vicious cycle. SBP and AS increase with age in most developed countries in the world. Age-related increase of SBP, however, is known to be absent in indigenous populations, in part because of extremely low salt intake and high potassium consumption. Age-related AS change in indigenous populations remain unsolved.
Purpose: The aim of this study is to analyze the relationship between SBP and AS, assessed by brachial-ankle pulse wave velocity (baPWV), with age among the indigenous Papuan highland people.
Methods: In 2014, we carried out a field survey as part of health promotion activities, on the indigenous population of a small village located in the central highlands of Papua, Indonesia. Most villagers maintain a traditional lifestyle even today; sweet potato is the staple food for them. One hundred twenty-seven native Papuans aged 16 to 75 years, of which 59% were women, were included in this study. baPWV was measured using a validated automatic device, which simultaneously measures bilateral brachial and ankle blood pressure. Semi-quantitative spot urine salt concentration was estimated using a salt titrator paper and spot urine sodium/potassium (Na/K) ratio was measured using a new device.
Results: Average age of subjects was 38 and 43 years for women and men, respectively. SBP increased with age only in women (r^2 =0.073). Prevalence of hypertension (SBP ≥140 and/or diastolic blood pressure ≥90 mmHg) was 6 (5%) and all were women. baPWV significantly increased with age (r^2 =0.323) in both sexes. Participants under 40 years of age (n=69) had higher body mass index (BMI) (22.3 vs. 19.6 kg/m^2, P<0.001), urine salt concentration (10 vs. 8 g/L, P=0.003) and urine Na/K ratio (1.9 vs. 1.1, P<0.001) than those aged 40 years and over. A multivariate analysis showed that urine salt concentration was independently associated with BMI (β =0.222) and age (β =–0.204). A multivariate stepwise analysis showed that SBP was independently associated with baPWV (β =0.669), salt paper (β =0.208), BMI (β =0.193) and sex (men, β =–0.264), but not with age. baPWV was independently associated with SBP (β =0.482), age (β =0.360), sex (men, β =0.174), pulse rate (β =0.135) and BMI (β =–0.197).
Conclusions: Age-related increase in SBP was still absent in indigenous highland Papuan populations. However, baPWV increased with age, indicating that AS may not always have a causative effect on SBP increase.

P5263 | BEDSIDE

Prevalence of hypertension and other cardiovascular risk factors in participants in the 2014 Hypertension World Day campaign in Italy

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Objective: Aim of our study was to obtain information on prevalence and awareness of hypertension and other cardiovascular risk factors in individuals participating in the 2014 "World Hypertension Day" in Italy.
Methods: During the 2014 "World Hypertension Day", health care providers from 50 hypertension centers affiliated to the Italian Society of Hypertension, spread all over the country, anonymously interviewed individuals spontaneously participating in this campaign. Information on demography, cardiovascular risk factors prevalence, awareness of hypertension and of its consequences was obtained. The average of two conventional blood pressure (BP) measurements, taken in seated position after a few min rest by a validated oscillometric device, was recorded.
Results: Data were collected from 6356 individuals (53.2% females, 46.8% males) aged 57.8 years. (18–105 years). 43.6% of subjects were aware of being hypertensive, 89.9% being treated. In this cohort active and former smokers were respectively 19.2% and 22%, 28.6% reported hypercholesterolemia and 8.3% diabetes. Mean systolic BP>139mmHg was found in 34.8% and mean diastolic BP>89mmHg in 18.3% of the entire cohort and in 47.7% and 23.5% of aware hypertensive individuals, respectively. In 14.5% of participating subjects and in 19.6% of aware hypertensives both systolic/diastolic BP were found above 139/89mmHg respectively. On average, BP was higher in aware hypertensive individuals, in spite of being treated, than in the overall cohort (139.6/81.7±19.7/14.5 vs 133.1/79.7±20.3/15 mmHg, respectively, p<0.005). Awareness of hypertension complications was imperfect, acute myocardial infarction, stroke and renal failure being recognized as consequences of hypertension by 85.1%, 61.6% and 28.6% of individuals, respectively.
Conclusions: Our data, obtained in Italy at the time of the 2014 World Hypertension Day show a yet high hypertension prevalence, accompanied by an unsatisfactory awareness of its complications and by a frequent occurrence of other cardiovascular risk factors in participants in this initiative. Even considering that these individuals may not be fully representative of the general Italian population, our results strongly indicate that more efforts are still needed to improve hypertension control and to increase patients' awareness of the risks associated to this condition.

P5264 | BENCH

Association between CXCL13 gene polymorphism and essential hypertension in Tatars from Russia

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Background: Genome-wide association studies have identified different hypertension-susceptibility loci in the populations of European ancestry. However, fine-mapping of blood pressure related loci has been complicated by the existing differences in genetic variation across populations. The population of Tatars residing in the Volga-Ural region of Russian Federation, particularly in the Republic of Bashkortostan, has a distinct genetic structure characterized by combination of Mongoloid and Caucasoid components, which makes it an interesting object for genetic study.
Aim: The aim of the present study was to investigate a possible association between hypertension and the loci in six candidate genes in individuals of Tatar origin.
Material and methods: We performed screening for SNPs in CXCL13, CCL8, CCL16, CCL17, CCL18, and CCL23 genes in the group of 522 Tatars from the Republic of Bashkortostan, Russia (213 patients with essential hypertension (mean age 42.24±8.27) and 309 healthy individuals (mean age 43.58±7.13) without history of cardiovascular or any other chronic disease).
Results: An association was detected between CXCL13 rs355689 polymorphism and essential hypertension: *T/T genotype and *T allele were associated with an increased risk of hypertension (OR=2.51, P=3.06*10–6 and OR=1.87, P=0.0001, respectively), while heterozygous genotype and *C allele carrier status indicated a decreased risk of the disease (OR=0.35, P=2.13*10–6 and OR=0.053, P=0.0001, respectively). Analysis of association between EH and allele/genotype combinations revealed many combinations, which differed in frequency in the group of EH patients and in control group. Eleven combinations remained significantly associated with EH after the correction for multiple testing was applied. The most significant association was observed for CXC13*T/T+CCL8*T+CCL17*C combination, that was more frequent in the group of patients with essential hypertension (OR=2.62, PBonf=0.0007), and two combinations that appeared to be protective against hypertension – CXCL13*C+CCL8*C+CCL18*T/T (OR=0.32, PBonf=0.0002), and CXCL13*C+CCL18*T/T (OR=0.33, PBonf=0.0002).
Conclusion: CXCL13 rs355689 polymorphism was found to be significantly associated with essential hypertension in Tatars., both individually and in combination with other chemokine genes.

POSTER SESSION 6

ATRIAL FIBRILLATION I

P5265 | BEDSIDE

Prognostic impact of resting heart rate in atrial fibrillation in octogenarians with systolic heart failure

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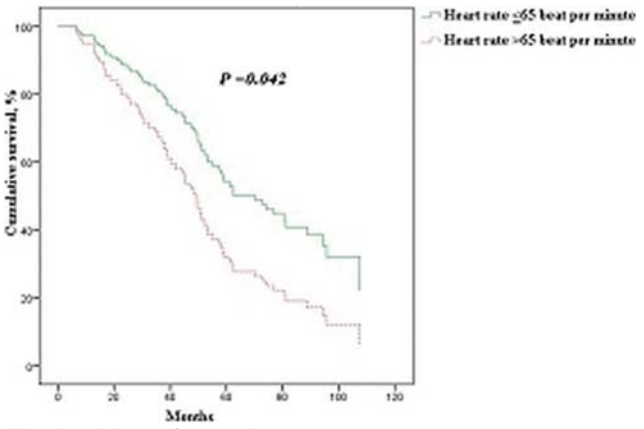
Background: In patients with heart failure with reduced ejection fraction (HFREF), it is well known that lower resting heart rate (HR) is associated with better survival. But whether this is true in octogenarians, in particular in heart failure concomitant with atrial fibrillation (AF), has not been studied. This is highly clinically relevant since main body of heart failure patients are elderly with high prevalence of AF.
Purpose: To study the prognostic impact of resting HR in patients with HFREF concomitant with AF in octogenarians after optimal uptitration of beta-blockers (BBs) and angiotensin converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs).
Methods and results: Patients (n=185) aged ≥80 years with HFREF and left ventricular ejection fraction ≤40% were included between January 2000 and January 2008 from two University hospitals. Of whole study population; 65% was male; 54% (n=100) had AF; mean age and mean EF were 83 years and 33%, respectively. After optimal uptitration of BBs and ACEIs/ ARBs, mean HR in patients with AF was 73 +15 beat per minute (BPM), 36% had resting HR <65 BPM. After ≥5 years of follow up, all-cause mortality in the whole population was 77%. Among patients with AF all-cause mortality was significantly lower in patients with HR ≤65/min (63%) compared with those with HR>65 (80%). Using Cox proportional-hazard regression analysis adjusted for clinically important baseline variables and doses of ACEIs/ARBs and BBs, resting HR ≤65/min remained an independent prognostic factor for improved survival from all-cause mortality compared with rest HR >65/min in patients with AF (HR 0.5, 95% CI 0.3–0.9, P 0.042).



Adjusted survival curves,Cox-regression

Conclusions: In Octogenarians with HFREF and AF, resting HR ≤65 BPM is associated with improved survival from all-cause mortality.

P5266 | BEDSIDE
Left atrium size further stratify the risk of left atrial thrombus in patients with non-valvular persistent atrial fibrillation

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Objective: This study sought to investigate the impact of left atrium size on left atrial (LA) thrombus in patients with non-valvular persistent atrial fibrillation (AF).
Methods: In a prospectively established database, patients with AF underwent transesophageal echocardiography prior to AF ablation were screened from January 2007 to June 2010. Exclusive criteria included paroxymal AF, vavular AF, deep vein thrombus, pulmonary embolism, on warfarin, redo procedure. Of 1524 patients, 367 patients (male 267, female 100) with mean age 56±11 (26–89) were enrolled.
Results: Thirty-two (8.7%) patients had LA thrombus. The LA diameter, left ventricular end diastolic diameter, left ventricular end systolic diameter were significantly larger in thrombus group than non-thrombus group. Left ventricular ejection fraction was significantly lower in thrombus group than non-thrombus group. CHA2DS2Vasc score did not differ between the two groups. The area under the receptor-operating curve for age predicting LA thrombus was 0.656 (0.563–0.750),the best cut-off point was 42.5mm. The incidence of LA thrombus was significantly higher in patients with LA diameter ≥42.5mm than those with LA <42.5mm (14.0% VS. 5.1%,P=0.003). In univariate analysis, LA diameter ≥42.5mm increased the risk of LA thrombus with odds ratio 3.05 [95% confidence interval (1.42–6.53), P=0.004]. In multivariate analysis, after adjustment of CHA2DS2Vasc score, left ventricular end diastolic diameter, left ventricular end systolic diameter, left ventricular ejection fraction, LA diameter ≥42.5mm was an independent risk factor of LA thrombus (odd s ratio 2.77, 95% confidence interval 1.17–6.57, P=0.021). In a subanalysis, LA ≥42.5mm helped to identify higher stroke risk only in patients with CHA2DS2Vasc score = 1 (Table 1)

Table 1

	n	LA thrombus (LA >42.5mm vs <42.5mm)	Odds ratio (LA >42.5mm vs <42.5mm)	95% CI	P
CHA_2DS_2-VASc = 0	97	4/32 (12.8%) VS2/65 (3.1%)	4.50	0.78–26.02	0.090
CHA_2DS_2-VASc = 1	108	8/46 (17.4%) VS2/62 (3.2%)	6.32	1.27-31.34	0.017
CHA_2DS_2-VASc ≥2	162	9/72 (12.5%) VS7/ 90 (7.8%)	1.69	0.60–4.80	0.317

Left atrial size further clarify stroke risk in different CHA2DS2Vasc score.

Conclusion: LA enlargement was an independent risk factor of LA thrombus in patients with non-vavular persistent AF.
Acknowledgement/Funding: High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)

P5267 | BEDSIDE
Effect of digoxin on all-cause mortality in patients with atrial fibrillation: a population-based cohort study

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Background: Previous studies on digoxin use in patients with atrial fibrillation (AF) and the risk of all-cause and cardiovascular mortality have reported conflicting results. Most of these studies were not able to take into account the severity of possible associated HF. We analyzed the effects of digoxin on mortality in unselected AF patients.

Methods: We conducted a population-based retrospective cohort study of patients admitted to a cardiology department from January 2000 to January 2011. Survival analysis used a Cox model controlled with propensity scores derived from multivariate logistic regression model based on all characteristics including NYHA functional class, eGFR, and BNP at baseline. In 8871 patients with AF, digoxin was prescribed to 2159 patients (24.3%) of whom 618 (28.6%) received it transiently. Digoxin was defined as "full dose" treatment (0.25mg daily) for 1202 patients (55.7%) and "low dose" treatment (0.125mg daily) for 957 patients (44.3%).
Results: Patients treated with digoxin were significantly older, with more heart failure and lower use of beta-blockers than non-users. Crude mortality was higher in patients on digoxin (17.1% vs 11.3%; Hazard Ratio [HR] 1.27; 95% Confidence Interval [CI] 1.12–1.44; p=0.0001), especially for those on low dose treatment (HR 1.54; 95% CI 1.32–1.81; p<0.0001). Based on individual propensity scores, there was no longer a significant difference in mortality related to digoxin use per se (HR 0.89; CI 95% 0.70–1.13), regardless of the presence (HR 0.90; 95% CI 0.78–1.04) or absence (HR 0.94; 95% CI 0.72–1.23) of underlying heart failure, digoxin dose regime (HR 1.16; 95% CI 0.92–1.45) or persistence of treatment (HR 1.06; 0.83–1.35).
Conclusion: In a large contemporary cohort of AF patients with more granular data than claims based studie, digoxin use was associated with an increased mortality. When differences in patient characteristics were accounted for, digoxin use had a non-significant effect on all-cause mortality regardless of dose, persistence of use, or underlying HF.

P5268 | BEDSIDE
Increased levels of both NT-proBNP and MR-proANP after initiation of atrial fibrillation: results from an invasive electrophysiological study

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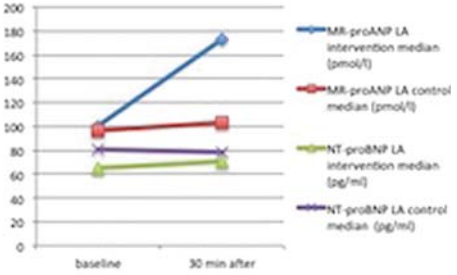
Background: It is known that natriuretic peptide levels are elevated in patients with atrial fibrillation (AF) but the effect on these levels of initiation of AF has not yet been studied.
Purpose: We aimed to study the reaction to initiation of AF on the N-terminal fragment of precursor B-natriuretic peptide (NT-proBNP) and the mid-regional fragment of the N-terminal precursor of atrial natriuretic peptide (MR-proANP) 30 minutes after the onset of AF.
Methods: 45 patients eligible for radiofrequency ablation (RFA) of AF were randomized to either AF initiation or to control. Freedom from AF prior to RFA was assured by transtelephonic ECG. Peptides were collected from the femoral vein (fv), the coronary sinus (CS) and the left atrium (LA) immediately after transseptal puncture, prior to AF initiation (baseline) and 30 minutes after AF initiation.
Results: In total, 26 patients were induced to AF and 19 served as controls. There were no differences in baseline characteristics between the groups. Using repeated measures analysis of variance after normalizing peptide levels with logarithmic transformation, we found that MR-proANP levels rose significantly after AF initiation compared to controls in all sites; fv (p<0,001), CS (p<0,001) and LA (p<0,001). NT-proBNP levels increased significantly only in LA in the AF group compared to controls (p<0,001).



Reaction of NT-proBNP and MR-proANP in LA after initiation of AF, LA:left atrium, AF:atrial fibrillation, NT-proBNP: N-terminal fragment of precursor B-natriuretic peptide, MR-proANP: mid-regional fragment of the N-terminal precursor of atrial natriuretic peptide(NT-proBNP: $p_{time*intervention}$<0,001, MR-proANP: $p_{time*intervention}$<0,001)

Conclusions: MR-proANP levels rose significantly as early as 30 minutes after AF initiation, possibly due to mobilization and release from atrial myocyte granule. Furthermore, the significant increase in NT-proBNP levels in LA after AF initiation is surprising since its synthesis time is about 90 minutes and there are no previous data indicating that NT-proBNP can be pre-produced and stored in myocyte granule.
Acknowledgement/Funding: County Council of Östergötland, the Carldavid Jönsson Research Foundation, the Heart Foundation, Linköping University and Biosense Webster

P5269 | BEDSIDE

Atrial fibrillation as an independent risk factor for depression in elderly population

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Background: Depression is a frequently comorbid condition in cardiovascular diseases. In contrast to coronary artery disease and heart failure we have a limited amount of data documenting the increased prevalence of depression in patients with atrial fibrillation (AF). Available results from studies with a small number of patients suggest a significant and perhaps two-way relationship between the two diseases. Due to the increasing with age incidence of both atrial fibrillation and its complications, the above issue is a particularly important in elderly patients.
Aim: To determine the frequency of depression in patients with a history of AF in a large group of patients≥65 years of age.
Methods: The data were collected as part of the nationwide PolSenior project (2007–2011). Of 4979 individuals (age range 65–104 years), data on self-reported history of AF were available for 4677 subjects (93.9%). Finally, the 4049 participants without suspected moderate or severe dementia in Mini Mental State Examination test were assessed with the 15-item Geriatric Depression Scale (GDS), and a score of 6 points and more was regarded as suspected depression.
Results: Mean age±SD of the study population was 78.1±8.3 years; 52% were males. The history of AF was reported by 788 (19.5%) subjects. The proportion of female subjects, obese individuals and the number of cardiovascular comorbidities, frequency of reported diabetes, strokes, falls, osteoporosis/fractures were higher in AF subgroup. In univariate analysis the self-reported AF history was connected with 41% increase of suspected depression (29% vs 41%; $p<0.0001$). In multivariate logistic regression AF remained an independent predictor of depression (OR=1.42, 95% CI: 1.16–1.73), stronger than heart failure, diabetes or coronary artery disease.
Conclusions: In geriatric population AF is connected with higher frequency of depression. This association is independent of other cardiovascular comorbidities and stroke history and certainly influences the quality of life of these subjects.
Acknowledgement/Funding: The study was implemented under the publicly-funded project No. PBZ-MEIN-9/2/2006 by the Ministry of Science and Higher Education in Poland

P5270 | BEDSIDE

Prevalence of erectile dysfunction in atrial fibrillation patients - cross-sectional, epidemiological study

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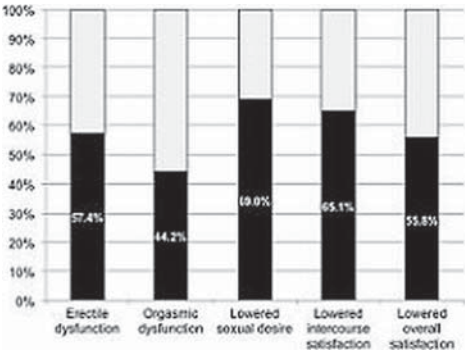
Introduction: Sexual dysfunctions, especially erectile dysfunction (ED) are a major problem in cardiovascular patients. They are caused by cardiovascular risk factors including low-grade inflammation process, endothelial dysfunction, oxidative stress, and vascular alterations. The same mechanisms are some of the main causes and/or consequences of atrial fibrillation (AF). To this day, literature provides no cross-sectional data on the prevalence of sexual dysfunction in AF.
Purpose: The study aimed to determine the prevalence of sexual dysfunction in consecutive male patients with AF.
Methods: A cross-sectional survey of adult male patients with a primary diagnosis of AF was conducted at University Cardiology Departments from 2013 to 2014. During the enrolment participants were either electively hospitalized with a primary diagnosis of AF, or had a scheduled outpatient visit. Sexual dysfunctions were assessed using IIEF score.
Results: 129 consecutive AF patients (mean age 57.0±11.8 years) were analyzed. Hypertension was present in 60.5%, diabetes in 22.5%, dyslipidemia in 46.5%, smoking in 18.6% and 45.7% had a family history of cardiovascular disease. 86.8% of patients had any kind of sexual dysfunction. ED was present in 57.4% of patients. 44.2% of patients had orgasmic dysfunction, 69.0% had lowered sexual desire, 65.1% had lowered intercourse satisfaction, and 55.8% had lowered overall satisfaction.



Conclusions: Sexual dysfunctions are highly prevalent in AF patients and are not only limited to ED, but also include dysfunction of orgasmic function, desire, or general satisfaction. In part, the presence of the sexual dysfunctions is probably caused by classical cardiovascular risk factors highly prevalent in AF patients, but the impact of AF itself, cannot be underestimated.

P5271 | BEDSIDE

The association of non-0 blood groups with spontaneous echo contrast. Is there a place for "A" blood group at thromboembolic risk scores in atrial fibrillation

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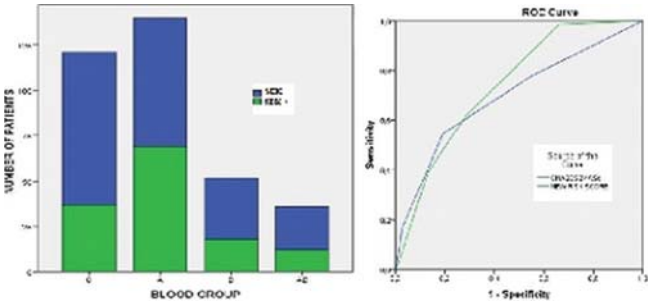
Introduction: Non-O blood groups have an association with a higher risk of the arterial and venous thrombosis owing to the relation of non-O blood groups with vWF and FVIII levels. Spontaneous echo contrast (SEC) as a manifestation of red cell aggregation, constitute a risk for thromboembolism and mortality. We aimed to assess the relation of ABO blood groups with SEC formation in non-valvular AF patients.
Materials and methods: 349 patients who were diagnosed as non-valvular AF and performed TEE before cardioversion or AF ablation procedure between 2010–2015, were included. The patients were categorized into two groups as non-O blood groups (228 patients) and 0 blood group (121 patients).
Results: Non-O blood groups had higher SEC prevalence than O blood group (30.6% vs 43.4% p=0.019). In the subgroup analysis, A blood group had higher SEC prevalence than other groups (49.3% p=0.013). CHA2DS2VASc score was correlated with the grade of SEC (β=0,534 $p<0.001$). Also, A blood group was quantified as an additional risk factor and incorporated into CHA2DS2VASc score by adding 1 point. New score was significantly correlated with SEC grade (β=0.577 $P<0.001$). In ROC analyses, a cut of value 1.5 score for new risk score has 61.8% sensitivity and 71.4% specificity for prediction of SEC with a higher area under the curve comparing with CHA2DS2VASc score (AUC=0.739 and AUC=0.697, respectively).



Conclusion: In conjunction with other risk factors, non-O blood types, especially A blood type, were demonstrated as independent predictors of SEC in non-valvular AF. Our study proposed A blood group as an additional risk factor to traditional risk scores for thromboembolism. There is a necessity of prospective, larger studies to evaluate the effect of blood groups on thromboembolic events.

P5272 | BEDSIDE

Sex-related differences in epidemiologic and clinical presentation of atrial fibrillation in the Balkan countries - insights from the BALKAN AF Snap Shot Survey

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Background: Compared to other European Regions, data on sex-related differences in epidemiologic and clinical aspects of atrial fibrillation (AF) in the Balkan Region are sparse.
Purpose: We report an interim analysis from the Balkan-AF Survey addressing sex-related differences in epidemiologic and clinical presentation of AF patients.
Methods: A 12-week prospective snapshot survey (December 2014-February 2015) of consecutive non-valvular AF patients seen by internal medicine specialists or cardiologists in university/non-university centres in- and outside the capital

cities was conducted in Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, Romania and Serbia (a region with ~45 million inhabitants). Data were collected via an electronic case report form.
Results: The interim analysis included a total of 2080 AF patients. Principal sex-related differences in clinical presentation are presented in the Table.

Differences in clinical presentation

Clinical characteristics	Females (n=936)	Males (n=1144)	P value
Age (mean±SD)	71.6±9.7	67.0±11.2	<0.001
Inclusion setting – hospitalization (%)	71.6	69.3	0.267
Emergency admissions (%)	73.1	65.4	0.002
First-diagnosed AF (%)	23.7	23.2	0.795
Paroxysmal AF (%)	30.7	24.9	0.011
Symptomatic AF (%)	80.9	77.2	0.040
Palpitations (%)	61.7	57.6	0.096
Chest pain (%)	30.9	29.4	0.518
Dyspnoea (%)	64.8	59.2	0.022
Fatigue (%)	54.4	48.8	0.026
General non-wellbeing (%)	30.5	25.4	0.023
Fear/anxiety (%)	16.3	9.6	<0.001
Hypertension (%)	82.3	78.6	0.041
Coronary artery disease (%)	27.6	34.6	0.001
Coronary angiography (%)	36.7	59.5	<0.001
Stent implantation (%)	18.6	33.3	<0.001
Heart failure, HF (%)	43.3	43.7	0.589
HF-preserved ejection fraction (%)	15.8	12.6	0.036
Mild valvular heart disease (%)	80.0	67.4	<0.001
Diabetes mellitus (%)	27.2	24.3	0.143
Peripheral arterial disease (%)	2.9	6.1	0.001
COPD (%)	9.6	15.8	<0.001
Chronic kidney disease (%)	13.6	16.3	0.085
Anaemia (%)	17.9	11.0	<0.001
Dementia (%)	4.1	1.8	0.003
Thyroid disease (%)	16.5	6.4	<0.001
Stroke/TIA (%)	13.9	12.3	0.295
Systemic embolism (%)	1.2	0.8	0.141
Pulmonary embolism (%)	2.7	1.2	0.022
Previous bleeding events (%)	5.8	5.2	0.561
CHA_2DS_2-VASc ≥2 (%)	87.1	77.6	<0.001
HASBLED >3 (%)	34.2	28.1	0.003

Conclusions: Female AF patients in the BALKAN AF Survey were older, more symptomatic, with more comorbidities and required more emergency hospitalizations. Uncontrolled hypertension was more prevalent in females and they were less likely to receive invasive diagnostic or therapeutic procedures for vascular disorders. Anemia and dementia were more prevalent, and thromboembolic and bleeding risk was higher in females, bearing implications for antithrombotic treatment.

P5273 | BEDSIDE
Do all AF patients with a CHA2DS2-VASc score of 2 (males) or 3 (females) have the same risk of ischemic stroke? A nationwide population-based cohort study

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Background: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and increases risk of stroke. The CHA2DS2-VASc score is recommended by American and European guidelines for stroke risk stratification in AF. However, not all risk factors in CHA2DS2-VASc score were associated with an equal risk. Even for patients with a same CHA2DS2-VASc score, their stroke risk may be different. Thus we aim to investigate the risk of stroke in patients with a score of 2 (males) or 3 (females) composed of different risk factors.
Methods: From 1996 to 2011, a total of 186,570 AF patients without use of anti-platelet or anti-coagulant agents were identified from the Taiwan AF cohort. Among these patients, 18,196 males having a CHA2DS2-VASc score of 2 and 13,022 females having a CHA2DS2-VASc score of 3 were enrolled. The study end point was ischemic stroke. Risks of ischemic stroke of patients with different combinations of risk components were analyzed.
Results: During the follow up, 2,832 males and 2,332 females experienced ischemic stroke. Age ≥75 years and hypertension plus age 65–74 years accounted for the risk score in more than 50% of patients. Patients with diabetes mellitus (DM) aged between 65–74 years had the highest risk of stroke (annual rate = 4.77% for males and 5.11% for females). Cox regression ananlyses demonstrated that the risk of stroke was highest for patients with an age ≥75 years or DM with an age 65–74 years compared to those with a CHA2DS2-VASc score of 0 (males) or 1 (females) with a hazard ratio greater than 4 (Figure 1).
Conclusions: In this nationwide cohort study, age ≥75 years and DM with an age 65–74 years possessed a higher risk of ischemic stroke in AF patients with a CHA2DS2-VASc score of 2 (males) or 3 (females) compared to other risk components.

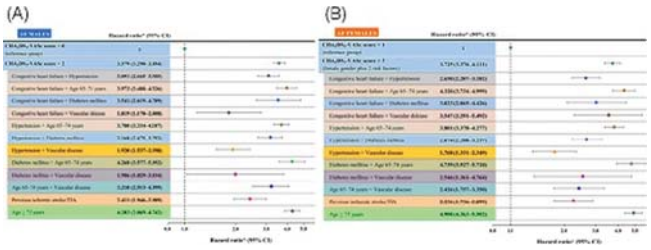

Figure 1. Risk of ischemic stroke

P5274 | BEDSIDE
CHA2DS2-VASc score predicted extensive substrate and poor outcome of catheter ablation of persistent atrial fibrillation

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Objective: This study sought to explore if CHA2DS2VASc score can predict substrate for persistent atrial fibrillation (AF) and outcome of catheter ablation of AF.
Methods: In this prospective study, 116 patients underwent catheter ablation of persistent AF were enrolled. Left atrial geometry (LA) was reconstructed with a 3.5 mm tip ablation catheter with fill-in threshold 10 in CARTO system. The mapping catheter was stabled at each endocardial location for at least 3 seconds for recording. The electrogram recordings at each endocardial location were analyzed with a custom software embedded in the CARTO mapping system. Interval confidence level (ICL) was used to characterize complex fractionated atrial electrograms (CFAEs). As the default setting of the software, ICL more than or equal to 7 was considered sites with a highly repetitive CFAEs complex. CFAEs index was defined as the fraction of area of ICL more than or equal to 7 to the left atrial surface. The CFAEs index and outcome of catheter ablation among different CHA2DS2VASc groups were compared.
Results: Of the 116 patients, 33 patients had CHA2DS2VASc = 0, 31 patients had CHA2DS2VASc = 1, 52 patients had CHA2DS2VASc ≥2. There are significant differences of left atrial surface (121.2±18.9 cm^2, 133.6±23.8 cm^2, 133.9±16.1 cm^2, P=0.008), left atrial volume (103.6±24.8 ml, 118.3±27.8 ml, 120.9±20.9 ml, P=0.05) and CFAEs index (44.6±22.4%, 54.2±22.2%, 58.7±23.1%, P=0.023) among the three groups. There are no difference of ICLmax, ICLmin, CFAEs spatial distribution among the three groups. After a mean follow-up of 13±8 months, the recurrence rate were 36.4%, 35.5%, 55.8% among the three groups (P=0.025) (Figure 1).

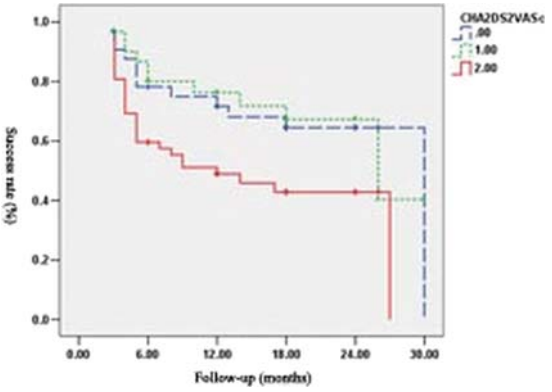

Figure 1

Conclusion: A high CHA2DS2VASc score was associated with extensive AF substrate and poor outcome of catheter ablation of persistent AF.
Acknowledgement/Funding: High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)

ATRIAL FIBRILLATION II

P5275 | BEDSIDE
Diastolic electrocardiographic parameters and diastolic index predict postoperative atrial fibrillation

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Background: Postoperative atrial fibrillation (POAF) is an important cause of morbidity and mortality. Diastolic dysfunction (DD) has significant pathological effects on atrial structure and function, many of which are proarrhythmic. It has been shown that diastolic ECG parameters like PQ, QTc, Tend-P, Tend-Q and a combined novel ECG index (Tend-P/[PQ x Age]) provides a good diagnostic performance for the recognition of DD. In our study, we aimed to investigate the relation between diastolic ECG parameters, novel diastolic ECG index and POAF in patients undergoing elective coronary artery bypass surgery (CABG).
Methods: Patients who will undergo CABG electively without a history of atrial fibrillation were included in the study. POAF was defined as at least 30-second

duration of AF detection. PQ interval was calculated from the beginning of the P wave to the beginning of the QRS complex manually. The QTc interval was calculated using the Bazett formula, Tend-P and Tend-Q intervals were calculated as: RR minus PQ minus QT for Tend-P and RR minus QT for Tend-Q. Diastolic ECG index was calculated as follows; Tend - P/[PQ x Age].
Results: A total number of 311 patients (age 60.1±8.7 years, %34,1 women) were included in our study prospectively. Only 71 (22.8%) of them developed POAF during their postoperative follow-up. Patients were divided into two groups according to observation of AF; Group-1 (POAF+) and Group-2 (POAF-). Demographics and transthoracic ECG parameters are similar between two groups.
QT intervals were similar in both groups, however PQ interval (161.4±32.6 vs 147.0±15.1 ms, $p<0.01$) and QTc (449.3±36.3 vs 426.9 vs 47.6) was significantly longer in Group-1. Mean heart rate was significantly higher in Group-1 and TendQ, TendP and QRS intervals were significantly shorter in Group-1. Diastolic ECG index was significantly different between two groups (0.040±0.017 vs 0.058±0.010, $p<0.01$). Diastolic ECG index was also significantly negatively correlated with POAF ($r=-0.463$, $p<0.01$). Univariate analysis revealed age, hypertension, preoperative calcium levels, heart rate, Tend-P, Tend-Q, PQ intervals and QTc may be predictors of POAF occurrence. Multivariate analysis showed ECG parameters like Tend-P, Tend-Q, QTc, PQ intervals with heart rate were only statistically significant predictor of POAF.
Conclusion: Diastolic ECG parameters and novel diatolic index predicts POAF after elective CABG operation. From clinical point of view, preoperative assessment of these parameters could allow identification of high risk patients who might benefit prophylactic treatment.
Acknowledgement/Funding: This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

P5276 | BEDSIDE
Risk prediction in atrial fibrillation. Comparison between the CHADS2, CHA2DS2-VASc score in a large contemporary cohort of patients with incident non-valvular atrial fibrillation

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Introduction: The 2 most commonly used risk scores to predict thromboembolic events in patients with atrial fibrillation - AF are the CHADS2 and the CHA2DS2-VASC. There is a controversy as to which score performs better.
Aim: To compare and describe the predictive ability of these risk scores in a large contemporary cohort of patients with non-valvular atrial fibrillation.
Methods: TWe used a computerized database of 2,420,000 adults, includes data of community clinic visits, hospital discharge records, medical diagnoses, medications, medical interventions and laboratory test results. During 2004–2012, 98,811 patients had nonvalvular AF.
Results: The distribution of risks is presented in figure. The rate of stroke and death (per 1000 person year) is shown based on risk category in table. The predictibe ability of CHADS2 was somewhat better for prediction of stroke (c-statistic 0.65) as compared to the CHADS VASC score (c statistic 0.64), and they performed similarly for predicting mortality (c -statistic of 0.69 for both) and the net reclassification index was decreased when moving from the CHADS2 to CHA2DS2-VASC score by 14% for mortality and by 7% for stroke.

Death and stroke based on risk category

Risk class	Percent in population (%)	Stroke rate (%)	Death rate (%)
CHADS2			
0	65.7	1.4	10
1	22	3.3	21
≥2	12.3	6.6	31
CHADS-VASc			
0	87	0.8	8.5
1	9	1.6	10
≥2	4	5.8	41

Conclusions: Both risk scores perform similarly but the CHADS2 performed somewhat better for ischemic stroke prediction and significantly better for prediction of mortality.
Acknowledgement/Funding: Pfizer

P5277 | BEDSIDE
Effectiveness of structured hospital based nurse-led atrial fibrillation clinics: A comparison of a real-world population versus a clinical trial population

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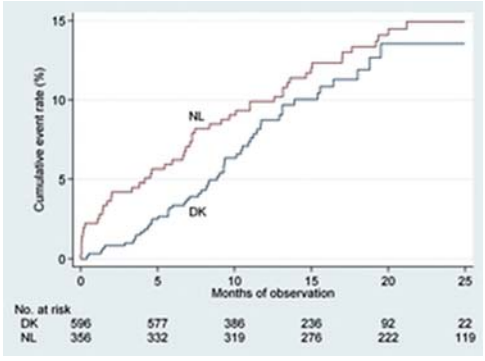
Aims: A randomized trial has documented that structured nurse-led Atrial Fibrillation (AF) service is superior to conventional AF service, but there is a need for more data, confirming feasibility and outcome in a real-world setting. We compared patient outcome in nurse-led structured hospital AF clinics between real-world patients from Denmark (DK) and from the randomised trial on efficacy of a nurse-led AF clinic reported from the Netherlands (NL), with respect to a composite outcome of CV hospitalization and CV death.
Methods: Real-world data consisted of baseline and follow-up data. All patients were referred by cardiologists. The AF nurse specialist provided patient education, risk factor control, and stimulated empowerment and compliance in these patients. During follow-up treatment was adjusted according to clinical guidelines, supervised by a cardiologist. Patient education was repeated and compliance was controlled. The study size was powered as a non-inferiority study. Outcome measures were adjudicated by same principles in both countries.
Results: 596 patients from DK and 356 patients from NL were included. There were no significant differences between groups with respect to age, body mass index, type of AF, CHA2DS2VASc score and co-morbidity. The composite primary end point occurred with an incidence rate of 8.0 in DK and 8.3 per 100 person years in NL, crude HR 0.83 (95% CI 0.56–1.23). Adjustment for covariates and medical treatment did not substantially change HR.



Cumulative event rate of primary outcome

Conclusion: Structured nurse-led hospital based AF service is feasible and effective, and patient outcome is in real life hospital based structured AF service is as least as good as in the setting of a randomized trial.

P5278 | BEDSIDE
Left atrial thrombosis in patients with atrial fibrillation undergoing cardioversion

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Introduction: According to published data, there is a small but significant risk of developing left atrial thrombosis (LAT) and potentially disastrous thromboembolism in patients with atrial fibrillation (AF) undergoing cardioversion, even if they are adequately anticoagulated in compliance with current guidelines. A predictor of LAT would be of great clinical value.
Aim: To establish whether there is an association between the serum concentration of fibrinogen and the prevalence of LAT in patients with AF undergoing cardioversion.
Methods: We conducted an observational study involving 287 patients with AF scheduled for cardioversion. Precardioversion transthoracic and transesophageal echocardiography was performed in 251 cases, regardless of their anticoagulation status. If LAT had been detected, the patient was rescheduled for cardioversion following 30 days of anticoagulation. Clinical, echocardiographic and biochemical data were recorded. Mann–Whitney U test was conducted to compare the differences between patients with LAT and patients without LAT in continuous variables and χ^2 test and Fisher's exact test for categorical variables. To assess the association of serum fibrinogen concentration with LAT, binary logistic regression models were built with LAT as outcome. For all analyses, a double-sided $p<0.05$ was considered statistically significant.
Results: 10% (25) of the patients were positive for left atrial thrombi. There was no difference between the LAT group and the no LAT group in the CHADS2-Vasc score or haemoststic parameters like INR and APTT. Patients with LAT had higher levels of fibrinogen 4 (3.3–4.6) vs. 3.4 (2.9–4.1) g/L, p=0.012. Among the patients with LAT who were rescheduled for cardioversion, there was a higher concentration of fibrinogen in patients with persistent LAT as opposed to patients in whom the thrombus had dissolved, 4.1 (4.1–4.7) vs. 3.6 (3.25–3.85) g/L respectively, p=0.035. The fibrinogen concentration was identified as an independent predictor of LAT in logistic regression models, OR=1.77, CI: 1.056–2.975, p=0.03.
Conclusions: The serum concentration of fibrinogen is positively associated with the prevalence of LAT in patients with AF undergoing cardioversion. It can also be a predictor of LAT resolution after anticoagulation therapy. Large-scale studies conducted in different populations are required to more comprehensively and reliably assess the relationship of serum fibrinogen concentration, and the occurrence of LAT in patients with AF.

P5279 | BEDSIDE

Urinary 11-dehydro-thromboxane B2 is associated with cardiovascular events and mortality in atrial fibrillation patients

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Background: Non-Valvular Atrial Fibrillation (AF) patients show high residual cardiovascular risk despite oral anticoagulants. Urinary 11-dehydro-thromboxane B2 (TxB2) is associated with an increased risk of cardiovascular events (CVEs), but its predictive value in AF patients is unknown.
Purpose: Aim of this study was to assess whether urinary 11-dehydro-TxB2 is a predictor of CVEs in anticoagulated patients with AF.
Methods: Prospective single-center cohort study, including 864 AF patients treated with vitamin K antagonists (VKAs). Mean time of follow-up was 30.0 months yielding 2062 person-years of observation. Urinary 11-dehydro-TxB2 was measured at baseline. The primary end-point was the occurrence of a CVE including fatal/nonfatal myocardial infarction and ischemic stroke, transient ischemic attack, cardiac revascularization and cardiovascular death.
Results: Mean age of patients was 73.1 years, and 43.6% were women. Median 11-dehydro-TxB2 levels were 100 [IQR 50–187] ng/mg of urinary creatinine. Overall, the anticoagulation control was adequate (63.9% of mean time in therapeutic range). A CVE occurred in 98 (11.3%) patients, 55 were cardiovascular deaths. At baseline, 11-dehydro-TxB2 levels were higher in patients with a CVE compared to those without (186 [107–400] vs. 98 [52–170], $p<0.001$). An increased rate of CVEs (log-rank test, $p<0.001$) and cardiovascular deaths ($p<0.001$) was observed across tertiles of 11-dehydro-TxB2. Cox proportional hazards analysis showed that tertile of 11-dehydro-TxB2 (3rd vs. 1st hazard ratio [HR]:4.71 95% confidence interval [CI] 2.46–9.03, $p<0.001$), age $\geq$75 years (HR: 1.79 95% CI1.17–2.74, p=0.007), diabetes (HR: 1.72 95% CI 1.07–2.76, p=0.0245), history of stroke/TIA (HR: 1.96 95% CI 1.24–3.10, p=0.0042) and MI/coronary heart disease (HR: 1.62 95% CI 1.04–2.53, p=0.0322) were predictors of CVEs.
Conclusions: Urinary 11-dehydro-TxB2 levels predict residual risk of CVEs and cardiovascular mortality in AF patients despite treatment with oral anticoagulants.

P5280 | BEDSIDE

Rate control or rhythm control - what do we choose more often in patients with higher thromboembolic risk? Data from a multicenter real-life registry

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Introduction: In atrial fibrillation (AF) patients both management strategies – rate control and rhythm control seem to be equally safe and effective. Decision on the way of patients treating depends on patients and doctors preferences. However, in everyday clinical practice we observe some disparities between patients on rate and rhythm control strategies.
Purpose: The aim of the study was to compare the group of persistent AF patients in whom rhythm control strategy is chosen to those with rate control, in terms of thromboembolic risk and general clinical characteristics.
Methods: We analyzed data from a prospective multicenter registry of continuous AF patients. All patients included in the study were hospitalized in one of the participating clinic with a primary diagnosis of paroxysmal AF between 2011 and 2014. Patients had their medical data collected by a qualified physician basing on the medical records or a de novo diagnosis during the current hospitalization. Thromboembolic risk of patients was assessed using CHADS2 and CHA2DS2-VASc scores.
Results: Out of the 1205 hospitalization due to AF occurring in the given time period we chose 341 cases of unique AF patients. Mean age of the study population was 69.6±13.2 years, a their mean body mass index (BMI) was 29.4±6.4 kg/m^2. 172 (50.4%) patients were in the rhythm control strategy group. Compared to the rate control group (permanent AF), patients in whom the rhythm control strategy was chosen were younger (65.2±13.6 vs. 74.0±11.1; $p<0.0001$). There were no differences in terms of sex, and hypertension or diabetes mellitus prevalence. Patients with rhythm control strategy had less often history of heart failure (38.4% vs. 75.7%; $p<0.0001$), stroke (8.1% vs. 16.0%; p=0.04), and vascular disease (24.4% vs. 47.3%; $p<0.0001$), which resulted in lower total thromboembolic risk. Mean CHADS2 score (2.0±1.4 vs. 2.9±1.4; $p<0.0001$) in rhythm control patients was lower than in rate control, the same applies to the CHA2DS2-VASc (3.2±2.1 vs. 4.6±1.9; $p<0.0001$).
Conclusions: Persistent AF patients in whom the rhythm control strategy is taken are younger and have less comorbidities, therefore their thromboembolic risk in both CHADS2 and CHA2DS2-VASc scores is lower than in patients on rate control strategy (permanent AF). Total thromboembolic risk is one of the factors taken into consideration in choosing treatment strategy in real-life AF patients.

P5281 | BEDSIDE

Being diagnosed with atrial fibrillation/flutter is associated with lower perceived physical health - a Danish cross sectional study

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Background: Reports on self-reported health-related quality of life and health status in patients living with atrial fibrillation (AF) have been deviating; from being similar to those of patients who have sustained and survived a myocardial infarction to no difference, when compared with healthy subjects. Low sample sizes have, however made stratification on gender impossible in earlier studies.
Purpose: To investigate the association between the diagnosis of AF and self-reported health status.
Methods: An observational, cross-sectional study was conducted, using data from the Danish Diet, Cancer and Health cohort. Information on health status was obtained using the Danish Short Form 36 version 2 (SF-36v2) questionnaire. The analyses were stratified on gender. In adjusted analyses, we considered potential confounding from comorbidity expressed by the Charlson Comorbidity Index and effect modification by age.
Results: We included 42,598 participants in the study; 873 of the participants had the diagnosis of AF and/or atrial flutter. We found a lower adjusted physical component score for a 60-year-old AF patient compared with a non-AF participant of 2.63 points [95% CI: 1.77; 3.48] for men and 3.44 points [95% CI: 1.84; 5.04] for women. The mental component score was 0.28 [95% CI: –0.63; 1.19] lower in men and 0.98 points [95% CI: –0.67; 2.63] lower in women.
Conclusion: Participants being diagnosed with AF report a clinically relevant and statistically significantly lower physical health component score compared with the remaining participants in the cohort, but no systematical differences in the mental component score. When caring for patients living with AF, it is important to be aware that even though patients with AF do not need much physical attention, they report a lower physical component score and therefore their individual perception of symptoms leading to physical limitations should be articulated.
Acknowledgement/Funding: The study was financially supported by a research grant from the Danish Council for Strategic Research (grant number 09-066965).

P5282 | BEDSIDE

Atrial fibrillation is underdiagnosed in general practice: the PROFIL FA awareness campaign results in patients above 80y

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Introduction: AF in patients above 65 y is a strong risk factor for stroke and anticoagulation should be considered. But early diagnosis is often difficult and in up to 20% of AF related strokes, AF is discovered too late at the time of the stroke. Use of a symptoms targeted questionnaire in general practice (GP) was shown to improve early AF diagnosis il the PROFIL FA campaign. In patients 80+, AF is highly prevalent and stroke is a big concern, in relation to disability and dementia burden.
Methods: During one week, GP asked all their consecutive patients above 65y about 4 symptoms (unexplained palpitations, chest pain, shortness of breath, or dizziness). If AF episodes could be suspected, the patient was referred to a cardiologist for confirmation or not. Risk scores for stroke and anticoagulation therapy were obtained
Results: 6301 patients from 622 GP were questioned, 2126 aged >80y (group 80+) (85y, 53% F) and 4175 aged <80y (group AF-) (71y, 42% F). AF was previously known more frequently in older patients: in 564 patients in 80+ (26%) vs 653 in 80- (16%). Following questionnaire, AF was similarly suspected in 232 in 80+ (11%) vs 422 in 80- (12%). Out of these AF suspected patients, AF was newly diagnosed by the cardiologist in 46 in 80+ (26%) vs 118 in 80- (30%). Symptoms of palpitations, dizziness, or chest pain, and more often shortness of breath were highly present in AF older patients, respectively for 23%, 14%, 6,2%, and 38% in 80+., and for 24%, 12%, 6,6% and 28% in 80-. an irregular pulse was related to AF only in 1 out of 2 patients, similarly in 80+ (49%) and in 80- (58%). CHADS2 scores were higher in 80+.
Following the campaign, anticoagulation was initiated similarly in 80+ (61%) and in 80- (70%), a high level as already 22% and 19% were on anticoagulation.
Conclusion: Systematic symptoms search is worthly in 80 y old patients, and can yield AF diagnosis in 26% of patients. Anticoagulation was incremented in 61% of these patients. A symptoms targeted questionnaire approach should be recommended in family practice.

P5283 | BEDSIDE

Stroke history as predictive criteria for further atrial fibrillation diagnostic: French screening campaign of atrial fibrillation (PROFIL FA) in general practice

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Purpose: Atrial fibrillation (AF) (750 000 patients in France) is a severe disease with important consequences in terms of morbidity and mortality but still underdiagnosed. Boehringer Ingelheim pursued in 2014 the screening campaign begun in 2013 (PROFIL FA) among family physicians in France, with a simple questionnaire based on heartbeat measurement, AF linked symptoms and thromboembolic patient risk.

The main objective of this second part of the study was to confirm or not the most predictive factors of the disease identified in the first part, and to provide a simple tool to improve screening and diagnosis of AF in patients over 65.

Methods: Main predictive factors of AF were identified, from questionnaire results, using a logistic regression model. A prognostic score was estimated and its predictive performance investigated using the ROC curve.

Results: 6 301 patients were screened, 612 were oriented to a cardiology specialist and 155 were diagnosed with AF. The statistical analysis was performed on the sample of oriented patients. The logistic regression model identified 3 predictive factors of AF: irregular heartbeat (OR=13.5, $p<0.0001$), stroke history, transient ischemic attack or peripheral embolism (OR=2.1, p=0.04) and presence of at least two of the following symptoms: faintness, palpitations, chest pain and shortness of breath (OR=2.7, $p<0.0001$). An AF prediction based only on irregular heartbeat (1st criteria) showed a sensibility of 77.2% and a specificity of 81.2%, its positive predictive value was 58.1%. It represents the main predictive criteria of AF.

The presence of at least two symptoms in patients having a stroke history improves sensibility (81.9%) while maintaining good specificity (78.7%).

Screening campaign showed that applying strictly those latest criteria to patients of the screened cohort could have potentially led to diagnosis of 94 additional AF. However, 27 patients (all with regular heartbeats) with FA would have been missed.

Further investigations were conducted on the sample of patients over 80. Two predictive factors of AF were identified: irregular heartbeat (OR=13.2, $p<0.0001$) and history of lipothymia (OR=2.6, p=0.02). Analyses are still underway.

Conclusion: This complementary study confirms that measure of heartbeat is the main predictive criteria in patients over 65, but patients with a regular heartbeat should also be considered. They should systematically be referred to a cardiologist in case they present at least two symptoms and a stroke history.

P5284 | BEDSIDE

Risk of incident atrial fibrillation in patients presenting with retinal artery or vein occlusion: a nationwide cohort study

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Background: Retinal artery or venous occlusions are associated with cardiovascular risk factors. Whether a presentation with retinal artery or venous occlusions may be an indicator for new onset cardiac arrhythmias is unknown. We examined the risk of new onset atrial fibrillation (AF) in patients with prior retinal arterial occlusions (RAO) and retinal venous occlusions (RVO).

Methods: From Danish nationwide registries, we identified all new cases of retinal occlusions from 1997–2011. The population was matched 1:5 according to sex and age. Unadjusted rates and hazard ratio (HR) of AF according to retinal vascular occlusions were determined.

Results: 1368 cases with retinal artery or venous occlusions were identified (mean age 69.7, 47.3% males) of which 706 (51.6%) were RAO and 529 (38.7%) were RVO. The rate of incident AF was 1.74 (1.47–2.06) events per 100 person-years for any retinal vascular occlusion versus 1.22 (1.12–1.33) for the matched control group. When stratified on type of occlusion, patients with RAO had a rate of AF of 2.01 (1.6–2.52), whereas patients with RVO had a rate of 1.52 (1.15–2.01). Hazard ratios of incident AF adjusted for cardiovascular comorbidities were 1.26 (95% CI; 1.04–1.53) for any retinal vascular occlusion. Adjusted HR according to RAO and RVO were 1.45 (95% CI; 1.10–1.89) and 1.02 (95% CI; 0.74–1.39), respectively as seen in Figure 1.

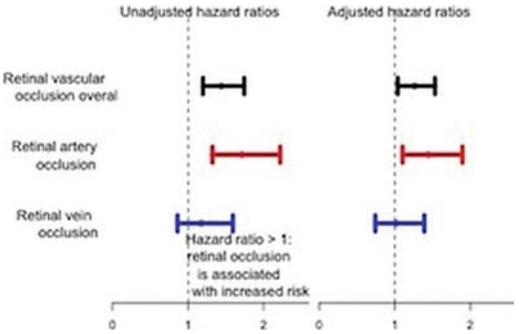

Figure 1. HR of AF according to retinal occlusion

Conclusion: In patients with a new diagnosis of retinal vascular occlusions, the risk of incident AF was increased, particularly in patients with RAO. Given that retinal vascular occlusions independently increases thromboembolism risk in AF, vigilance for incident AF amongst newly diagnosed patients with retinal vascular occlusions is recommended

P5285 | BEDSIDE

Prevalence and predictors of subclinical atrial tachyarrythmias in high risk patients detected by prolonged continuous Holter monitoring

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Background: One quarter of strokes are of unknown cause, and subclinical atrial tachyarrythmias (AT) may be a common etiologic factor. Data of the real prevalence and predictors of silent AT are scarce, and the proper diagnostic test for its diagnosis has not been established, yet. The aim is to assess prevalence and predictors of subclinical AT with continuous 7-day ECG Holter monitoring applied in patients at risk for AT.

Methods: We enrolled consecutive patients, 65 years of age or older, with left atrium dilation at echocardiographic exam, defined as left atrium indexed volume >33 ml/mq detected at transthoracic echocardiography (TTE), and the presence of at least one of the following clinical risk factors: hypertension with left ventricular hypertrophy, defined as left ventricular mass >108 g/mq for women and >131 mg/mq for men, detected at TTE, heart failure with left ventricular ejection fraction ≤35%, previous myocardial infarction with left ventricular ejection fraction ≤35%, or mitral stenosis. Exclusion criteria were history of AT, detection AT at basal ECG, previous implantation of pacemaker or defibrillator, and history of stroke or transient cerebral ischemic attack. All patients underwent continuous 7-day ECG Holter monitoring and TTE.

Results: Of 1712 screened patients, 142 were included in the study (mean age 72.6±7.4 yrs, 65% males). The mean CHA2DS2 VASc Score was 3.5±1.3, with a mean HAS-BLED score of 2.0±0.5. Subclinical AT detected by continuous 7-day Holter monitoring had occurred in 31 patients (22%). Mean duration was 30 s (10s-90s), with a mean of 6 episodes/patient. At the univariate comparison, patients with AT had a higher body mass index (BMI; 23±3 vs 29±5; P=0.002), had more often significant mitral stenosis (27 vs 5%; P=0.006) and interventricular septum thicknes (14±3 vs 12±2 mm; P=0.02). At the multivariate logistic regression analysis, mitral stenosis (OR=8.09, CI 95% 1.65–39.8, P=0.01) and interventricular septum thickness (OR=1.46 CI 95% 1.11–1.94, P=0.01) were identified as independent predictors of AF, whereas a higher BMI had a protective effect (OR=0.81, CI 95% 0.66–0.99, P=0.03).

Conclusions: In a high risk population, the occurrence of silent AT detected is not unfrequent and is predicted by mitral stenosis, interventricular septum thickness, and BMI.

P5286 | BEDSIDE

The relationship between the frequency of paroxysmal episodes of atrial fibrillation and left atrial function as measured by strain imaging

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Objective: The objective of the study were (i) to reveal the role of strain (S) and strain rate (SR) imaging (SRI) and their prognostic power in the left atrial (LA) function changes among patients (pts) with paroxysmal atrial fibrillation (PAF); and (ii) to establish the LA reservoir function by SRI for the relationship between the frequency of symptomatic arrhythmic episodes and echocardiographic data.

Methods: 54 pts with lone PAF (age 45±7 years, 36 men) were assessed by the standard echo-Doppler study (LA diameter, maximum and minimum volumes, LA compliance index) and by Doppler myocardial imaging (velocity, S, and SR of LA). The difference between LA maximum and minimum volumes divided by the minimum LA volume was used as an index of LA compliance.

Pts were divided into two groups, based on the frequency of their symptomatic AF paroxysms. The first group (n=28) included pts with paroxysms frequency of no more than one time in a three-month period. The pts of the second group (n=26) had more than one paroxysm during the same three-month period. AF paroxysms anamneses in all groups were between 1 to 12 months.

Results: In the second group the S from both the septal (S-LAs) and lateral (S-LAe) portion of the LA were significantly lower compared to the first group (S-LAs (%) 24.1±5.2 vs. 13.5±4.1, P<001; S-LAe (%) 8.0±2.5 vs. –0.5±2.1, P<001). Frequent AF paroxysms correlated significantly with LA ejection force (r=–0.57; $P<0.005$), emptying fraction (r=–0.61; $p<0.005$) and S-LAs (r=–0.54; $P<0.005$). Both the LA diameter and volumes were significantly increased in the second group ($P<0.005$). Atrial myocardial velocities and deformation indices were sig-

nificantly compromised in the second group (P<0.005). Significant negative correlation was found between the LA myocardial velocity and LA volumes (R=–0.58; P<0.05). Peak systolic LA myocardial S and SR were significantly correlated with LA volumes (S: R=–0.56; P<0.05; SR: R=–0.49; P<0.05), compliance index (S: R=0.47; P<0.05; SR: R=0.48; P<0.05), ejection fraction (S: R=0.53; P<0.05; SR: R=0.51; P<0.05).
In multivariate analysis, the best predictor of repeated AF paroxysms was LA peak systolic SR average with a sensitivity of 85%, specificity of 81%.
Conclusion: LA myocardial deformation properties, assessed by SRI, are abnormal in frequent AF paroxysms group. The degree of this impairment is predictor of AF paroxysms and this could be used as an indicator of gradual mechanical remodeling of the LA, which may favor recurrence and perpetuation of AF.

ATRIAL FIBRILLATION III

P5287 | BENCH
Predictors of rheumatic atrial fibrillation: Late Gadolinium Enhancement MRI study to assess atrial fibrosis

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Introduction - Atrial fibrillation (AF) is a common arrhythmia in patients with rheumatic heart disease (RHD). Late Gadolinium Enhancement (LGE) MRI can identify atrial scarring. Data on in-vivo distribution of atrial scarring in RHD patients is lacking. We aimed to use LGE to quantify atrial scarring in RHD and to define predictors for developing AF
Methods: Consecutive patients with mild to moderate rheumatic mitral valve disease were prospectively studied. After sample-size calculation, we planned to include 30 patients in AF and 30 in sinus rhythm (SR). Clinical, echo and LGE MRI data were analyzed.
Results: Mean age was 32.6 years, 63% were females and 83% had isolated mitral stenosis with mean mitral valve area1.25±0.17 cm^2. Mean left atrial (LA) diameter was 4.82±0.51cm and volume was 73.03±7.73 ml. All patients were on beta blockers and 7 were on amiodarone. Median duration of AF was 12 months (range 6 - 48). Atrial fibrosis was more common in AF patients compared to those in SR (100% vs. 33%, P<0.001) with more involvement of the LA than the right atrium (44% vs. 20% in the SR group and 86.7% vs. 63.3 in the AF group). The posterior wall was the most frequently involved (26.7% in the SR group and 86.7% in the AF group). Severe fibrosis was more common in long standing AF (n=11) compared to persistent (n=9) and paroxysmal (n=10) (100% vs. 44% vs. 0, P<0.001). LA fibrosis was the most important predictor of AF (OR 5.8, 95% CI 2.63–13, P<0.001). Atrial fibrosis maintained its statistical significance among clinical and echocardiographic data using Stepwise multiple regression analysis with R=0.8 and P<0.001 (Standardized Coefficients Beta was 0.58, 0.56 and 0.26, P value was <0.001, <0.001 and 0.047 for LA fibrosis, LA volume and mitral valve area respectively).
Conclusions: AF is associated with more atrial fibrosis in RHD patients. Severity of atrial fibrosis is a stronger predictor of AF compared to valve disease severity or LA size which may play a role for patient selection for catheter ablation in this subset of AF.

P5288 | BEDSIDE
Predictors for atrial fibrillation in patients with coronary artery disease: a cross-sectional analysis of BOREAS registry data

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Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with increased cardiovascular morbidity and mortality. Previous studies have shown that hypertension, valvular disease, heart failure, age and male gender are the predictors of AF in general population. However, differences in the prevalence and risk factors of AF between patients with coronary artery disease (CAD) and those without CAD have not been clarified.
Methods and results: We analyzed data for 1,871 consecutive patients who underwent coronary angiography from August 2014 to December 2014 in 12 hospitals joined for BOREAS-CAG2 Registry. Patients with moderate or severe mitral valve disease and those with history of coronary angioplasty were excluded (n=960), and thus 911 patients contributed to the present analysis. Patients were divided into a group with CAD (CAD group, n=494) and a group without CAD (non-CAD group, n=417). CAD was defined as presence of a coronary stenosis ≥75% in AHA criteria in the proximal legion of at least one coronary artery. Diagnosis of AF was based on ECG and/or medical history of AF in hospital records; 15.6% of patients in the non-CAD group and 6.9% of patients in the CAD group had AF. In both the non-CAD and CAD groups, age, and proportions of males, hypertension and diabetes were similar in patients with and without AF. In the non-CAD group, patients with AF had larger left atrial dimension (LAD: 45.3±7.8 vs. 36.1±6.9 mm), lower left ventricular ejection fraction (LVEF: 55.6±13.9 vs. 61.8±11.8%), lower estimated glomerular filtration rate (eGFR: 56.9±21.7 vs. 67.1±23.4 ml/min/1.73m^2) and higher brain natriuretic peptide (BNP: 274±276 vs. 113±209 pg/ml) than those without AF, while body mass index (BMI) was similar in patients with or without AF. In the CAD group, AF patients had larger LAD, lower LVEF, lower eGFR (51.7±26.8 vs. 65.7±36.5 ml/min/1.73m^2), higher BNP, higher uric acid (6.6±2.8 vs. 6.0±1.7 mg/dl) and lower BMI (22.4±3.9 vs. 24.5±3.8 kg/m^2) than patients without AF. Multivariate logistic regression analysis revealed that larger LAD and higher BNP were significantly associated with AF in the non-CAD group and that lower eGFR, higher uric acid and lower BMI were significantly associated with AF in the CAD group.
Conclusions: Predictive factors for AF are different between patients with and without CAD. Renal dysfunction may have greater impact on the development of AF in patients with CAD that in those without CAD.

P5289 | BEDSIDE
Prevalence of non valvular atrial fibrillation in a large cohort of ambulatory patients. A survey from a large data base of a GP group

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Background: Non Valvular Atrial Fibrillation (NVAF) is a common condition in the general population. The prevalence of NAVF is reported to be ≈ 2% in several studies. However, prevalence varies with age and sex. Furthermore, there is evidence of significant regional heterogeneity in estimations and availability of population-based data. In our area General Practioners (GPs) are organized in groups and work with a common medical practice management software (Millewin). All clinical information from patients are prospectively recorded and collected in a common data-base. Aim of this survey was to evaluate the prevalence, age distribution and therapeutic choices from the common data base offered by the common informatic platform of the GPs.
Methods: We identified 10 GPs with a sufficient quality of data recording and a large number of assisted patients. Data recording quality was checked by veryfying the adherence to a program of proactive assistance which included the assessment of the cardiovascular risk in their patients. Only those GPs reaching a target >90% of adherence to the protocol were invited to the data collection of this survey.
Results: Data from 14731 pts >16 years were collected and analysed. NVAF was found in 563 Patients, thus representing a prevalence in this population of 3.82%. The gender distribution wa similar (50.8% Males, 49.2% Females). Among the NVAF Group, 9.2% of the patients were less than 65 years old, while the large majority was older (62.7% in the Group 65–84 years old). 30% of patients with NVAF was older than 85. Patients older than 85 years old represent 5.22% of the whole population examined. In this older group of patients the prevalence of NVAF was 18%. Fifty-seven percent of these NVAF patients were on treatment with oral anticoagulation (VKA and NOAC). The percentage of treated patients increased to 68% when considering only permanent NVAF.
Conclusions: The prevalence of NVAF in this population-based cohort is higher than that reported in previous studies. This may depend on a different age distribution of our population wth respect to previous studies. Our results confirm and reinforce the concept that NVAF is a common condition in the general population particularly in the oldest subjects. In the real world more than 40% of NVAF patients do not receive an adeguate antithrombotic therapy. Access to GPs Medical records allow to gain real-world information that can be used to promote and monitor public health actions.

P5290 | BEDSIDE
Critical coronary atherosclerosis in patients with recent onset atrial fibrillation and troponin rise

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Background: In patients with atrial fibrillation (AF), the presence of comorbidities including coronary artery disease (CAD) could contribute to excess mortality, beyond systemic embolism. Evidence to look for the presence of CAD is lacking and the mechanism underlying the troponin rise during AF without acute coronary syndrome (ACS) is unclear. This study investigates the relationship between adverse outcomes and CAD in patients with troponin rise.
Patients and methods: Patients with a recent onset AF and without severe comorbidities were enrolled. Baseline characteristics in those with troponin rise versus those without were adjusted with the propensity score matching for possible confounders. SPSS software allowed estimation of the propensity-score using logistic regression and specifying nearest neighbor matching in prior-stroke, heart-rate, hypertension, TIMI-risk score, GRACE score, CHA2DS2Vasc score. Patients with a troponin rise or adverse cardiovascular event (CVE) were considered for angiography. The primary endpoint was the composite of ACS, critical CAD stenosis >70%, revascularization and cardiac death at the follow-up; the secondary endpoint was stroke.
Results: Out of 10250 patients with supraventricular tachyarrhytmias, 6203 with AF and without severe comorbidities were considered, 3627 with recent onset AF

were enrolled and 3541 completed the study (86 patients lost at follow-up); finally 202 (6%) showed a troponin rise, 91 (3%) a CVE. After matching no difference existed in baseline characteristics. On multivariate analysis, in the entire cohort, troponin rise, know CAD and hypertension were predictors of the primary endpoint, whereas only troponin rise (Odd Ratio, OR: 10, Confidence Interval 95%, CI: 4–22, p<0.001) and TIMI score >2 (OR 4, CI 2–9, p<0.001) in the matching cohort, suggesting the role of CAD in poor outcomes. Patients with or without troponin rise achieved the endpoint in 38 (19%) and 43 (1%), respectively (p<0.001). Stroke occurred in 4 (2%) and 20 (1%), respectively (p=0.018). "Critical" CAD account for 23 (12%) and 15 (1%), respectively (p<0,001). In the matching cohort, only stroke did not reach the statistical significance. Interestingly, the best cut/off of troponin level for decision making was 0.30 ng/L which, on Receiver Operator Curve analysis, was associated with 68% of sensitivity and 60% specificity; the value >0.50 ng/L was associated with 55% and 75%, respectively.
Conclusions: Patients with a recent-onset AF and troponin rise showed a high prevalence of CVE excluding stroke, thus CAD might have a role in poor outcomes.

P5291 | BEDSIDE
Clinical efficacy of antazoline in rapid cardioversion of paroxysmal atrial fibrillation: a single centre, randomized, double blind, placebo controlled study

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Introduction: Rapid pharmacological conversion of atrial fibrillation (AF) to sinus rhythm is widely employed in clinical practice. Antazoline is a first generation antihistaminic agent with chinidin-like properties. Intravenous administration of antazoline exerts a strong antiarrhythmic effect on AF facilitating rapid conversion to sinus rhythm. Despite lack of recognition in renowned clinical guidelines and scarcity of published data, antazoline has been used in cardiology wards and emergency rooms in Poland due to its clinical effectiveness, safety and rapid onset of action within minutes of administration.
Purpose: The aim of the study was to assess clinical efficacy of antazoline in rapid conversion of paroxysmal AF to sinus rhythm in patients with paroxysmal AF without significant valvular disease or advanced heart failure.
Methods: This study was a single center, randomized, double blind, placebo-controlled, superiority clinical trial. We enrolled patients with an AF episode lasting less than 43 hours, in a stable cardio-pulmonary condition and with no prior history of advanced heart failure or significant valvular disease. Subjects who fulfilled selection criteria were randomly assigned to receive intravenously either placebo or antazoline up to 250mg in divided doses and observed for 1.5 hour after conversion to sinus rhythm or after last iv. bolus. The primary end point was conversion of AF to sinus rhythm confirmed in ECG during the observation period. Due to presumed lack of statistical power the secondary end points and safety endpoints were considered exploratory. All analyses were conducted according to intention-to-treat principle.
Results: Between November 2012 and December 2014 we enrolled 74 patients: 36 (48.6%) in antazoline group and 38 (51.4%) in control group. The mean age was 68.4±12.1 years [range 31–90 years] and 39 (53.3%) patients were male. Successful conversion of AF do sinus rhythm during observation period was achieved in 26 (72.2%) patients treated with antazoline and 4 (10.5%) in control group: RB 6.86 [95% CI: 2.66–17.72]. The adverse effects were rare and mild but one patient was hospitalized due to exacerbation of previously diagnosed heart failure and recovered without consequences. There were no cases of pro arrhythmic effect of antazoline.
Conclusion: Intravenous antazoline was effective and safe in the rapid conversion of paroxysmal atrial fibrillation to sinus rhythm in patients without significant valvular disease or advanced heart failure.

P5292 | BEDSIDE
Patient profile in non-valvular atrial fibrillation (NVAF) and stroke: findings from a real-world setting in Spain

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Background: Atrial Fibrillation (AF) increases the risk of ischaemic stroke five-fold and doubles the risk of death from AF-related stroke. In practice, many patients with AF do not receive appropriate anticoagulant therapy (AC) and thus may be inadequately protected against stroke.
Purpose: To describe demographic, clinical, and AC treatment characteristics of patients with NVAF, according to occurrence or absence of stroke following NVAF diagnosis.
Methods: We undertook a retrospective cohort study of patients newly diagnosed with NVAF (without prior history of stroke) between Jan. 1, 2003 and Dec. 31, 2013 using the Badalona Serveis Assistencials SA (BSA) database, which contains data from hospitals, primary-care and ambulatory-care centres for a sanitary area of 120,000 inhabitants in Catalonia. We identified clinical events using ICD-9 codes. We calculated summary statistics of demographic, clinical, and AC-treatment characteristics of patients with NVAF, overall and separately for those who did and did not experience stroke during follow-up.
Results: We identified 3,052 eligible patients with NVAF. At time of NVAF diagnosis: average age 74.3 (SD 10.8; IQR 67–82); 52.8% women; mean CHA2DS2-VASc 2.9 (SD 1.45; IQR 2–4); 56.8% hypertension (HT); and 24.5% diabetes (DM). Median follow-up duration was 1,230 days (IQR 455–2,291). In eligible NVAF patients, 70% received at least one vitamin-k antagonists (VKA) or novel oral anticoagulant (NOAC) prescription during follow-up (2,127 and 300 patients, respectively). Overall, 341 (11.2%) patients had ≥1 stroke during follow-up; median time from NVAF diagnosis to first stroke was 335 days (IQR 1–1,359); and mean number of stroke events per patient was 1.7 (SD 0.8; IQR 1–2). Patients experiencing stroke were older and more likely female, had a higher CHA2DS2-VASc score, had more HT and DM, and were more likely to receive VKA/NOAC (100% vs. 66.2%). In stroke patients, 35.2% did not receive VKA/NOAC between NVAF diagnosis and stroke; 53.4% received VKA/NOAC in this period but discontinued therapy before stroke; and 11.4% received VKA/NOAC only at time of stroke.
Conclusion: In this real-life study, Spanish patients newly diagnosed with NVAF were elderly, with a small majority of women, and frequently had comorbidities of cardiovascular importance such as hypertension and diabetes. VKA was the most prescribed anticoagulant for AF in this time period. As more patients treated with NOACs accumulate in Spain, research should continue to address NVAF patient profile, AC treatment patterns, and the occurrence of stroke.
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P5293 | BEDSIDE
Does renal function affect clinical course and management in patients with atrial fibrillation?

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Background: There are scarce data concerning renal function in population with valvular and non-valvular atrial fibrillation (AF).
Aim: To assess renal function in patients with AF, the association between eGFR and AF perpetuation and in-hospital mortality.
Methods: We studied 1800 patients with AF. Patients with chronic kidney disease (CKD) were compared to population with preserved renal function.
Results: There were 828 (48%) out of 1800 patients with impaired renal function. The patients with impaired renal function (eGFR <60ml/min) were older (p<0.001), they were more frequently females (p<0.001), had more often permanent AF (p<0.001), diabetes (p<0.001) anaemia (p<0.001), history of stroke (p=0.02) and myocardial infarction (p=0.004). They had higher CHA2DS2VASc and HAS-BLED score (p<0.001, p<0.001, respectively). The reason of admission to hospital was more frequently exacerbation of chronic heart failure (p<0.001), acute heart failure (p<0.001) and non-ST elevation myocardial infarction (p=0.006). They were more frequently given reduced dose of non-VKA (p<0.001), also less often VKA (p=0.01) and not given antithrombotic treatment at all despite it was indicated (p=0.05). The use of non-VKA was similar in both groups (p=0.7). Cardioversion in the group with CKD was done less frequently (p=0.03). Patients with eGFR <60ml/min had also lower ejection fraction (p<0.001) and larger left atrium (p=0.004). They had higher in-hospital mortality (p=0.04). Paroxysmal type of AF was less often observed (p=0.001). If eGFR decrease by 10ml/min, odds of permanent AF are increased by 10% (OR=0.9, p<0.0001,95% CI1.05- 1.15).
Conclusions: Almost half of the patients with AF are diagnosed with impaired renal function. This group is significantly older, has more serious comorbidities, higher risk of stroke, also higher risk of bleeding and higher mortality. Although prognosis in patients with AF and CKD is worse than in patients without CKD, anticoagulant treatment and rhythm control management are less intensive. There is the correlation between CKD and AF perpetuation.
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P5294 | BEDSIDE
The impact of new onset atrial fibrillation on mortality and morbidity in patients with acute coronary syndrome

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Background: There is a strong evidence that patients (pts) with atrial fibrillation (AF) and acute coronary syndrome (ACS) constitute a high-risk population, however the prognostic importance of new onset AF in these pts remains unclear.
Aim: The aim of this study was to determine in-hospital and long-term mortality in pts with ACS and new onset AF.
Methods: We conducted the cohort study, which included consecutive 644 pts with ACS diagnosed according to the ESC guidelines, hospitalized in the Depart-

ment of Coronary Disease and Heart Failure in Cracow between January 2008 and June 2010. We excluded pts with valvular heart disease, LV hypertrophy, pericarditis, permanent AF, active thyroid disease and cancer. Patients were divided into two groups: ACS-AF group- 87 pts with new onset AF during ACS (43 M, mean age72.5±9.7) and ACS-noAF group- 573 pts without new onset AF during ACS (374 M, mean age 63.7±11.4). After the follow-up period of 43–73 months we have contacted with 75 (86.2%) pts from ACS-AF group and 441 (76.9%) pts from the ACS-noAF group.
Results: Patients with ACS-AF in comparison to the ACS-noAF group were characterized by: older age (72.5 vs. 63.7 lat; p<0.001), women prevalence (50.5 vs. 32.8%; p<0.001), higher heart rate at admission to the hospital (111 vs. 78/min; p<0.001). Blood examination revealed higher serum creatinine level (101 vs. 87 umol/l; p<0.001). TTE showed larger LVEDD (53.1 vs. 50.8 mm; p=0.04), whereas in coronary angiography more often left main coronary artery disease was diagnosed (14.1% vs. 6.5%; p=0.01), in contrary to one-vessel disease (24.4 vs. 39.4%; p=0.007). In these pts we also observed higher rate of cardiac arrest during hospitalization (9.8 vs. 1.6%; p<0.001). In-hospital mortality rate in the ACS-AF group was 2.3 vs. 0.7% (p=0.15). Follow up revealed differences in both groups in all-cause mortality (24.7 vs. 6.1%; p<0.001), stroke-related mortality (4.3 vs. 0.6%; p=0.009) and cardiovascular disease- related mortality (8.5 vs. 2.5%; p=0.008). Cox proportional hazards model revealed three independent predictors of all-cause mortality in both groups: new onset AF during ACS (RR 2.1; 95% CI (1.1–3.8); p=0.01), age (RR 1.09; 95% CI (1.05–1.13); p<0.001) and LVEF in TTE (RR 0.95; 95% CI (0.93–0.97); p<0.001).
Conclusions: In pts with ACS and new onset AF follow-up revealed higher rate of all-cause mortality, stroke-related mortality and cardiovascular disease - related mortality. Age, AF during ACS and LVEF were independent predictors of all-cause mortality in follow-up, in pts with ACS.

P5295 | BEDSIDE
Lone atrial fibrillation: work up and predictors of recurrences

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Background: Mechanisms and best treatment choice of "lone atrial fibrillation (AF)" are still debated. Due to the risk of major complications and recurrences after ablation procedure, antiarrhythmic drugs (AADs) are often considered as first line therapy. The aim of this study was to report on clinical work up and long term efficacy and safety of ablation procedure in the highly selected subgroup of lone AF patients.
Methods: We retrospectively analyzed 855 patients referred to our centre for a first AF ablation between 2011 and 2014. Among them 72 (8%) met diagnostic criteria for lone AF (mean age 45±4 years; 68% males; mean LA diameter 34±3 mm; no cardiovascular comorbidities). 58 (81%) patients underwent pulmonary veins isolation (PVI) for paroxysmal AF, 14 (19%) underwent PVI and additional substrate modification, including complex fractionated atrial electrograms (CFAE) ablation and/or linear lesions for persistent AF. Immediately after ablation, all AAD were stopped in all patients.
Results: The median preoperative AF history was 24 [9;48] months. 12 (16%) patients were unsuccessfully treated with AADs as first line therapy. After a mean follow up of 458±347 days, 78% of patients were free from recurrences without AADs. The risk of recurrences after ablation procedure was not influenced either from AF duration, or from type of AF (paroxysmal vs persistent). In the Cox-regression model smoke (p=0.017; HR=3.9), atrioventricular block I (p=0.001; HR=30.2) and early recurrences in the blanking period (p=0.001; HR=11.8) were associated with a higher risk of clinical recurrences in the long term follow up. Major peri-procedural adverse events did not occur, no strokes or mortalities were registered during long-term follow-up.
Conclusions: This retrospective study shows that catheter ablation in young healthy patients with AF is highly effective and safe. The outcomes are maintained at long-term follow-up, irrespective of preoperative AF history. Smoke, AV Block I and early recurrences are associated with higher risk of recurrences at long term follow up.

P5296 | BEDSIDE
More advanced electroanatomical remodeling of left atrium and contractile dysfunction of left atrial appendage increase the risk of stroke for women in comparison to men in atrial fibrillation

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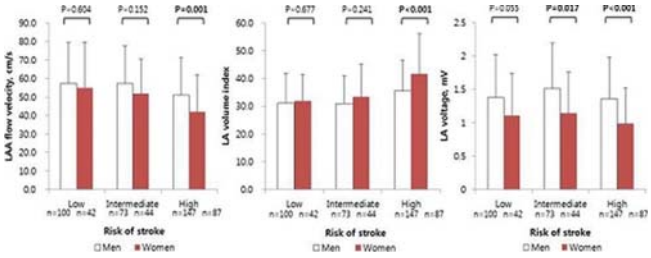
Background: The risk of stroke imposed by atrial fibrillation (AF) is significantly greater in women than in men; however, the mechanism behind the observed differences is still unclear.
Purpose: We hypothesized that the higher stroke rate in women with AF can be explained by gender differences in electroanatomical remodeling of left atrium (LA) and contractile function of LA appendage (LAA) in association with left ventricular (LV) diastolic function.
Methods: A total of 493 AF patients (173 women and age- and AF type matched 320 men, 60.7±10.4 years old, 73.6% paroxysmal AF) who underwent AF catheter ablation were enrolled in the study. Gender differences of LA volume index (TTE), LAA emptying flow velocity (FV, TEE) and LA voltage were analyzed in low (0 for men, 1 for women), intermediate (1 for men, 2 for women) and high (≥2 for men, ≥3 for women) risk groups, into which patients were divided according to their CHA2DS2-VASc scores.
Results: 1. Contractile dysfunction of LAA (LAA-FV) was more significant in women with a high stroke risk than in men of the same risk (p=0.001), but not in the low or intermediate risk groups. 2. Women also showed a greater LA volume index than their male counterpart in the high risk (p<0.001) group, but not in the low or intermediate risk groups. 3. Women showed lower LA voltage than men in the intermediate (p=0.017) and high (p<0.001) risk groups. 4. LA volume index (OR 1.134, CI 1.013–1.269, p=0.029) was independently associated with the history of stroke in women but not in men among AF patients.



Conclusions: More extensive LA remodeling and deterioration in mechanical function of LAA were noted in women with intermediate to high risk of stroke in AF, but not in those with a low risk.

P5297 | BEDSIDE
Atrial fibrillation with or without valvular disease: is the prognosis different?

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Background: European guidelines defined valvular atrial fibrillation (V-AF) in the presence of prosthetic valve or rheumatic heart disease. Recently it was proposed to restrict V-AF to mitral stenosis and mechanical prosthetic valves. The remaining pts with AF are therefore those without valvular disease (AF-WVD) or with other valvular disease/prosthetic valves (AF-VD). There are scarse data directly comparing these two populations.
Aim: We assessed demographic and clinical baseline characteristics and incidence of thromboembolic (TE) and major events (hospital admissions, major bleeding and death) during follow up, in a real-world population of outpatients with AF-WVD and AF-VD.
Methods: Between calendar 2009 and 2013 years, we enrolled 3379 AF-WVD pts and 1268 AF-VD pts. Clinical data were derived from the E-data chart for outpatient clinic. After a median follow up of 29 months we considered the incidence of TE and major events in the two groups. Data were obtained from Hospital Discharge Database and ICD9 code reports and regional Registry of Births and Deaths.
Results: Considering baseline characteristics of 3379 AF-WVD pts (mean age 75, males 58%) versus (vs) 1238 AF-VD pts (mean age 78, males 50%), the prevalence of obesity was 21% vs 16% (p<0.001), coronary artery disease 27 vs 3% (p<0,001), Charlson Index was >5 in 9.4 vs 13.9% (p<0.001), median CHA2DS22VASC 4 (2–5) vs 4 (3–5) (p<0.001), HASBLED ≥3 in 30% vs 39% (p<0.001), previous stroke/TIA 11.8 vs 11.4% (p=ns), glomerular filtration rate (GFR)<60ml/min/mq 27% vs 35% (p<0.001), ≥5 drugs 62 vs 72% (p<0.001), oral anticoagulants (AT) 53 vs 63% (p<0.001). During follow up we recorded TE events in 7.5% AF-WVD vs 8.7% AF-VD pts (p=NS), hospital admission in 53% vs 60% (p<0.001), CV hospitalizations 27% vs 37% (p<0.001), major bleeding 9.4% vs 13% (p<0.001), deaths 13% vs 19% (p<0.001). Also considering patients treated with AT, less TE occurred in AF-WVD vs AF-VD: 6.9 vs 9% (p=0.03)
Conclusions: 1) In a real world registry, AF-WVD vs AF-VD pts are different groups, being the former pts are younger, more obese, without complex heart disease or comorbidities, lower CHA2DS2VASc/HASBLED and less frequent on AT treatment; 2) During follow up TE events in the 2 groups were not different, but considering patients on AT therapy, TE events were significantly increased in AF-VD pts; 3) During follow-up, the incidence of hard prognostic events was higher in AF-VD pts, probably related to demographic and clinical characteristic of these more complex and frail pts.

P5298 | BEDSIDE
Guideline adherence for stroke prevention and risk of mortality in patients with atrial fibrillation

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Background: Although the current European guideline had clear recommenda-

tions for stroke prevention in patients with atrial fibrillation (AF), whether patients who received treatments adherent to guidelines had a lower risk of mortality remained unknown.
Methods: This study used the "National Health Insurance Research Database" in Taiwan. According to the 2012 ESC AF guideline, adherences to guideline recommendations were defined as the following (1) For AF males with a CHA2DS2-VASc score of 0 and AF females with a score of 1 (only gender), no any antithrombotic drug was necessary (2) For AF patients with one risk factor in addition to gender, oral anticoagulants should be prescribed. Patients who received treatments different from these recommendations were defined as "non-adherence".
Results: From 1996–2011, the Taiwan AF cohort included 354,652 AF patients. Among the study population, 45,595 and 309,057 patients were defined as guideline adherence and non-adherence groups, respectively. During the follow up, 133,552 patients experienced mortality. The risk of mortality was lower among AF patients who were adherent to the guideline recommendation for stroke prevention (annual risk of mortality = 4.3% versus 10.0%). Patients who were not adherent to the ESC guideline had a higher risk of mortality with a hazard ratio of 1.25 (95% confidence interval = 1.23–1.28, p value <0.001) after the adjustments for age, gender, CHA2DS2-VASc score and baseline differences (Figure 1). The finding was consistently observed after the propensity match analysis.

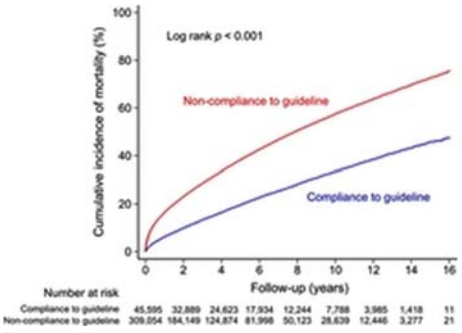

Figure 1. K-M curve

Conclusions: In this nationwide AF cohort, the risk of mortality was lower for patients who were adherent to ESC guideline for stroke prevention. The finding of the present study emphasized the importance of guideline adherence.

ATRIAL FIBRILLATION IV

P5299 | BEDSIDE
Combination of bilevel positive airway pressure and oral airway insertion is an effective strategy during atrial fibrillation ablation

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Background: Adaptive servo-ventilation was reported to be useful during pulmonary vein isolation (PVI). However, airway management influences this non-invasive positive pressure ventilation (NPPV) system. Hence, we assessed if combination of NPPV and oral airway insertion could have an effective strategy during atrial fibrillation (AF) ablation.
Methods: Two hundred twenty seven AF patients who underwent PVI using NavX were studied (paroxysmal AF, n=155; non-paroxysmal AF, n=72). Combination of dexmedetomidine and thiopental, or prorofol was used for sedation. We divided into 3 groups: they underwent AF ablation using bilevel positive airway pressure (BiPAP) system (BiPAP group, n=70), using BiPAP system and oral airway insertion (BiPAP-Airway group, n=31), and not using respiratory device (control group, n=126). We compared ablation procedure data and AF-free probability among the 3 groups.
Results: BiPAP-Airway group was lower frequency of patient restlessness compared with BiPAP and control groups (1.2±1.3 times versus 1.6±1.7 and 2.4±1.8 times, P<0.05 and P<0.01, respectively) and minimum SpO2 was higher in only BiPAP-Airway group than in control (98.8±1.1% versus 97.9±1.8%, P<0.05). At the ablation procedure data, procedure duration for PVI was shorter in BiPAP-Airway group than in BiPAP and control groups (66±16 minutes versus 79±19 and 81±23 minutes, P<0.01 and P<0.05, respectively). In addition, duration of radiofrequency energy delivery was shorter and total energy requirement was lower in BiPAP-Airway group than in control (2235±556 sec versus 2546±590 sec, P<0.05; 57±12 KJ versus 63±14 KJ, P<0.05), although there was no significant difference between BiPAP and control groups. In the non-paroxysmal AF patients (BiPAP group, n=30; BiPAP-Airway group, n=10; Control group, n=32), BiPAP-Airway group was lower frequency of respiratory compensation using NavX as compared with BiPAP and control groups (P<0.05, respectively). AF-free probability was higher in BiPAP-Airway and BiPAP groups than in control (P<0.05, respectively), although there was not significant difference in AF-free probability among the 3 groups in the paroxysmal AF patients.
Conclusions: Combination of BiPAP and oral airway insertion during AF ablation suppresses patient restless and stabilized patient respiratory condition as compared with BiPAP only and this improved ablation procedure data. Therefore, this respiratory strategy may be effective during AF ablation and may lead to reduce AF recurrence.

P5300 | BEDSIDE
Which components of the CHA2DS2-VASc score are the most important in obstructive sleep apnea patients with atrial fibrillation?

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Introduction: Elevated thromboembolic risk is observed in patients with several different diseases of the cardiovascular system, with the most prevalent of them being atrial fibrillation. The arrhythmia often co-exists with other diseases like obstructive sleep apnea (OSA). In this settings common risk factors of both diseases add to the thrombogenic profile and make the proper assessment of thromboembolic risk difficult.
Purpose: The aim of the present study was to establish which thromboembolic risk factors are more prevalent in atrial fibrillation patients with obstructive sleep apnea.
Methods: CHA2DS2VASc score was used to assess thromboembolic risk in continuous atrial fibrillation patients pre-qualified for atrial fibrillation ablation in a high-volume tertiary, university hospital. In each case the diagnosis of diseases included in the score (congestive heart failure, hypertension, diabetes, stroke, vascular disease) was based on the current guidelines. All 266 patients included in the study had a whole-night polygraphy examination performed. Patients were subsequently into a group with apnea-hypopnea index (AHI) <15/h, and those with AHI ≥15/h who were considered as having moderate to severe OSA.
Results: The mean age of the study population was 57.6±10.1 years, and 65.0% of the subjects were male. Moderate to severe OSA was diagnosed in in 16.5% of patients. In OSA patients the following risk factors included in the CHA2DS2VASc score were significantly higher prevalent: congestive heart failure (6.5 vs. 0.5%; p=0.02), hypertension (93.5 vs. 70.9%; p=0.01), diabetes mellitus (26.1 vs. 6.8%; p=0.003), history of vascular disease (23.9 vs. 8.2%; p=0.006). Non-significant differences were noticed in the history of stroke, age categories, or sex. After dividing patients into 4 groups: non-OSA, mild OSA (AHI >5 and <15/h), moderate OSA (AHI ≥15 and <30/h), and severe OSA (AHI ≥30/h) the same risk factors as previously remained significant (p<0.05).
Conclusions: The strongest contributors responsible for the elevated thromboembolic risk observed in atrial fibrillation patients with OSA are higher prevalence of congestive heart failure, hypertension, diabetes mellitus and vascular disease. Higher comorbidity burden is another argument for including OSA into the risk assessment schemes in atrial fibrillation patients.

P5301 | BEDSIDE
Twenty-four hours holter monitoring and clinical predictors for new onset atrial fibrillation in a non-selected population

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Introduction: Due to its high prevalence and morbimortality, atrial fibrillation (AF) represents a tremendous challenge. Despite some studies have defined clinical predictors for new onset AF, only few of them have focused in 24h Holter monitoring (HM) characteristics.
Purpose: Our aim is to define clinical and HM predictors for AF in a non-selected population.
Methods: After the only exclusion criterion of AF prior to or during the index HM we retrospectively included 299 patients from an initial cohort of 468 consecutive patients undergoing HM for any cause. Clinical and echocardiographic characteristics were also assessed in all patients.
Results: Age at inclusion was 62±18 years (46.5% women). Hypertension (HTN), diabetes mellitus (DM) and heart failure/structural heart disease (HF/SHD) were present in 52%, 17% and 8% respectively. Averaged left ventricle ejection fraction (LVEF) and left atrium diameter (LAD) were 62±10% and 37±6 mm respectively. Percentage of premature atrial complexes (PAC), number of non-sustained supraventricular tachycardias (NSSVT) and maximum number of beats during a NSSVT (MNB) during HM were 1±3%, 10±80 and 4.5±13 beats, respectively. Atrio-ventricular conduction disturbances were observed in 16% patients, being the mean PR interval 175±42 milliseconds. With a follow up of 36±8 months, the incidence of new onset AF was 10.5%, and 6% patients died, any of them due to cardiovascular causes. In the univariate analysis, age >65 years (HR 14.3, p<0.001), history of HTN (HR 4.7, p=0.002), DM (HR 2.8, p=0.007), HF/SHD (HR 4.4, p<0.001), creatinine clearance <60 ml/min (HR 3.3, p=0.003), CHA2DS2VASc score ≥4 (HR 7.1, p<0.001), LVEF <50% (HR 3, p=0.02), LAD >40mm (HR 2.8, p=0.01), a percentage of PAC >0.2% (HR 3.6, p<0.001), Atrial Burden >15, defined by the product of NSSVT and MNB (HR 2.86, p=0.004;) and PR interval >180ms (HR 2.7, p=0.008) demonstrated a strong association with new onset AF episodes during the follow up. Multivariate model showed age >65 years, percentage of PAC >0.2%, PR interval >180 ms and HF/SHD as independent predictors for AF (HR 8.5, p=0.004; HR 2.7, p=0.01; HR 2.4, p=0.02 and HR 5.4, p<0.001, respectively). We created an AF risk score based on multivariate model predictors (Age=3 points, HF/SHD=2 points, PAC >0.2% and PR interval >180 ms=1 point each). A Score of ≥4 predicted a high incidence of long-term new onset AF (>25%, vs <10% for <4 points).

Conclusions: Clinical and HM parameters are able to predict new onset AF at long term in a non-selected population. These patients should be closely followed in order to assess AF incidence.

P5302 | BEDSIDE
Opportunistic screening for atrial fibrillation in hospitalized geriatric patients

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Introduction: The clinical presentation of atrial fibrillation (AF) in the elderly is often atypical. Nevertheless it is a major source of increased morbidity especially because of the increased risk of stroke in this population.
Purpose: To assess (1) the added value of daily short-term rhythm strip recordings in AF detection in hospitalized geriatric patients (pts) on top of routine clinical care (history, physical examination, ECG and 24 hour ECG recording in selected pts) and (2) to assess its potential therapeutic implications.
Methods: A hand held device storing a bipolar electrogram during one minute automatically classifying the rhythm as AF or non-AF was used for daily recordings. During 2 months all patients (n=327) admitted to the Department of Geriatric Medicine were screened. Patients with severe mental (n=29) or motoric impairment (n=24) and implantable cardiac stimulators (n=38) were excluded (n=224 eligible patients). All rhythm strips were evaluated by experts.
Results: Based upon routine clinical care (detailed results available in 214 pts), AF was known in 71 pts (33%). If experts only reviewed tracings automatically labeled as AF, another 15 pts with AF (7%) were identified. If experts reviewed all tracings, 28 patients (13%) with AF were identified on top of routine clinical care. All of these patients had a CHADS2VA2Sc score of at least 3. No contraindications for anticoagulation were present in respectively 10/15 (67%) and 21/28 (75%) of identified patients.
Conclusions: On top of routine clinical care, daily short-term rhythm strip recordings identifies another 7% to 13% (depending on the screening approach) of elderly hospitalized patients with AF. This has significant therapeutic implications with respect to initiation of anticoagulation.

P5303 | BEDSIDE
The clinical impact of atrial fibrillation complicating ST-segment elevation myocardial infarction depends on location of infarction and timing of arrhythmia - data from a 10-year prospective study

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Introduction: Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia in patients with ST-segment elevation myocardial infarction (STEMI). AF is a well-established marker of poor short- and long-term prognosis in STEMI-patients. However, little is known as to the impact of new-onset AF on in-hospital outcome in patients with different locations of STEMI.
Purpose: The aim of the study was to assess the clinical significance of new-onset AF in patients with STEMI according to a location of infarction and timing of arrhythmia.
Methods: We analyzed 4363 consecutive STEMI-patients treated invasively, who were admitted to our center between 2003 and 2013. Finally, 4099 subjects were included into further analysis, as 264 patients were excluded because of previous permanent/paroxysmal AF. Among them, 1800 (43.91%) subjects with anterior infarction were included into Group 1, whereas Group 2 encompassed 2299 (56.09%) patients with non-anterior infarction. Data on in-hospital follow up were screened to identify subjects who experienced major adverse cardiovascular events during index hospitalization.
Results: New-onset AF was recognized in 225 patients (5.49%) during index hospitalization – 96 (5.33%) with anterior infarction (Group AF1) and 129 (5.61%) with non-anterior infarction (Group AF2). The incidence of arrhythmia onset within 24 hours (early onset) after admission was significantly higher in Group AF2 than in Group AF1: 71.33% vs. 35.42% ($p<0.001$). In Group 2, only late onset of AF (>24 hours after admission) was associated with significantly higher in-hospital mortality (13.51% vs. 4.24%; $p<0.05$), whereas mortality in patients with early onset of AF did not differ significantly in comparison with AF-free subjects (7.61% vs. 4.24%; p=NS). On the contrary, in Group 1 in-hospital mortality in patients with early and late onset of AF was 2- and 4-fold increased compared with AF-free population (17.65% and 27.42% respectively vs. 6.34%; $p<0.05$). Additionally, new-onset AF was the independent predictor of death only in Group 1 (HR 2.16) and this effect was even stronger for AF developing after 24 hours (HR3.07).
Conclusions: New-onset AF was associated with significantly worse in-hospital outcome in STEMI-patients treated invasively. However, the predictive value of this arrhythmia was strongly related with STEMI location and AF timing.

P5304 | BEDSIDE
Prognostic usefulness of the glomerular filtration rate estimation equations in patients with non-valvular atrial fibrillation on vitamin K antagonists: the new CKD-EPI versus the re-expressed MDRD-4

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Background: In atrial fibrillation, renal dysfunction entails more adverse events. Limited data exist on the prognostic value of the re-expressed Modification of Diet in Renal Disease equation (MDRD-4) versus the new Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) in atrial fibrillation.
Purpose: We compared the performance of the re-expressed MDRD-4 equation versus the new CKD-EPI equation at predicting major adverse outcomes in a real world cohort of patients with non-valvular atrial fibrillation (NVAF) on vitamin K antagonists (VKAs).
Methods: Retrospectively, we identified 911 consecutive patients with NVAF on VKAs who were attending the outpatient Cardiology consultation of a tertiary hospital between January 2011 and February 2013. The performance of each equation with respect to either a composite endpoint of major bleeding, thromboembolic events and all-cause mortality or each individual component of the composite endpoint was assessed using continuous and categorical ≥60, 59–30, and <30 ml/min/1.73 m^2 estimated glomerular filtration rate.
Results: During 10±3 months of follow up, the composite endpoint occurred in 98 (10.8%) patients: 30 patients developed major bleeding, 18 had thromboembolic events, and 60 died. The new CKD-EPI equation provided lower prevalence of renal dysfunction <60 ml/min/1.73m^2 (32.9%), compared with the re-expressed MDRD-4 equation (34.1%)
Estimated glomerular filtration rate from both equations was an independent predictor of the composite endpoint (hazard ratio=0.98 and 0.97 for the re-expressed MDRD-4 and the new CKD-EPI, respectively; $p<0.0001$) and all-cause mortality (hazard ratio=0.98 for both equations, $p<0.01$). Strong association with thromboembolic events was observed only when estimated glomerular filtration rate was <30 ml/min/1.73m^2: hazard ratio=5.1 for the re-expressed MDRD-4 equation, and hazard ratio=5.0 for the new CKD-EPI.
No significant association with major bleeding was observed for both equations.
Conclusions: The new CKD-EPI equation reduced the prevalence of renal dysfunction in a community based cohort of patients with NVAF on VKAs. Both equations performed similarly in predicting major adverse outcomes.

P5305 | BEDSIDE
Atrial ectopy and NT-proBNP as predictors of atrial fibrillation

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Background: Atrial fibrillation (AF) is a common arrhythmia associated with increased morbidity. Models for prediction of AF can be relevant in identifying subjects at increased risk for AF and for employing the appropriate therapy. Framingham Heart Study AF risk score is validated risk score that predicts the 10-year risk for incident AF. Studies have shown an association between increased risk of AF and increased rate of premature atrial contractions (PAC) and elevated levels of N-terminal pro-BNP (NT-proBNP).
Purpose: We aimed to investigate whether addition of the biomarkers NT-proBNP and PAC improved the model performance of the Framingham AF risk score.
Methods: Subjects from the population-based cohort in the Copenhagen Holter Study, consisting of 646 men and women between 55 and 75 years of age and with no history of prior atrial fibrillation, stroke or cardiovascular disease, were followed for the diagnosis of incident AF or death (median follow-up time 14.4 years). Baseline examination included physical examination, laboratory testing and 48-hour ambulatory ECG monitoring. In order to investigate the predictive ability of PAC (log-scale) and NT-proBNP (log-scale) we computed the time-dependent area under the ROC curve (AUC) for the AF status 10 years after the baseline examination. Risk reclassification and calibration of the models was assessed and the overall predictive performance was assessed by Brier score.
Results: Two hundred and sixty nine subjects (41.6%) were women, mean systolic blood pressure was 156.2 mmHg and 72 subjects (11.1%) had diabetes. Median NT-proBNP was 6.7 mmol/L (IQR: 3.6–13.5) and median PAC count was 1.4 beats/hour (IQR: 0.6–4.5). During the 14.4 years of observation 71 (11.0%) subjects developed AF and 224 (33.0%) died. In multiple Cox model adjusted for Framingham AF risk score log-transformed NT-proBNP and log-transformed PAC was associated with a significant increase in AF risk (HR 1.44 [95% CI: 1.16–1.78], p=0.001; HR 1.22 [95% CI: 1.08–1.37] p=0.002). The addition of PAC to the Framingham AF risk model significantly improved AF risk discrimination (AUC 65.7 vs. 72.2; p=0.0072), while the addition of NT-proBNP did not (AUC 68.4; p=0.23). The addition of both PAC and NT-proBNP to the Framingham risk score also improved the AF discrimination capability (AUC 72.1; p=0.013).
Conclusion: AF risk discrimination was significantly improved by addition of PAC to the Framingham AF risk prediction model, but not by addition of NT-proBNP.

P5306 | BEDSIDE

Anthropometric measures and risk of atrial fibrillation - a cohort study of 1.2 million young men

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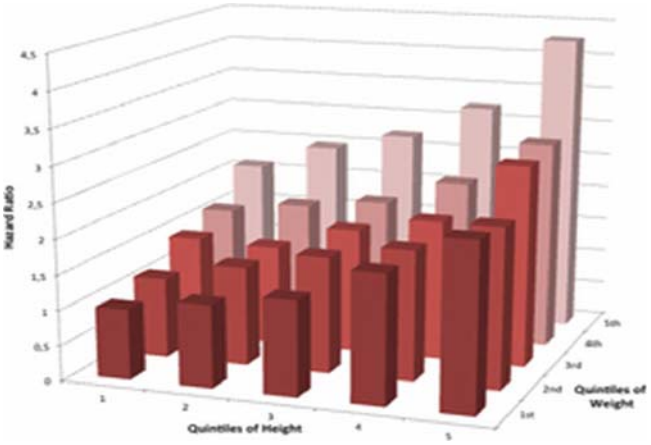
Background: While tall stature has been related to lower risk of cardiovascular disease, tall stature has been proposed as a risk factor for atrial fibrillation.
Aim: To investigate associations of body height, body weight, body surface area and body mass index with risk of atrial fibrillation, and to investigate joint effects of these measures and potential mediators of effect.
Study design: Cohort study
Study population: All Swedish men who participated in the mandatory military conscription at age 18 between August 1st 1972 and December 31st 1995. Outcomes were defined using the national in-patient and cause-of-death registries
Results: During a median of 26.3 years of follow-up of 1,173,547 men, higher body height was associated with higher risk of atrial fibrillation (HR 2.80; 95% CI 2.63–2.98; for 5th vs. 1st quintile) and so was weight (HR 2.52; 95% CI 2.34–2.70; for 5th vs. 1st quintile). Higher body surface area was also associated with higher risk of atrial fibrillation (HR 3.23; 95% CI 3.02–3.45; for 5th vs. 1st quintile). Body mass index was inconsistently associated with risk of atrial fibrillation. We found a multiplicative joint effect of higher height and higher weight (Figure).



Conclusion: Higher body height and weight in adolescence are strongly associated with higher subsequent risk of atrial fibrillation. These associations are multiplicative, and are reflected in a strong association of body surface area with risk of atrial fibrillation. The mechanisms remain unknown but we suggest that the increased volume load related to larger body size could be a mediating factor.
Acknowledgement/Funding: The Swedish Heart-Lung Foundation (grant 20041151) and the Swedish Research Council (grants 2007-5942 and 2010-1078).

P5307 | BEDSIDE

The incidence of atrial fibrillation increased significantly among men in their sixties and seventies

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Background: There has been a remarkable increase in the incidence of atrial fibrillation in Japan. Atrial fibrillation is known to increase with age. Although the increase in the incidence of atrial fibrillation may be due to the increase in the size of the elderly population, it is not clear as to whether or not the incidence of atrial fibrillation is increasing at a rate greater than the increase in the size of the elderly population due to other factors.
Subjects and methods: We annually recorded and analyzed the electrocardiograms of healthy residents of Iwate Prefecture, Japan who are living on their own using 16 specially equipped buses capable of recording electrocardiograms. In this study, we divided subjects ranging in ages from 40 to 79 years old into four groups for every 10 years of age, and investigated the incidence of atrial fibrillation at five year intervals during the 15 year period from 1997 to 2012.
Results: The average number of subjects during the four rounds of analysis was 201,000, and the population coverage rate was 29.1% of the number of residents in the prefecture of the same age groups of 690,000 (as of 2012). The incidence of atrial fibrillation, as determined by correcting the age composition in each analyzed year for the age composition in 2012, among men was 1.47% in 1997, 1.55% in 2002, 1.71% in 2007 and 1.79% in 2012, thereby demonstrating a significant increase. On the other hand, there were no significant increases observed among women. In looking at individual age groups, although the incidence among men in their forties in 2012 was 0.33% and that among men in the fifties was 0.33% and there were no significant differences observed, the incidence among men in their sixties increased from 2.27% in 1997 to 2.95% in 2012 and the incidence among men in their seventies increased from 4.17% in 1997 to 5.63% in 2012, demonstrating significant increases of 0.68% and 1.46%, respectively. In addition, the size of the increase was larger among men in their seventies than men in their sixties.
Conclusion: Although the incidence of atrial fibrillation among men in Iwate Prefecture during the 15 year period from 1997 to 2012 did not exhibit any changes among men in their forties and fifties, significant increases were observed among men in their sixties and seventies. Thus, there were clearly determined to be factors responsible for the increased incidence of atrial fibrillation other than changes in the population pyramid attributable to an increase in the size of the elderly population.

P5308 | BEDSIDE

Duration of diabetes mellitus and thromboembolic events in atrial fibrillation: a nationwide cohort study

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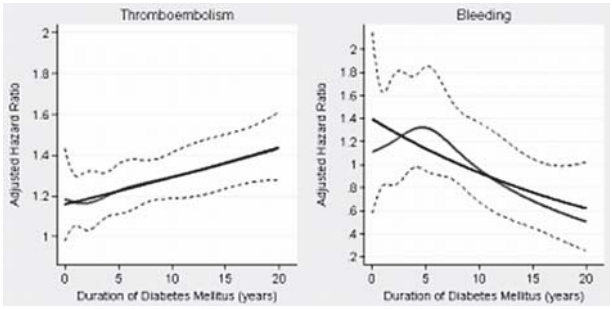
Background: Guidelines advocate anticoagulant treatment to all patients with atrial fibrillation and concomitant diabetes mellitus. The potential refinement to thromboembolic risk stratification that may spring from subdividing diabetes mellitus is unexplored.
Purpose: To investigate duration of diabetes mellitus as a predictor of thromboembolism and anticoagulant-related bleeding in patients with atrial fibrillation.
Methods: Using nationwide Danish registries, we identified all patients discharged from hospital with incident atrial fibrillation from 2000–2011. Hazard ratios [HRs] with 95% confidence intervals [CIs] for thromboembolism and bleeding according to years of diabetes duration in categories (0–4, 5–9, 10–14, and ≥15) and as a continuous variable were calculated using Cox regression.
Results: The study population comprised 137,222 patients with atrial fibrillation, of which 12.4% had diabetes mellitus. Compared with patients without diabetes and after adjustment for anticoagulant treatment and CHA2DS2-VASc components, the risk of thromboembolism was lowest in the 0–4 years duration category (HR 1.11, 95% CI: 1.03–1.20), and highest in the longest duration category of ≥15 years (HR 1.48, 95% CI: 1.29–1.70). As a continuous variable, duration of diabetes was associated with risk of thromboembolism in a dose-response dependent manner, but not with a higher risk of bleeding during anticoagulant treatment (Figure).



Thromboembolism and bleeding

Conclusions: In patients with atrial fibrillation, longer duration of diabetes mellitus was associated with a higher risk of thromboembolism, but not with a higher risk of anticoagulant-related bleeding. Considering the critical balance between preventing thromboembolism and avoiding bleeding, longer duration of diabetes mellitus may favour initiation of anticoagulant therapy.

P5309 | BEDSIDE

Acute ranolazine plus amiodarone vs amiodarone alone for conversion of recent-onset atrial fibrillation: a prospective clinical study

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Background and introduction: Amiodarone (AMIO) is frequently used to convert atrial fibrillation (AF) in patients with or without heart failure. However, because AMIO needs several hours or days for converting AF into sinus rhythm, it has recently been started to combine it with ranolazine (RAN) in an attempt to accelerate termination of this arrhythmia in clinical practice. RAN is a new antianginal agent with additional electrophysiologic properties, partially consisting of a selective open-state Na+ channel inhibition at atrial level.
Purpose: To compare the antiarrhythmic effectiveness of AMIO + RAN vs AMIO alone in a prospective, single-blinded, randomized study.
Methods: We enrolled 65 patients with recent-onset (<48 h duration) AF who

were eligible for pharmacologic cardioversion. A number of 29 patients (16 male/13 female, 62±11 years) received only AMIO infusion (loading dose 5 mg/kg followed by maintenace dose of 50 mg/h), while the remaining 36 patients (9 male/27 female, 67±10 years) were treated with AMIO plus a single oral dose of RAN 1g. Left ventricular ejection fraction (LVEF), left atrial diameter (LAd), and P-wave duration (PWD) were evaluated in all patients.
Results: Patients in the AMIO+RAN group compared with the AMIO-only group showed significantly shorter time to conversion intervals (8.1±2.2 vs 24.4±4.1 h; $P<0.0001$, Mann-Whitney test). AMIO+RAN vs AMIO-only patients had LVEF (54.3±5.9 vs 54.5±3.8%, P=NS), LAd (39.1±3.8 vs 39.1±7.7 mm, P=NS), and PWD (90.2±28 vs 91.1±26 ms, P=NS), respectively. All aforementioned values were expressed as mean±SD and considered significant at the 0.05 level. No sinus bradycardia or QTc excessive prolongation (≥440 ms) were observed after cessation of AF in the AMIO+RAN group.
Conclusion: These findings demonstrate a superior antiarrhythmic efficacy of AMIO+RAN therapy to AMIO alone in patients with recent-onset AF and LAd ≤46 mm. We suppose that RAN might selectively depress atrial conduction and increase postrepolarization refractoriness more than AMIO alone thereby potentially enhancing its antiarrhythmic effect.

P5310 | BEDSIDE
A multidisciplinary atrial fibrillation clinic is superior to standard outpatient treatment

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Background: Atrial fibrillation (AF) is the most common taky-arrhythmia and it is associated with an increased risk of stroke and mortality. Anticoagulation therapy reduces the risk of stroke in patients with AF.
Despite a simple empiric scoring system (CHA2DS2-VASc) only 50–80% of patients receive correct anticoagulation therapy according to guidelines.
We hypothesized that a structured multidisciplinary approach to AF patients will ensure optimal anticoagulation therapy superior to standard outpatient treatment.
Methods: The present study compares the proportion of patients with AF in anticoagulation treatment according to guidelines in three different settings.
In the "AF clinic group" patients were treated in a structured multidisciplinary AF clinic that comprised of two dedicated cardiologists and two nurses, one nurse with expert knowledge of anticoagulation treatment, and another with echocardiographic skills. The "first usual care group" comprised of patients with AF seen in the same outpatient setting prior to the establishment of the AF clinic. The "second usual care group" comprised of data from the EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry.
We evaluated the proportion of patients with indication for anticoagulation (CHA2DS2-VASc ≥1) actually treated with anticoagulation, and the proportion of patients treated with multi-anticoagulation/ antithrombotic drugs not indicated by the guidelines.
Results: In the "AF clinic group" correct anticoagulation treatment according to guidelines was achieved in 99% (170 out of 172 patients) compared to 79% (143 out of 179 patients) in the "first usual care group" and 80% (2435 out of 3044 patients) in the "secondusual care group" ($p<0.01$, both).
The proportion of patients in the "AF clinic group" treated with multi-anticoagulation/antithrombotic drugs not indicated by the guidelines was <1% (1 out of 172 patients) compared to 19% (34 out of 179 patients) in the "first usual care group" and 20% in the "second usual care group" ($p<0.01$, both).
Conclusions: This study demonstrates that a structured multidisciplinary approach ensures optimal anticoagulation therapy in patients with atrial fibrillation. This contributes to a better protection against stroke and a lower bleeding risk.
We encourage establishment of structured multidisciplinary AF clinics to ensure optimal antithrombotic treatment and adherence to current guidelines.

ATRIAL FIBRILLATION V

P5311 | BEDSIDE
Stroke severity in relation to duration of atrial fibrillation and supraventricular runs in patients with cerebral ischemia

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Background: Atrial fibrillation (AF) is a frequent cause of ischemic strokes. The AF-definition includes only typical episodes ≥30 seconds, but the minimal duration of AF that increases the risk of thromboembolism is unknown. The relevance of shorter supraventricular (SV-) runs, which are frequently revealed by enhanced ECG-monitoring, remains unclear. As AF-related strokes are known to be more severe, we applied stroke-related physical impairment as a surrogate marker for cardioembolic pathogenesis in patients with various durations of paroxysmal AF and SV-runs.
Methods: Retrospective analysis from the prospective observational Find-AF-trial (ISRCTN46104198). Those without AF at presentation received 7-day Holter-ECG-monitoring. The longest SV-run was determined in a 24-hour interval free from AF. Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS).
Results: 258 patients were analysed. 43 had AF at presentation. 215 received Holter-monitoring: 27 (12.5%) had paroxysmal AF, 69 had SV-runs >5 beats and 119 had neither AF nor SV-runs. Stroke severity was equally increased in those with various durations of manifest AF. Even those with prolonged SV-runs had significantly milder strokes, in the range of those without any supraventricular arrhythmias.
Conclusion: Although stroke-related physical impairment is only a surrogate-marker of cardioembolic pathogenesis, our results imply that even short AF-episodes could be associated with thromboembolic events. On the other hand, even prolonged SV-runs do not appear to induce cardioembolism. It remains to be determined, whether subgroups with short AF-episodes or those with SV-runs effectively benefit from oral anticoagulation.
Acknowledgement/Funding: grants by German Ministry of Education and Research (German Heart Failure Network, TP 7 (FKZ 01GI0205) and unrestricted grant by Roche diagnostics

P5312 | BEDSIDE
A severity of sleep-disordered breathing with atrial fibrillation ablation candidates is associated with the long-term outcome after pulmonary vein antrum isolation

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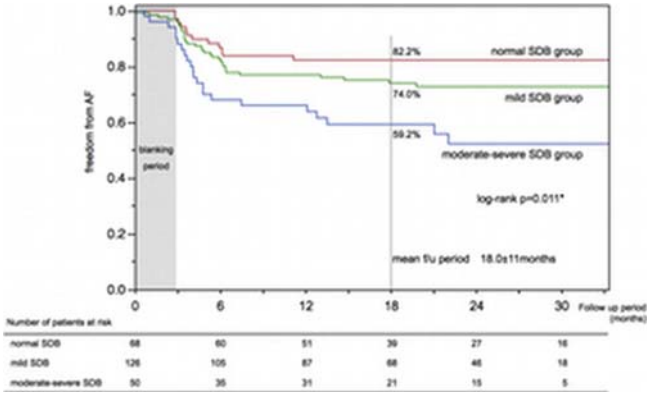
Background: Sleep-disordered breathing (SDB) may be associated with pulmonary vein antrum isolation (PVAI) failure.
Purpose: The aim of the present study was to investigate the impact of the severity of SDB for the outcome after PVAI.
Methods: From December 2011 to March 2014, 269 consecutive patients underwent PVAI. Known SDB cases with continuous positive airway pressure (CPAP) therapy, cases without appropriate oxygen desaturation data, and ablation failure cases due to the complications were excluded. A total of 244 patients were analyzed. Before the procedure, we measured the oxygen desaturation index (ODI) by pulse oximetry overnight as an indicator of SDB, and classified SDB severity by 3% ODI as normal (ODI <5 events/h), mild (ODI ≥5 to <15 events/h) or moderate-severe (ODI ≥15 events/h).
Results: At the mean follow-up period (18±11 months), 82.2% of normal, 74.0% of mild, and 59.2% of moderate-severe SDB group were free of atrial fibrillation after the single procedure (log-rank P=0.011). The severity (moderate-severe) of SDB was only predictor of recurrence after single PVAI (hazard ratio, 2.23; 95% CI, 1.05–4.96 P=0.038) including with other known risk factors such as LAVI (< or ≥34ml/m^2), AF type (paroxysmal or non-paroxysmal), and concomitance of left ventricular diastolic dysfunction adjusting with age and gender. Even after multiple sessions, Kaplan-Meier analysis shows that recurrences of moderate-severe SDB group significantly more frequent during mid-term follow-up (log-rank P=0.047).



Kaplan-Meier curve after PVAI

Conclusions: Our study suggests that baseline SDB is associated with increased PVAI failure and the moderate-severe SDB was an independent predictor for the recurrence after single PVAI. We recommend that pulse oximeter testing become a routine part of the procedural work-up before AF ablation.

P5313 | BEDSIDE
Causes of death and influencing factors in a cohort study of patients with atrial fibrillation

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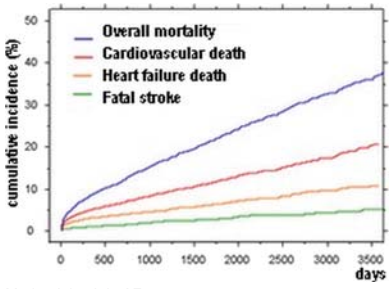
Background: Atrial fibrillation (AF) is associated with a higher mortality. However, the causes of death and their predictors are poorly known in unselected patients with AF seen outside the context of a randomized trial.
Methods: We examined the clinical course of 8962 consecutive patients with AF seen between 2000–2010 in an academic institution and identified their causes of death.
Results: In these 8962 patients (age 70±10 years, CHA2DS2VASc score 3.1±1.7), 1253 deaths were recorded during a follow-up of 929±1082 days (yearly rate of death 5.5%) and 97% of causes of death were identified. Cardiovascular deaths accounted for 54% and 43% for non-cardiovascular. The three main causes of death were heart failure (29%), infection (18%) and cancer (12%). Fatal stroke or fatal bleeding each accounted for 7% of all deaths. In multivariate analysis, the prescription of oral anticoagulation was independently associated with a lower risk of all-cause mortality (Hazard Ratio HR 0.62, 95% CI: 0.54–0.71, $p<0.0001$) and cardiovascular mortality (HR 0.60, 95% CI 0.49–0.72, $p<0.0001$). In addition, permanent AF, history of heart failure or major bleeding and renal failure were independently associated with an increase in the risk of all cause mortality (35%, 78%, 42% and 79% respectively), of cardiovascular mortality (43%, 129%, 46% and 93% respectively) and non-cardiovascular mortality (21%, 45%, 40% and 50% respectively).



Mode of death in AF

Conclusion: Oral anticoagulation was associated with lower risk of overall mortality and cardiovascular death but stroke- and haemorrhage-related mortality represented a relatively small proportion of deaths in unselected patients with AF. An optimal management of underlying heart disease and associated comorbidities should be a relevant target to reduce mortality in AF.

P5314 | BEDSIDE
Time course of atrial fibrillation in patients with a congenital heart defects

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Background: Regular atrial tachycardia (AT) and atrial fibrillation (AF) occur frequently in patients with congenital heart defects (CHD). Whereas regular AT has extensively been studied, studies about AF in CHD patients are rare, despite the increasing incidence of AF.
Purpose: The aim of this international multicenter study was 1) to examine the development of AF in patients with a variety of CHD 2) to investigate the co-existence of AF with regular AT 3) to study the progression of paroxysmal to long-standing persistent/permanent AF during long-term follow-up.
Methods: CHD patients derived from databases of the participating centers with documented AF episodes on an ECG or 24-hour Holter registration were included. All available ECGs and 24-hour Holter registrations were also reviewed for the presence of regular AT.
Results: Patients (N=199) with 15 different CHD and a documented AF episode were studied. AF developed at the age of 49±17 years. Patients with an atrial septal defect (N=58; 57±6 years) and aortic valve disease (N=34; 53±15 years) were older at the time of initial AF than patients with transposition of the great arteries (N=17; 35±7 years) or univentricular hearts (N=16; 29±11 years. Co-existence of AF with regular AT was observed in 65 (33%) patients; 42 (65%) first developed regular AT 5±5 years before the first AF episode. The remaining 23 (35%) patients with co-existence first presented with AF, 5±5 years before regular AT. Of the patients with a yearly ECG (N=112), progression to long-standing persistent/permanent AF was observed in 29 (26%) patients after only 3 (0–18) years of the initial AF episode. In all the patients, ischemic cerebrovascular events were found in 26 patients (13%). However, the majority (N=16) occurred years before patients were diagnosed with AF.
Conclusion: Patients with CHD develop AF at a relative young age compared to patients without CHD, especially patients with "complex" CHD. Thirty-three percent of the patients with AF also developed regular AT; initial episodes of AF were documented before as well as after regular AT. Progression of paroxysmal to long-standing persistent/permanent AF was frequently observed and occurred relative fast; therefore, aggressive therapy of regular AT and AF is reasonable.

P5315 | BEDSIDE
Does renal dysfunction predict new onset of atrial fibrillation in the Japanese general population?

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Purpose: Several conditions have been proposed as a risk factor contributing to the new onset of atrial fibrillation (AF). Chronic kidney disease is reported as a risk factor for the new onset AF in hypertensive patients, whereas their relationship has not been intensively investigated in general population. We tested the hypothesis that the risk of new AF increases with deterioration of estimated glomerular filtration rate (eGFR) in the general population.
Methods: Consecutive 14,558 participants without a history of AF (male=8,924, 52.0±12.2 year-old) who visited our hospital for a physical check-up from July 2001 to June 2013 were enrolled in this study. After baseline evaluation, they were followed up for the median of 1,838 days with the endpoint being the new onset of AF. The relationship between baseline eGFR and the incidence of AF during the follow-up was analyzed. Kidney function was categorized into 4 groups according to the classification of chronic kidney disease: stage 1, $eGFR \geq 90$; stage 2, $90 > eGFR \geq 60$; stage 3, $60 > eGFR \geq 30$; stage 4+5, $eGFR < 30$ (mL/min per 1.73 m^2).
Results: During the follow-up, 99 subjects suffered from paroxysmal or chronic AF (1.19 per 1000 person-year), with the incidence being more frequent in male than in female subjects (1.55 vs. 0.58 per 1000 person-year, $p<0.0001$). The incidence of AF in stage 1, 2, 3, and 4+5 was 0.59, 1.58, 3.77 and 27.46 per 1000 person-year, respectively. The risk of new AF increased across the kidney function categories at baseline (the hazard ratio [95% confidence interval] in stage 1, 2, 3, and 4+5 was 1 [reference], 2.653 [1.649–4.269], 6.739 [3.207–14.164] and 60.428 [8.127–449.313], respectively). After adjustment for gender, body mass index, systolic blood pressure, heart rate, uric acid, fasting plasma glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and current smoking habit at baseline, multivariate Cox proportional hazard regression analysis, where eGFR was taken as a continuous variable, revealed that decreased eGFR was the significant predictor of new AF (hazard ratio [95% confidence interval: 0.981 [0.967–0.996]).
Conclusions: The risk of the new onset of AF increases with decreasing eGFR. Renal dysfunction may be a useful predictive factor for the incidence of AF in the general population.

P5316 | BEDSIDE
Impact of non-rheumatic valvular heart disease on mortality in patients with atrial fibrillation: Results from the German AFNET registry

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Atrial fibrillation (AF), the most common arrhythmia, is associated with substantial morbidity and an increased risk of death. Recent data from large randomized trials have highlighted that mortality in anticoagulated AF patients remains high and is often due to heart failure or sudden death. Data on the impact of valvular disease on mortality in AF patients are limited. We therefore analysed mortality rates and baseline prognostic factors for all-cause mortality in AF patients with and without native valve disease.
Methods: A total of 9574 AF patients were enrolled 2004–2006 in the prospective long-term registry of the German Atrial Fibrillation Competence NETwork (AFNET). Survival information was available for 96.8% of patients. Corresponding to the definition of non-valvular AF, patients with mitral stenosis or valve prostheses were excluded for this study. After excluding patients with missing values on prognostic factors, the study population consisted of 8260 patients (5169 men, mean age 66.2±11.2 years; 3091 women, 71.6±10 years). Patients were grouped by type of valvular disease (VD) to aortic stenosis (AS, n=314 (3.8%)), Other VD (n=2382 (28.8%)), and No VD (n=5564 (67.4%)) as assessed by the enrolling physician.
Results: Median follow-up time was 6.4 years and total number of deaths was 2259. Patients with AS were older, had higher NYHA classes, and more comor-

bidities. All-cause mortality rate was 12.9 and 14.6 per 100 person-years in men and women with AS, respectively. Mortality was 6.6 (men) and 6.2 (women) per 100 person-years in Other VD, and 4.5 per 100 person-years in both men and women with No VD. In a multivariable Cox model (with interactions), only AS was associated with all-cause mortality, while Other VD was not (adjusted hazard ratio compared to No VD: AS, 1.89 (1.53–2.34); Other VD, HR 1.10 (0.98–1.23)). The most relevant independent predictors of all-cause mortality in patients with and without VD were age, heart failure, as either assessed by the NYHA classification or EF, peripheral vascular disease, chronic renal failure, chronic obstructive pulmonary disease, diabetes mellitus, prior myocardial infarction, and, in patients with No VD only, malignancy.
Conclusion: In this large real world cohort of patients with "non-valvular" AF, aortic stenosis was independently associated with an increased risk of death from any cause, whereas other valvular disease was not. Specific diseases therefore have a major impact on mortality in AF, illustrating the need to target concomitant diseases to improve survival in AF.
Acknowledgement/Funding: Supported by the German Federal Ministry for Education and Research [BMBF 01GI0204]

P5317 | BEDSIDE
Chronic osteomyelitis as a new risk factor for incident atrial fibrillation: evidence from a nationwide cohort of 23 million people

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Objectives: Chronic inflammation is an important predisposing factor for the development of atrial fibrillation (AF). This study aimed to determine whether chronic osteomyelitis (COM), a chronic inflammatory disease, is linked to an increased risk of AF.
Methods: A national insurance claim dataset of more than 23 million enrollees was used to identify 19,002 patients with newly-diagnosed COM and 76,008 randomly selected age- and gender-matched controls between January 1, 2000 and December 31, 2009 for comparing the risk and incidence of AF. The study period was from the entry date to the first date of the following events: the diagnosis of AF, death, withdrawal from the Taiwan National Health Insurance program or the end of 2010. The analysis of the AF risk was performed using Cox proportional hazards regression model.
Results: During a follow-up period of 91,927 person-years, the overall incidence rate of AF in COM cohort was 1.42-fold higher than non-COM cohort (4.54 vs. 3.19 per 1000 person-years). After adjusting for age, gender and classical AF risk factors including hypertension, diabetes, heart failure, coronary artery disease, valvular heart disease, hyperlipidemia, and chronic obstructive lung disease, the risk remained significantly higher in the COM cohort than the control group (hazard ratio [HR] 1.36, 95% confidence interval [CI] 1.22–1.53, $p<0.001$). In age-stratified analysis, the younger population carried higher AF risk than the elderly (from HR 2.17, 95% CI 1.21–3.90 in age <50 to HR 1.21, 95% CI 0.97–1.51 in age ≥ 80). Additionally, patients with COM showed a disease severity-dependent increased risk of AF (mild COM: HR 0.88, 95% CI 0.74–1.06; moderate COM: HR 1.32, 95% CI 1.11–1.58; and severe COM: HR 3.43, 95% CI 2.86–4.12).
Conclusions: This study demonstrates that COM is an independent risk factor for incident AF, particularly in the younger population. Further studies are required to explore the underlying mechanisms linking COM and AF.

P5318 | BEDSIDE
Presentation, treatment, and outcome of patients with Atrial Fibrillation and Chronic Kidney Disease. A prospective national study

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Background: Atrial fibrillation (AF) is more prevalent among patients with chronic kidney disease (CKD) than among individuals with normal renal function. Patients with CKD are more likely to suffer from ischemic stroke, thromboembolism or major bleeding. We examine the correlations between renal function on treatment and outcomes in a historical cohort of AF patients with varying degrees of kidney disease.
Methods: A prospective historical cohort study, conducted using our Services database, between 2004 and 2011. Patients with nonvalvular AF (NVAF) were stratified into five CKD stages (eGFR >90, 89–60, 59–30, 29–15 and <15 mL/min/1.73 m^2). Primary endpoints were cerebro-vascular stroke, death, major bleeding and the composite endpoint of death and stroke.
Results: During the study period, 98,811 patients with new onset of non-valvular AF were identified. Mean follow-up time was 48.8 months. The incidence rate of stroke was 12.5 per 1,000 person-years (PY). Mortality rate was 87.5/1,000PY, and of major bleeding 5.2/1,000PY. The average age was highest among the stage 3 CKD group (average age 79). Patients with stage 4 and 5 CKD had higher incidence of heart failure, hypertension, diabetes and dyslipidemia, and had a lower chance of being treated with Warfarin (only 15.2% of the patients compared with average of 25%). Mortality was directly correlated severity of CKD. Highest stroke rates were observed among patients with stage 3 CKD, and the lowest among patients with normal kidney function. On multivariate analyses eGFR was not an independent predictor of stroke risk, but a strong predictor of mortality. In the groups of patients with CKD stage 4 and 5, Warfarin did not influence the incidence rate of the composite endpoint of stroke or death (190 per 1000PY), but Warfarin usage was associated with a significantly longer time before reaching the endpoint (22.7 months vs. 37.6).
Conclusion: In this large contemporary study of patients with AF, stroke incidence was highest among patients with moderate CKD, but mortality rate increased with decreased eGFR throughout the entire range of CKD. The use of Warfarin among patients with severe renal impairment was associated with improved survival.

P5319 | BEDSIDE
Comparison of emerging blood biomarkers, NTproBNP and the CHA2DS2-VASc score in the prediction of paroxysmal atrial fibrillation in patients with continuous rhythm monitoring

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia associated with increased morbidity and risk of stroke. Paroxysmal AF (PAF) is often asymptomatic, and diagnosis and management may be delayed with sporadic rhythm monitoring. Risk factors combined in the CHA2DS2-VASc score (heart failure, age, diabetes, hypertension, stroke, vascular disease, gender) and also serum biomarkers (e.g. NTproBNP) have been associated with AF. We compared the predictive value of emerging biomarkers, NTproBNP and CHA2DS2-VAsc for AF in patients with continous rhythm monitoring.
Methods: Patients with dual chamber pacemaker and sinus rhythm at presentation were divided according to the absence (SR, N=44) or presence (PAF, N=49) of atrial tachyarrhythmias >6 min duration in the device event history. CHA2DS2-VASc score was assessed and set of biomarkers were determined in serum or plasma taken during sinus rhythm from all patients. Regulation of 16 selected biomarkers was tested in univariate analysis in two subgroups of patients with the highest incidence of AF (N=20) and no (0 min) AF (N=20). The predictive value (AUC) of signifcantly regulated biomarkers was tested than in all patients in univariate and bivariate models.
Results: In the PAF and SR subgroups levels of Hsp27, TGFβ1, cysteine C, matrix metalloproteinases MMP-2, -3, -9, albumin and serum uric acid were not different between SR and PAF. In contrast, tissue inhibitors of metalloproteinases (TIMP)-1, -2, -4; proANP (1–98), NTproBNP, IL-6 and serum amyloid protein A (SAA) were significantly different in PAF vs. SR (subgroups and full cohort; $p<0.05$), with the highest AUC for TIMP-4 (78%). Patients with NTproBNP value >150 pg/ml had an odds ratio of 12,9 for AF (sensitivity: 92%, specificity: 46,5%). Combining two of the best performing biomarkers vs. a single biomaker added predictive value for AF detection (e.g. TIMP-4 vs TIMP-4 with NTproBNP, TIMP-4 vs TIMP-4 with proANP (1–98); both $P<0.05$). AUC for CHA2DS2-VASc was lower than for the top biomarkers (TIMP-1, proANP (1–98), NTproBNP). Combination of CHA2DS2-VASc with the top biomarkers significantly added prognostic value.
Summary: We identified biomarkers (TIMP -1, -2, -4; proANP (1–98), NTproBNP, IL-6 and SAA) that are regulated in patients with a history of PAF presenting in sinus rhythm. TIMP-1, proANP (1–98), NTproBNP performed better that the CHA2DS2-VASc score in identifying patients with PAF.

P5320 | SPOTLIGHT
Increasing incidence of non-valvular atrial fibrillation (AF) between 2001-2013 in the UK: largely due to non-primary AF hospital diagnosis in the elderly

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Background: The incidence of non-valvular atrial fibrillation (AF) is increasing, though many studies have calculated incidence rates from only one source, usually hospital discharges, disregarding any contribution of general practice to AF diagnosis.
Purpose: To examine recent temporal trends in AF incidence rate and place of AF presentation.
Methods: The UK Clinical Practice Research Datalink with additional hospital discharge data from Hospital Episode Statistics (HES) was used to identify a cohort of 91,707 patients aged over 45 with incident AF from 2001 to 2013. Age and gender-standardized incidence rates of AF in the UK population were calculated and stratified by calendar year and place of AF presentation.
Results: Overall, 39% of incident AF presentations were in general practice (GP), 15% were primary admissions to hospital with AF, and 46% were diagnosed during a hospital admission with a non-AF primary diagnosis. There was a gradual linear increase of incidence rate from 5.9 to 6.9 new AF/1000 person-years between 2001 and 2013, almost entirely due to an increase of non-primary hospital AF diagnoses, while incidence rates in GP and for primary AF hospital admis-

sions were static (Figure 1, upper panel). When non-primary HES were stratified by age, the rise in incidence rates was most marked for those >80 (Figure 1, lower panel).

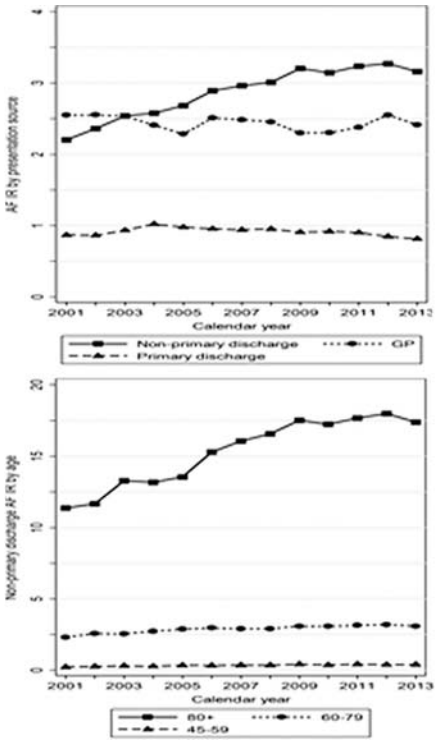

Figure 1. AF incidence rate/1000 patient yrs

Conclusions: GP diagnosis of AF without hospital admission constitutes a large proportion of incident AF, often overlooked in epidemiological studies. There has been a gradual and significant rise in incidence rates of AF in the last 13 years, largely due to an increasing incidence of hospital diagnosis of AF in the elderly admitted for a cause other than AF. This needs to be considered when addressing the increasing burden of AF forecast as the population ages.

P5321 | BEDSIDE

Ventricular rate is not related to survival in patients with heart failure and atrial fibrillation

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Introduction: Atrial fibrillation (AF) is common in patients with chronic heart failure (CHF), and is associated with significant morbidity and mortality. Although there is robust evidence that heart rate is a risk factor in CHF and that reducing elevated heart rates improves survival in patients who are in sinus rhythm, the importance of strict heart rate control in AF is still not clear. This study sought to investigate the influence of resting ventricular rate on survival in CHF, comparing those who are in sinus rhythm to those in AF.
Methods: A total of 1415 CHF patients (mean age 76±11 years, 36% females, 65% IHD, 41% NYHA II, 44% NYHA III, 14% NYHA IV), of whom 62% (n=875) were in sinus rhythm and 38% (n=540) in permanent AF were evaluated from the BIOSTAT-CHF Scotland study. Patients from both in-patient and out-patient settings were included. We analysed the heart rate and rhythm data recorded on a 12 lead ECG at the baseline review. Multivariate Cox proportional hazards models & Kaplan-Meier curves were used to assess the influence of heart rate on survival in CHF patients with AF or sinus rhythm.
Results: During a median per-person follow-up of 1.5 yrs (QIR 0.7–2.2), there were 330 (23%) all-cause deaths. Although Kaplan-Meier survival curves displayed significant differences between the AF and sinus rhythm groups (log-rank test p=0.014), multivariate Cox survival models showed no significant difference between the 2 groups (hazard ratio [HR]: 0.98, 95% CI: 0.75–1.29; p=0.9). When assessing the influence of heart rate, multivariate Cox models showed that higher heart rates (per 10 beats/min increments) were associated with worse survival in patients in sinus rhythm (HR: 1.14, 95% CI: 1.03–1.25; p=0.008), but not for those in AF (HR: 0.98, 95% CI: 0.91–1.07, p=0.7), for both preserved and reduced ejection fraction heart failure. When separated into two categories (heart rate <80bpm vs. ≥80bpm), those in sinus rhythm with a heart rate ≥80bpm had a significantly worse survival than those with a heart rate <80bpm (HR: 1.57, 95% CI: 1.10–2.23, p=0.012).
Conclusion: Although higher heart rate was associated with worse survival for CHF patients in sinus rhythm, it does not appear to be associated with survival in those who are in AF. These findings question the value of strict heart rate control in CHF patients with atrial fibrillation, thus necessitating further research in this area.

P5322 | BEDSIDE

Usual blood pressure, atrial fibrillation and vascular risk: evidence from 4.3 million adults

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Purpose: To determine the age-specific association between usual blood pressure and risk of atrial fibrillation and to further determine the associations between atrial fibrillation and a range of vascular events in a large contemporary cohort.
Methods: Linked electronic health records, validated for epidemiological research, were used to assemble a cohort of 4.3 million adults, aged 30 to 90 years and free of pre-existing vascular disease. Cox proportional hazards models were used to examine the association between baseline blood pressure and incident atrial fibrillation, and the association between baseline atrial fibrillation and risk of nine different vascular events.
Results: After adjusting for regression dilution, a 20 mm Hg higher systolic blood pressure was associated with a higher risk of atrial fibrillation (hazard ratio [HR] 1.21 95% confidence interval [CI] 1.19, 1.22). The strength of the association declined with increasing age, from an HR of 1.91 (CI 1.75, 2.09) in age 30–40 to an HR of 1.01 (CI 0.97 1.04) at age 80–90 years.
Atrial fibrillation without antithrombotic use at baseline was associated with a greater risk of any vascular event than atrial fibrillation with antithrombotic usage (2.15 CI 2.05, 2.24 vs. HR 1.15 CI 1.12, 1.18; p interaction <0.0001). Atrial fibrillation without baseline antithrombotic usage was associated with an increased risk of ischemic stroke (HR 2.72 CI 2.19, 3.38), hemmorhagic stroke (HR 2.22, CI 1.60, 3.08), unspecified stroke (HR 2.59 CI 2.25, 2.99), ischemic heart disease (HR 2.52 CI 2.23, 2.84), heart failure (HR 3.80 CI 3.50, 4.12), chronic kidney disease, peripheral arterial disease and vascular dementia, but not aortic aneurysm.
Conclusions: The association between elevated blood pressure and atrial fibrillation attenuates significantly with increasing age. Atrial fibrillation without antithrombotic usage is, in turn, associated with increased risk of stroke, ischemic heart disease, heart failure, chronic kidney disease, peripheral arterial disease and vascular dementia.

ATRIAL FIBRILLATION VI

P5323 | BEDSIDE

Accessory pathway ablation is enough to suppress atrial fibrillation in patients without elevated B-type natriuretic peptide level among those with WPW syndrome and atrial fibrillation (WPW-AF study)

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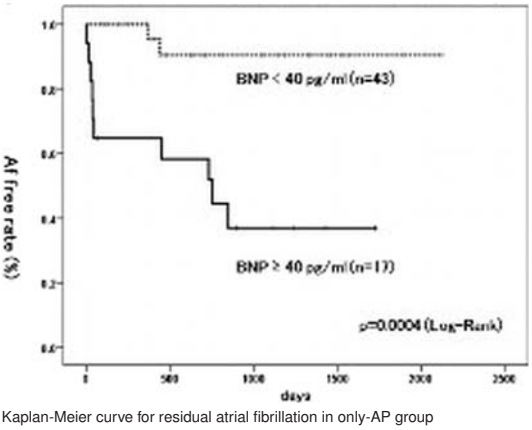
Introduction: Paroxysmal atrial fibrillation (AF) often occurs in patients with Wolff-Parkinson-White (WPW) syndrome. It has been reported that successful accessory pathway (AP) ablation suppressed AF.
Methods: Ninety-one WPW syndrome patients (55±14 years, 70 men) with clinical AF underwent catheter ablation between 2008 and 2014 at 8 centers.
Results: Sixty patients underwent only AP ablation (only-AP group) and 31 underwent pulmonary vein isolation simultaneously (+PVI group). There was no significant difference in terms of basic clinical data and electrophysiological findings between the groups. During follow-up (median 711 days), AF was observed in



Kaplan-Meier curve for residual atrial fibrillation in only-AP group

21 (23%). The incidence of AF after the ablation did not show a significant difference between the groups. In the only-AP group, those with residual AF were significantly older and had significantly higher BNP level and more concomitant hypertension than those without AF. Among risk factors for residual AF (age≥60 years, BNP≥40pg/ml, or accompanied hypertension), BNP≥40pg/ml was the only independent predictor of remaining AF (95% confidence interval 0.023 to 0.491; p=0.004) using multivariate Cox regression.
Conclusion: In WPW syndrome patients with AF, a BNP level≥40 pg/ml is a strong and independent predictor of AF after AP ablation. This finding has important implications for identifying patients at higher risk of post-procedural AF who could be considered for additional ablation for AF.

P5324 | BEDSIDE
Increased cardiovascular risk after treatment for hyperthyroidism

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Background: Hyperthyroidism is a common disease affecting 1–2% of the population at some time. Previous studies have shown increased long-time morbidity in patients treated for hyperthyroidism, largely due to cardiovascular disease. However, controversy remains regarding which cardiovascular subgroups are responsible for this increased risk. It is also not clear whether the type of hyperthyroidism - Graves disease (GD) or Toxic Nodular Goiter (TNG) – matters.
Purpose: To perform a detailed investigation of incident cardiovascular disease in previously hyperthyroid subjects.
Methods: We analysed a register of 29 662 patients treated for hyperthyroidism with either radioiodine or surgery between the years 1976–2012. An additional cohort of 42 630 euthyroid patients was used as a control group. Data on comorbidities and outcomes was collected from the Swedish National Inpatient Register. Age, sex, and cardiovascular risk factors at baseline were adjusted for.
Results: For hyperthyroidism as a whole, statistically significant increases in hazard ratios (HR) were seen for the following overall categories of cardiovascular diagnoses: Valvular disease (1.20, 95% confidence interval (CI) 1.09–1.30), ischaemic heart disease (HR 1.05, CI 1.01–1.10), arrhythmias (HR 1.15, CI 1.10–1.20), heart failure (HR 1.41, CI 1.35–1.47) and cerebrovascular disease (HR 1.18, CI 1.13–1.24). No significant excess risk was seen for disorders of the pulmonary circulation or arterial disease. When GD and TNG were analysed separately, few significant differences between GD patients and controls remained, while HR:s were further increased among TNG patients in all cardiovascular disease categories examined. Additional analyses of more specific diagnosis groups revealed increased risk for pulmonary embolism (HR 1.16, CI 1.02–1.32), bradycardias (HR 1.30, CI 1.14–1.50), atrial fibrillation (HR 1.31, CI 1.23–1.38) and cardiac arrest (HR 2.03, CI 1.58–2.60) among TNG patients but not among patients with GD.
Conclusion: In our cohort, hyperthyroidism is associated with an increased risk of hospitalization for several types of cardiovascular disease. This excess risk appears to be almost solely attributed to patients with a TNG diagnosis. Furthermore, the connections seen between TNG and pulmonary embolism, bradycardia and cardiac arrest have to our knowledge not been previously described.

P5325 | BEDSIDE
Effect of colchiciNe on the inciDence of Atrial Fibrillation in open heart surgery patients: end-AF Trial

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Background: Atrial fibrillation (AF) is a common dysrhythmia in patients undergoing open heart surgery (OHS). It occurs in up to 25% of such patients and results in significant morbidity and increased hospital stay. Different strategies have been tested to decrease its incidence with variable success.
Purpose: We sought to determine if colchicine administered preoperatively to patients undergoing OHS and continued during their hospitalization is effective in reducing the incidence of postoperative AF.
Methods: This is a multicentre prospective randomized open label study. Consecutive patients with no history of supraventricular arrhythmia and scheduled to undergo elective OHS (n=360) were randomized to colchicine (n=179) or no-colchicine (n=181). Main exclusion criteria were history of supraventricular arrhythmias or absence of sinus rhythm at enrolment, and contraindications to colchicine. Colchicine was orally administered 12 to 24 hours preoperatively and continued until hospital discharge (2 mg at enrolment and 0.5 mg twice daily in patients≥70 kg, or 1 mg at enrolment and 0.5 mg once daily in patients <70 kg). Cardiac rhythm was monitored continuously in the coronary care unit, and, by daily and symptom-prompted 12-lead electrocardiograms in the ward. The primary efficacy end point was documented AF lasting more than 5 minutes. Safety end point was colchicine side effects.
Results: The baseline characteristics were similar in both groups. In-hospital mortality was 3.3% (12 patients, 5 in the colchicine and 7 in the no-colchicine groups). The primary end point of AF occurred in 63 patients (17.5%), 26 (14.5%) in the colchicine group and 37 (20.5%) in the no-colchicine group; RRR 29.3% (p=0.17). Of the 63 patients who developed AF, 33 (52.4%) developed their AF on the second post-operative day, and the majority of AF episodes (n=53, 84.1%) occurred in the first 3 days after surgery. Diarrhoea occurred in 54 patients, 44 (24.6%) on colchicine and 10 (5.5%) on no-colchicine (p<0.0001). Colchicine was discontinued in 23 patients (52%) because of diarrhoea.
Conclusion: 1. Colchicine administered preoperatively to patients undergoing OHS and continued until hospital discharge failed to reduce the incidence of early postoperative AF. 2. Most AF episodes developed shortly after OHS. 3. Diarrhoea was the most common side effect of colchicine prompting discontinuation in more than half of patients.

P5326 | BEDSIDE
Ectopies with a short coupling interval may trigger atrial fibrillation

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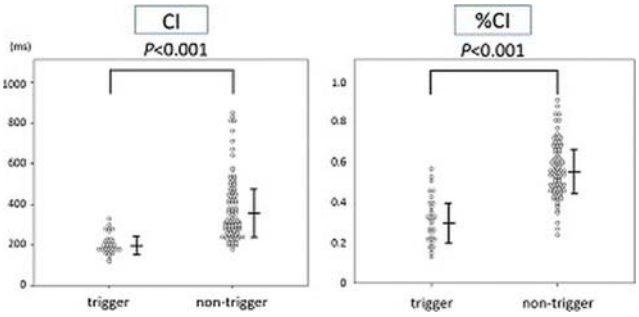
Background: The elimination of atrial fibrillation (AF)-trigger ectopies is an essential procedure in AF ablation. However, the identification of AF-trigger ectopies is often difficult because of insufficient AF inducibility by drugs such as an isoprpterenol infusion.
Purpose: To compare the coupling intervals (CI) between AF-trigger and non-AF-trigger ectopies.
Methods: This study consisted of 59 patients with AF (paroxysmal AF, 35 (59%) patients; male, 43 (73%) patients; age, 66±10 years old) who underwent an initial radiofrequency catheter ablation. Prior to the ablation procedure, we investigated the AF triggers as follows. If patients were in AF, they were converted to sinus rhythm by electrical cardioversion. Then, isoproterenol was infused to provoke ectopies and AF. We measured the CI of all ectopies provoked by an isoproterenol infusion. An ectopy was defined as an AF-trigger ectopy when it preceded AF or atrial firing. The %CI was calculated as the CI of the ectopy/P-P interval of the preceding 2 beats.
Results: Out of a total of 132 ectopies, 32 (24%) were AF-trigger ectopies. Most (97%) originated from pulmonary veins. AF-trigger ectopies had a significantly shorter CI (202±50ms vs. 374±152ms, p<0.001) and %CI (0.31±0.11 vs. 0.56±0.13, p<0.001) than those of non-trigger ectopies (Figure). An ROC analysis revealed that a %CI of 0.40 was the best cut-off value for the differentiation between AF-trigger and non-AF-trigger ectopies. (AUC=0.92, sensitivity=93%, specificity=78%).



Distribution of CI and %CI

Conclusion: AF-trigger ectopies had a short CI and %CI. These findings may be useful for estimating whether the ectopies are AF-trigger or not.
Acknowledgement/Funding: none

P5327 | BEDSIDE
Comparisons of the effect of anticoagulation therapies on the coagulation systemincluding the tissue factor pathway between vitamin K antagonist and the factor Xa inhibitors

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Background and introduction: The effects of the factor Xa inhibitors (FXa-inh) on the tissue factor pathway, are unclear. In addition, the anti-coagulation effect of NOACs during the trough drug concentration periods has not been well clarified.
Purpose: The purpose of this study was to evaluate the effects of FXa-inh and vitamin K antagonist (VKA) on the coagulation system including the tissue factor pathway.
Methods: In the consecutive 16 patients with atrial fibrillation who underwent catheter ablation therapy and 6 patients with paroxysmal supraventricular tachycardia or idiopathic ventricular tachycardia as control, we assayed the various markers of the coagulation system including tissue factor pathway inhibitor (TFPI). Of those 22, 11 were treated with factor Xa inhibitors (FXa-inh group), 5 with vitamin K antagonist (VKA) and 6 controls without anticoagulation therapy. The markers of the coagulation system were collected before punctures of femoral artery

and veins (corresponding to the trough concentration periods of FXa-inh), 15 minute after administration of 3,000 unit of unfractionated heparin intravenously, and 15 minute after punctures of femoral artery and veins during catheter operation.
Results: (1) The non-endothelial binding TFPI level was not different among the three groups (P=0.22, ANOVA) (control group: 94±32 ng/dl, VKA group: 69±28 ng/dl, and FXa-inh group: 93±20 ng/dl, respectively). However, the endothelial binding TFPI level was significantly higher in the FXa-inh group than in the control group (P=0.02, 280±55 ng/dl vs. 199±43 ng/dl) and in the VKA group (P=0.01, 280±55 ng/dl vs. 187±58 ng/dl).
(2) The basal levels of protein C, protein S and factor VII were lower in the VKA group than in other two groups.
(3) The prothrombin fragment 1+2 (F1+2) level, a marker of thrombin generation, before the punctures was higher in the control group (228±92 pmol/L) compared with other two groups (P<0.01, vs. VKA group: 47±34 pmol/L) (P<0.01, vs. FXa-inh group: 113±41 pmol/L).In addition, F1+2 after the punctures was lower in the VKA group (67±34 pmol/L) compared with other two groups (P<0.01, vs. control group: 246±82 pmol/L) (P=0.03, vs. FXa-inh group: 171±75 pmol/L).
Conclusion(s): Endothelial TFPI was augmented by FXa inhibitor treatment, which could account for the anticoagulation effect in the period of the trough drug concentration. As compared to FXa-inh, VKA inhibited thrombin generation in response to vascular injury, which could explain about the lower risk of hemorrhagic complications in patients treated with FXa-inh.

P5328 | BEDSIDE
The prevalence and risk factors for atrial fibrillation in beta-thalassemia major: a cross-sectional study in a UK specialist cardio-haematology clinic

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Background: Management of the severe monogenetic anaemia, Beta-thalassemia major (TM), has undergone transformative change over the last two decades. Improved prognosis has unveiled new management challenges including identification and management of atrial fibrillation (AF). Historically AF was associated with acute decompensation secondary to iron overload, but we present evidence of a rising tide of AF prevalence in TM survivors.
Purpose: To determine the prevalence of and risk factors for AF within a stable cohort of UK TM patients undergoing routine cardiovascular surveillance in our specialist clinic.
Methods: We undertook a cross-sectional analysis of TM patients under review in our specialist-lead, cardio-haematology clinic over a 12-month period. Electrocardiographic evidence of atrial fibrillation were determined, and cardiac magnetic resonance T2* and clinical history tabulated.
Results: Out of 80 TM patients (39 male), aged 20–57 years of age (mean 38.3, median 38); 7 patients had current AF, and a further 20 had paroxysmal AF, providing an overall prevalence of 33.8% within this cohort. By age group, the prevalence was: 0–34 years: 24.1%; 35–44: 31.0% and 45–54:52.3%, representing a 400-fold greater prevalence than that seen in aged-matched cohorts of the general UK population.
In common with the general population, the presence of diabetes was found to represent a significant risk factor in the development of AF, with an odds ratio (OR) of 3.85 (95% CI 1.44 to 10.29, p=0.007). However, the strongest risk factor for the development of AF was a history of heart failure: OR 18.20 (2.10–157.48, p=0.008), followed by the presence of conduction disease, OR 5.83 (1.37–24.83, p=0.017). There was no correlation between AF and current T2* (a measure of cardiac iron load), but a history of previous moderate to severe cardiac iron overload (T2*<15msec) was also associated with increased risk: OR 3.45 (1.44–9.54, p=0.017).
Left atrial enlargement was not a risk factor in TM and significant mitral valve disease was absent in this group. Similarly diastolic dysfunction, pulmonary hypertension, thyroid disease or history of hepatitis C infection was not predictive.
Conclusion: In TM the prevalence of AF is extremely high; the presence of diabetes, history of heart failure, conduction disease and previous iron overload are each strongly associated with the risk of developing AF. Given the increased thromboembolic risk in this group of patients, scrupulous attention needs to be paid towards the identification of AF and initiation of thrombo-prophylaxis against stroke.
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P5329 | BEDSIDE
Electrocardiographic differences between symptomatic and asymptomatic paroxysmal atrial fibrillation

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Purpose: The reason why some episodes of atrial fibrillation are symptomatic while others are asymptomatic remains unclear. The purpose of this study is to evaluate the electrocardiographic (ECG) differences between these episodes of paroxysmal atrial fibrillation (PAF).
Methods: Thirty consecutive patients (mean age 67±9 years; 14 men) who received an implantable loop recorder-ILR (Reveal XT 9529; Medtronic, Minneapolis, Minnesota, USA) after the first symptomatic episode of paroxysmal or persistent atrial fibrillation (AF) were enrolled. All the patients were instructed to activate the device after the onset of symptoms indicative of the arrhythmia. We analyzed episodes of PAF that initially were asymptomatic but became symptomatic later on. In all these episodes we calculated the heart rate (HR) and the heart rate variability (HRV) the first 2 minutes of the episode and 2 minutes before the activation of the device by the patient. HRV was defined as the standard deviation (SD) of RR intervals. Coefficient of variation (CV) defined as SD/mean RR X 100.
Results: In our analysis, we included 73 episodes of PAF from 17 patients (10 male). The major symptom was palpitation. The average time between the onset of AF and the activation of the device was 244 min (range 30–645 min). The mean duration of the episodes was 13±9h. The average HR at the onset of AF was 104±28bpm while during the symptomatic period was 145±30bpm (p<0,001). The mean HRV was 170±68msec and 84+32msec (p<0,001), while the mean CV was 24,5±3,9% and 18±4,5% (p<0,001) respectively.
Conclusions: In this study we found that in episodes of PAF recorded by an ILR with an asymptomatic period preceding the symptomatic, onset of symptoms was characterized by higher HR and lower HRV. If this finding constitutes a consequence of autonomic imbalance due to the arrhythmia remains to be investigated.

P5330 | BEDSIDE
Relationship between inflammatory markers and coagulation cascade in patients with atrial fibrillation

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Background: Atrial fibrillation (AF) is associated with a prothrombotic or hypercoagulable state, which may be contributed to an increased risk for stroke and systemic embolism. There is a plausible evidence linking inflammation to the initiation and perpetuation of AF and AF-related thrombosis. Various inflammation markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) have been associated with AF. Several prothrombotic factors have been found to be elevated in AF, indicating abnormal thrombogenesis. Abnormalities of haemostasis, fibrinolysis, endothelium and platelets have all been described increasing the risk of stroke and thromboembolism. The aim of this study is to investigate a relationship between inflammation and the prothrombotic state in the setting of AF, including the impact of this relationship on clinical presentation and outcome of AF patients.
Methods: 141 patients with non-valvular AF (mean age 64.6±9.7) where enrolled in this study. After the enrollment the echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. We measured plasma indexes of inflammation (CRP, IL-6) and the prothrombotic state, including markers of the coagulation cascade such as tissue factor (TF) and fibrinogen (F) in all observed patients with AF and 21 healthy control subjects. Sample calculated for 80% power, assuming a standard deviation difference of 1/3; significant p if it is <0.05. All data were analyzed by SPSS 13.
Results: The obtained results shown that compared with controls, AF patients had higher levels of IL-6 (p=0.043), CRP (p=0.002), TF (p=0.026), and F (p=0.025). Plasma CRP levels were higher among AF patients at "high" risk of stroke (p=0.003). Moreover the levels of CRP and IL-6 are markedly elevated in patients with dilated left atrium, poorly functioning left atrial appendage and longer duration of AF.
Conclusions: Increased plasma of IL-6 and CRP are related to indexes of the coagulation cascade and may be contribute structural remodeling of left atrium in patients with AF.

P5331 | BEDSIDE
Comparison among CHADS2, CHA2DS2-VASc and R2CHADS2 score in Japanese patients with paroxysmal non-valvular atrial fibrillation without receiving anticoagulant therapy

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Aim: It remains unclear which of CHADS2, CHA2DS2-VASc or R2CHADS2 score is most available for the risk stratification of ischemic stroke/systemic thromboembolism (IS/SE) in Japanese patients with paroxysmal non-valvular atrial fibrillation (PNVAF). We retrospectively investigated incidence of IS/SE on the basis of CHADS2, CHA2DS2-VASc, and R2CHADS2 scores in 332 paroxysmal non-valvular atrial fibrillation (PNVAF) patients (224 men, mean age 65±13 years) who was not administered anticoagulation therapy but who administered antiarrhythmic drug therapy to maintain sinus rhythm between August 1995 to July 2008 before the Japanese Circulation Society guideline was issued (mean follow-up periods 53±35months).
Results: (1)Annual rates of IS/SE underlying antiarrhythmic drugs therapy were as follow (Table). All higher CHADS2, CHA2DS2-VASc and R2CHADS2 scores

were associated with greater annual rates of IS/SE (P<0.001). (2)In a multivariate logistic regression analysis adjusted for the potentially confounding variables, CHADS2 scores (odds ratio[OR]:4.74,95% confidence interval[CI]:2.80–8.00, p<0.001), CHA2DS2-VASc scores (OR: 4.15,95% CI: 2.57–6.71, p<0.001), and R2CHADS2 scores (OR: 1.94,95% CI: 1.48–2.53, p<0.001) were significant independent predictors for IS/SE, respectively. (3)Area under receiver-operator characteristic curve for predicting IS/SE were 0.89 in CHA2DS2-VASc scores, 0.87 in CHADS2 scores and 0.85 in R2CHADS2 scores (all, P<0.001), respectively, whereas there were not a significant difference among three scores.
Conclusion: In Japanese patients with PNVAF, all CHADS2, CHA2DS2-VASc and R2CHADS2 scores are useful schemes for the risk stratification of ischemic stroke or systemic embolism.

P5332 | BENCH
The prevalence of left atrial enlargement in unselected atrial fibrillation patients

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Introduction: Echocardiographic parameters such as left atrium (LA) enlargement are useful in assessment and clinical decision making in atrial fibrillation (AF) patients.
Purpose: The aim of this study was to evaluate the prevalence of the LA enlargement in a cohort of unselected non-valvular AF patients.
Methods: Data on 582 hospitalizations with primary diagnosis of AF, either paroxysmal, persistent or permanent were analyzed. All patients underwent a standard transthoracic echocardiography (TTE) with the asssessement of LA in accordance with the current guidelines. All patients also had their thromboembolic risk assessed in both CHADS2 and CHA2DS2-VASc scores.

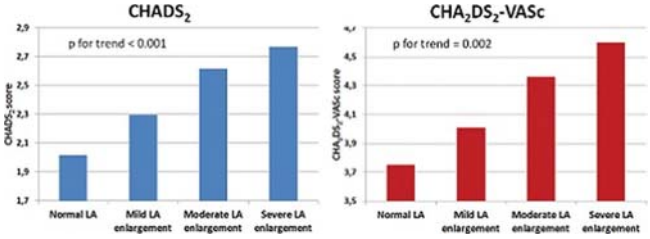

Figure 1

Results: Out of the initial cohort, 494 patients were chosen. In the enrolled patients (48.5% male; mean age 73.4±11.5 years) AF was classified as paroxysmal in 233 (47.3%), as persistent in 109 (22.1%), and as permanent in 151 (30.6%) patients. LA was enlarged in 426 (86.2%) patients. Enlargement was classified as mild in 99 (20.0%) patients, as moderate in 130 (26.3%) patients, and as severe in 196 (39.7%) patients. Paroxysmal AF was more often present (76.5% vs. 42.6%; p<0.0001) in the group with normal LA size, while persistent and permanent AF was more often in patients with LA enlargement then in those with normal LA size (23.8% vs. 11.8%; p=0.04 and 33.6% vs. 11.8%; p=0.0005, respectively). Patients with enlarged LA had higher mean CHADS2 (2.0±1.5 vs. 2.6±1.3; p=0.0005) and CHA2DS2-VASc (3.8±2.0 vs. 4.4±1.8; p=0.02) score. The both mean scores rose along with rising LA diameter. (Figure 1.) Conclusions: LA enlargement is highly prevalent in AF patients. Echocardiographically assessed LA size may be an additional parameter useful in thromboembolic risk stratification of AF patients.

CORONARY ARTERY DISEASE AND COMORBIDITIES I

P5333 | BEDSIDE
Relationship between abdominal aortic and coronary artery calcification as detected by computed tomography in chronic kidney disease patients

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Purpose: Coronary artery calcification (CAC) is highly sensitive for the detection of coronary artery disease (CAD) as well as predictive of future cardiovascular (CV) events in various population. Abdominal aortic calcification (AAC) is common in the chronic kidney disease (CKD) and its presence is also associated with increased risk of CV events. However, few studies have examined the association of CAC and AAC in CKD patients. The purpose of this study was to investigate relationships between CAC and AAC in these patients.
Methods: We evaluated 138 asymptomatic CKD patients (90, 38 and 10 patients in stages G3, G4 and G5, respectively). A non-contrast computed tomography scan was used to determine the abdominal aortic calcification index (ACI) and CAC score were measured using Agatston scoring system. Both CAC score and ACI were quantified and these relationships were investigated.
Results: Among the subjects, abdominal aortic calcification was present in 121 patients (88.0%) as defined by ACI >0 and median ACI was 12.9%. severe CAC score (≧400 AU) was present in 35 patients (25.4%). ACI showed a significant positive correlation with CAC score in CKD patients. (r=0.549, p<0.001) After adjusting for age, diabetes, systolic blood pressure, eGFR, and intact-PTH, ACI was independently associated with severe CAC score (OR1.09, p<0.001). ROC curve analysis showed that the ACI optimal cut-off value predicting severe CAC score was 15.5% (AUC 0.833, p<0.001).
Conclusion: High abdominal aortic calcification is strongly associated with severe coronary artery calcification in CKD patients. The value of ACI 15.5% allows us to predict the presence of severe coronary artery calcification in these patients.

P5334 | BEDSIDE
Obesity paradox in patients with coronary artery disease treated with percutaneous coronary intervention

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Background: Obesity is known as a risk factor for coronary artery disease (CAD). However, the relation between obesity and clinical outcomes in patients treated with percutaneous coronary intervention (PCI) remains controversial.
Methods: We analyzed 4,673 CAD patients who underwent PCI from single center registry between 2007 and 2012. Patients were divided into four different body mass index (BMI) categories based on the suggestion by the World Health Organization for the Asian population: underweight group (BMI <18.5 kg/m^2, n=100); normal weight group (18.5 ≤ BMI <23.0 kg/m^2, n=1,221); overweight group (23.0 ≤ BMI <27.5 kg/m^2, n=2,348); and obese group (BMI ≥27.5 kg/m^2, n=1004).
Results: Higher BMI group was older and had higher incidence of hypertension, diabetes and dyslipidemia. But, lower BMI group was younger and had higher incidence of cerebral vascular attack, chronic kidney disease, dialysis, chronic lung disease, and smoking. Higher BMI group had more stable angina, but less acute myocardial infarction. Higher BMI group showed poor lipid and glycemic laboratory profiles. But, Lower BMI group showed higher high sensitive C-reactive protein level. Higher BMI group had high-risk coronary anatomy and treated with larger diameter of stent(s). Medications at discharge were similar among the groups. In-hospital mortality (4.0%, 2.9%, 2.0%, and 4.9%, p<0.001) and 1-year mortality (13.0%, 7.7%, 4.8%, and 7.0%, p<0.001) was higher in the underweight and obese group.
Conclusion: This study shows that the relation between obesity and mortality is U-shape. This result provides the concept of obesity paradox in CAD patients treated with PCI.

P5335 | BEDSIDE
Predictors of chronic total occlusion in a non-culprit artery in patients undergoing coronary angiography for acute coronary syndrome: mean platelet volume and serum uric acid

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Background: In patients with acute coronary syndrome (ACS), the presence of a chronic total occlusion (CTO) in a non-infarct related artery (non-IRA) is an independent predictor of early and late mortality. Both mean platelet volume (MPV) and serum uric acid (SUA) are associated with adverse cardiovascular events in patients with ACS.
Purpose: We aimed to investigate the relationship between presence of non-IRA-CTO with MPV and SUA levels in ACS.
Methods: A total of 1024 patients who underwent urgent coronary angiography (CA) for ACS were included in this study. Blood samples were drawn on admission before CA. Patients were categorized into two groups: non-IRA-CTO (–) group and non-IRA-CTO (+) group.
Results: 230 patients (22.5%) had a non-IRA-CTO. MPV and SUA levels on admission were significantly higher in non-IRA-CTO (+) group when compared with non-IRA-CTO (–) group (9.26±0.98 vs. 8.35±0.69, P<0.001 and 7.08±1.73 vs. 5.26±1.29, P<0.001, respectively). At multivariate analysis, MPV [odds ratio (OR) 4.705, 95% confidence interval (CI) 2.842–7.790; P<0.001] and SUA (OR 2.535, 95% CI 1.891–3.398; P<0.001) levels were still independent predictors of non-IRA-CTO as well as age, hemoglobin, LVEF, and NSTE-ACS.
Conclusion: MPV and SUA levels were significant and independent predictors for presence of non-IRA-CTO in patients with ACS.

P5336 | BEDSIDE
The impact of subclinical hypothyroidism or thyroid autoimmunity on coronary vasospasm in patients without associated cardiovascular risk factors

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Background and objectives: Subclinical hypothyroidism is associated with

endothelial dysfunction and impaired coronary flow reserve. However, the effect of subclinical hypothyroidism or thyroid autoimmunity on variant angina has yet to be determined.
Materials and methods: Among 385 consecutive patients without associated cardiovascular risk factors, who underwent coronary angiography with the ergonovine provocation test (EPT), 165 had a positive EPT {EPT(+)} and 220 had a negative EPT {EPT(–)}. The relationship between coronary artery spasm and the presence of subclinical thyroid dysfunction as well as serum thyroid peroxidase autoantibody (TPO Ab) was evaluated.
Results: The proportion of patients with subclinical hypothyroidism among those who were EPT(+) was significantly higher than that in those who were EPT(–) (18% vs. 11%, p=0.001). However, there was no significant difference in the proportion of patients with subclinical hyperthyroidism between the groups. Moreover, EPT(+) patients showed more positive TPO Ab (33% vs. 14%, p<0.0001) than those with EPT(–). There was a positive correlation between EPT(+) and TPO positivity (r=0.226, p<0.001), subclinical hypothyroidism (r=0.112, p=0.033), and body mass index (r=0.123, p=0.018). Binary logistic regression analysis revealed that the significant predictors of EPT(+) were body mass index {adjusted odds ratio (OR)=1.042, 95% confidence interval (CI)=1.005–1.080}, presence of subclinical hypothyroidism (OR=3.047, 95% CI: 1.083–8.572), TPO Ab titer (OR=1.028, 95% CI: 1.015–1.041) and the presence of TPO Ab (OR=4.904, 95% CI: 1.544–15.567).
Conclusion: Subclinical hypothyroidism and the presence of TPO Ab are significantly associated with coronary vasospasm in patients without cardiovascular risk factors.

P5337 | BEDSIDE
Impact of coronary artery disease on outcomes after transcatheter aortic valve implantation

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Background: Cornary artery disease (CAD) negatively prognosis of patients undergoing surgical aortic valve replacement and revascularization is generally recommended at the time of surgery. Implications of CAD in the setting of transcatheter aortic valve implantation (TAVI) are not known. The aim of this study was to determine the prevalence and impact having coronary artery disease in patients undergoing percutaneous valve implantation.
Methods: Between April 2008 and December, 2013 372 patients with severe symptomatic aortic stenosis were treated with high surgical risk, percutaneous aortic CoreValve prosthesis. All patients underwent coronary angiography prior.
Results: A total of 150 p (40.3%) had coronary disease. In 95 patients were performed PCI, 23 p CABG and 23 and 8 p both techniques. Revascularization was complete in 64.6%. Patients with CAD were characterized by increased ventricular dysfunction than patients without CAD (24.8% vs. 12.6%, p=0.002) and predominantly male (55% vs. 31.8%, p<0.001). The occurrence of periprocedural myocardial infarction was 1.1%. After a mean follow-up of 26±17 months, there was a slightly higher mortality in patients with CAD (22.7% vs. 15.3%, p=0.072) and lower mortality for patients with complete revascularization versus partial, 15 9% vs.31.1%, [OR=0.417 (95% CI 0.176 to 0.992), p=0.044].
Conclusions: The prevalence of coronary artery disease in patients undergoing TAVI is high. The type of revascularization seems to influence on survival in the follow-up.

P5338 | BEDSIDE
Acute coronary syndrome in patients with pre-existing severe aortic stenosis

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Purpose: Severe aortic stenosis (sAE), specially when symptomatic, is associated with a poor outcome. The coexistence of significant coronary artery disease is common, however, little is known about sAE clinical significance in patients (P) with acute coronary syndromes (ACS). We sought to determine the prevalence and prognostic value of sAE in P with ACS.
Methods: Retrospective, unicentric study including 2389 P admitted with ACS over 5 years and during a minimal 6 months (6m) follow-up. sAE was defined by the presence of >1 echocardiographic criteria: mean transaortic gradient >40 mmHg; valve area <1cm^2; or aortic valve area index (AVAi) <0,6 cm^2/m^2.
Results: Of the 2389 P with ACS 2% had sAE, the majority (75%) presenting with a non ST elevation ACS. These P were older (78±8 vs 64±13 y; p<0,001), more often had hypertension (83% vs 64%; p=0,006), non-coronary atherosclerotic disease (19% vs 4%; p<0,001) and atrial fibrillation (25% vs 5%; p<0,001). At admission, they had lower mean levels of hemoglobin (12,2±1,8 vs 13,9±1,9 g/dL; p<0,001) and glomerular filtration rate (GFR) (55,9 vs 87,3 mL/min; p<0,001); higher levels of troponin (35,2±95,7 vs 19,6±51,2 ng/mL; p=0,027) and type B natriuretic peptide (9469±12715 vs 2792±574 pg/mL; p<0,001). At echocardiographic evaluation, they had more often moderate/severe left ventricular hypertrophy (46% vs 9,6%; p<0,001), left ventricular systolic dysfunction (LVSD) (83% vs 53%; p<0,001) and higher levels of pulmonary artery systolic pressure (44±15 vs 34±10 mmHg; p<0,001). P with sAE had more often left main stem disease (32% vs 11%; p<0,001). Coronary artery bypass surgery were more likely done in these P (31% vs 10,8%; p<0,001). During hospitalization, they had more often heart failure (75% vs 29%; p<0,001), high grade AV block (13% vs 5%; p=0,03) and "de novo" atrial fibrillation (19% vs 8%; p=0,01). In-hospital (23% vs 3,4%; p<0,001) and 6m (35,4% vs 7,5%; p<0,001) mortality were higher in P with sAE. After multivariate analysis, sAE persisted as independent predictor of in-hospital (OR 4,7; CI 95%; p<0,001) and 6m (HR 2,1; CI 95%, p=0,001) mortality. P with sAE had higher 6m mortality when presenting with GFR<60 mL/min (48% vs 13%; p=0,024), severe LVSD (63% vs 27%; p=0,04), lower mean AVAi (0,2±0,1 vs 0,4±0,2; p=0,03) and higher euroSCORE (11,6±9,6; 7,1±5,2; p=0,04). P who did not undergone aortic valve replacement also had higher 6 m mortality (48% vs 15%; p=0,03). Only AVAi and aortic valve replacement persisted as independent predictors of 6m mortality in sAE.
Conclusion: The coexistence of sAE and ACS is rare, but is associated with a poor in-hospital and medium term outcome.

P5339 | BEDSIDE
Lipid profile and paraoxonase 1 enzyme activity in patients with type 2 diabetes mellitus and different genotypes of paraoxonase 1 gene

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Aim of study: We assumed lipid profile and paraoxonase 1 (PON 1) activity in patients with type 2 diabetes mellitus and different genotypes of paraoxonase 1 gene.
Material and methods: PON 1 enzyme activity, lipid profile and PON 1 192 gene polymorphism were determined in 118 patients (27 males and 91 females) with type 2 diabetes mellitus (DM) (age - 48.7 ±10.7 years old). 110 patients (93.2%) were overweight and obesity. 112 patients (94.9%) had arterial hypertension. 20 patients (17.2%) were smokers. Family history of cardiovascular disease was in 63 patients (53.4%) and family history of DM was in 43 patients (36.8%). 77 patients (67.5%) had hypercholesterolemia, 73 patients (61.9%) had ischemic heart disease and 16 patients (13.6%) had myocardial infarction (MI). PON 1 enzyme activity was evaluated by kinetic method, parameters of lipid profile - by enzyme method. PON 1 192 gene polymorphism were determined by PCR.
Results: We identified PON 1 genotype Q192Q in 76 patients (64.4%), PON 1 genotype Q192R - in 39 patients (33.1%). PON 1 genotype R192R was revealed only in 3 patients (2.5%). PON 1 enzyme activity was higher in patients with PON 1 Q192Q genotype versus patients with PON 1 Q192R and PON 1 R192R genotypes (9.8±5.7 FA/ml·min and 7.3±4.9 FA/ml·min, p<0.05). Lipid profile in patients with type 2 DM and different PON1 192 genotypes didn't differ. We revealed correlations between level of high density lipoproteins and PON 1 enzyme activity (r=0.2, p=0.04). Lipid profile in patient with and without MI didn't differ.
Conclusion: Paraoxonase 1 enzyme activity was significantly higher in patients with type 2 diabetes mellitus and paraoxonase 1 Q192Q genotype. Lipid profile in patients with type 2 diabetes mellitus and different PON1 192 genotypes didn't differ.

P5340 | BEDSIDE
Prognostic value of elevated high-sensitivity cardiac troponin T levels in patients with stable coronary artery disease

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Background: Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide despite advanced primary and secondary prevention.
Purpose: To investigate the prognostic implications of elevated high-sensitivity cardiac troponin T (hs-cTnT) values in presumably stable ambulatory CAD patients treated for secondary and non-secondary prevention.
Methods: We conducted a retrospective, single-center pilot observational study in a low-risk population. All patients received routine measurement of hs-cTnT at index visit and follow-up visits. Endpoints were all-cause mortality and a composite of all-cause mortality, acute myocardial infarction, stroke and rehospitalization for acute coronary syndrome and heart failure.
Results: 965 consecutive patients presenting to our outpatient clinic between June 2009 and June 2010 were screened for eligibility. 693 patients with a stable clinical course at index visit, at least one hs-cTnT value and at least one follow-up visit qualified for analysis. Follow-up was 796 days. 547 patients (78.9%) had hs-cTnT values below and 146 patients (21.1%) had values above 14 ng/L. We observed 13 deaths (all-cause mortality) including 4 patients with a cardiovascular death. Age, NT-proBNP levels and impaired renal function were independently associated with an elevated hs-cTnT in a mulitvariate analysis. Hs-cTnT values >14 ng/L were strongly associated with all-cause mortality (HR 12.9, 95% CI:

3.5–46.9, p=0.0001, Figure 1), the composite clinical endpoint (HR 2.35, 95% CI: 1.48–3.72, p=0.0003) and rehospitalsation for heartfailure (HR 3.36, 95% CI: 1.73–6.53, p=0.0004). Compared to the multivariable Framingham score hs-cTnT revealed a significantly better performance (AUC hs-cTnT: 0.882 vs AUC Framingham score 0.639, p=0.0005).
Conclusions: Hs-cTnT levels exceeding the 99th percentile of a reference population (i.e. 14 ng/L) provide excellent prognostic information regarding all-cause mortality and a combined clinical endpoint in presumably stable ambulatory CAD outpatients presenting to a cardiology clinic for routine evaluation.
Acknowledgement/Funding: AstraZeneca, Wedel, Germany

P5341 | BENCH
Circulating miRNAs as potential biomarkers of coronary artery calcification and their roles of predicting coronary artery disease

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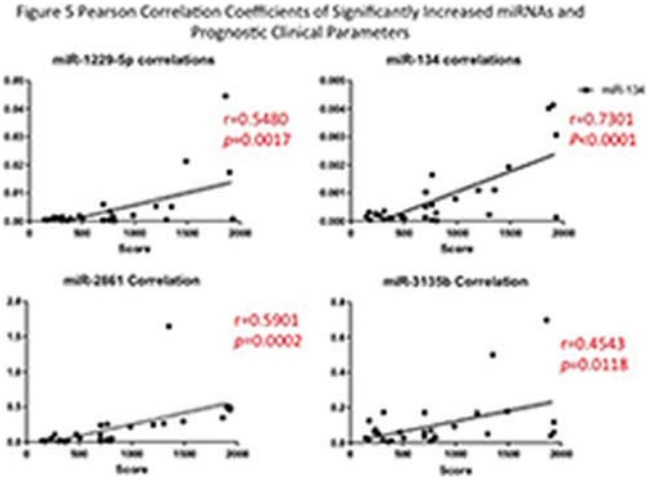
Objectives: The purpose of this study was to find the changed circulating microRNAs (miRNAs) co-related with coronary artery calcification (CAC), and identify the miRNAs that can be used as a potential biomarkers for predicting the risk of coronary artery disease.
Background: The signatures of circulating miRNAs for CAC remain to be disclosed.
Methods: Patients with moderated risk for CAD were characterized with coronary artery calcium score (CACS) from cardiac computed tomography (CT). We analyzed plasma miRNA levels of clinical matched 11 CAC (CACS >100) and 6 non-CAC (CACS = 0) subjects by microarray profile. The levels of miRNAs that existed significant difference between CAC and non-CAC group were further assessed by quantitative real-time polymerase chain reaction in an independent clinical matched cohort (non-CAC subjects, 40; CAC patients, 30). The specificity and correlation of these miRNAs with CAC were analyzed by ROC curve and correlation analysis, respectively. The selected miRNAs were validated in a larger cohort (200 patients) with moderated possibility of CAD.
Results: Microarray analysis identified 34 differentially expressed miRNAs between CAC and non CAC groups. Among them, the levels of 8 miRNAs were significantly increased in CAC plasma in an independent clinical matched cohort. However, only 4 miRNAs (miR-2861, 134, 1229 and 3135b) were correlated with the degree of CAC. Validation test showed that miR-134, miR 1229–5p, miR 3135b were significantly changed in patients with CAD.



Pearson correlation coefficients of sign

Conclusions: In this experiment, we identified four significantly up-regulated circulating miRNAs (miR-2861, 134, miR-3135b and 1229) co-related with CAC, miRNA 134, miR 3135b and 1229 could predict CAD.
Acknowledgement/Funding: This work was supported by National Natural Science Foundation of China Project (31325012, 31170811, 31271225, 31300698 and 81470429)

P5342 | BEDSIDE
Lack of association between HbA1c and cardiovascular outcome in Japanese type 2 diabetic patients with coronary artery disease

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Background: Much effort has been made for the Identification of appropriate target levels of blood glucose for anti-diabetic treatments that provide the best outcome with high-risk patients with type 2 diabetes but they remain unclear. Although randomised controlled trials are the best ways to address such clinical questions, observational studies have some advantages over RCTs because of feasibility and generalizability of results. We thus conducted a historical cohort study that registered type 2 diabetic patients with established coronary artery diseases (CAD) and examined association of HbA1c with cardiovascular outcome and mortality.
Methods: We consecutively registered 4248 type 2 diabetic patients with CAD based on results from coronary angiography and history of PCI, CABG and acute coronary syndrome since 2005 and followed up through 2014. Primary outcome was all-cause death, nonfatal myocardial infarction and nonfatal stoke. Patients were categorized as having very tight if their averaged HbA1c below 6%, tight if 6 to 7%, usual if 7–8% and uncontrolled if above 8% during the follow up.
Results: During 15717 patients-years of follow-up, 630 primary outcomes occurred. There was no association between baseline Hb A1c (below or above 7%) and primary outcome. Risk for primary outcome (HR1.52. p=0.0014) and all-cause death (HR 1.51, p=0.0077) in very tight glycemic control group was significantly higher than that in tight control group. Risk for primary outcome in either usual control group or uncontrolled group was not higher than that in tight control group.
Conclusion: Tight glycaemic control among type 2 patients with CAD was not associated with improved cardiovascular outcomes compared with usual control.
Conclusion: Tight glycaemic control among type 2 diabetic patients with CAD was not associated with improved cardiovascular outcomes compared with patients having usually controlled or even uncontrolled HbA1c
Acknowledgement/Funding: Grant-in -aid from Ministry of health, labour and welfare

CORONARY ARTERY DISEASE AND COMORBIDITIES II

P5343 | BEDSIDE
Myocardial revascularization using exclusive skeletonized internal thoracic artery grafting in diabetic multivessel-disease patients

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Objectives: The left internal thoracic artery (ITA) is acknowledged as the best coronary conduit for coronary artery bypass grafting surgery (CABG).
In diabetic multivessel-disease patients, CABG can be performed by using exclusively both ITAs with multiple sequential side-to-side coronary anastomoses. The purpose of this study is to evaluate the clinical status of the patients by stress test and the patency of ITA, and the quality of ITA grafts, and coronary anastomoses by angiographic control.
Methods: Between May 2008 and February 2014, 112 diabetic and multiple vessel disease patients underwent CABG by exclusive ITAs. The technique consisted of connecting the right ITA divided at its origin and connected to the left ITA left in situ, in a Y fashion; the left ITA is used to revascularize anterior coronary arteries, and the right ITA, coronary arteries of lateral and posterior aspect of the heart. A total of 409 anastomoses were performed (3.6 anastomoses per patients; range, 3 to 5).
Results: There was 1 death on the seventh post operative day by right ventricular failure. There was no postoperative myocardial infarction or stroke. There was no mediastinitis or wound infection or sternal healing problem. Ninety three patients (83%) had stress test control with no major abnormalities. except 3 patients in whom the test was interrupted because of arrhythmia for two patients and high blood pressure for the other one. Angiographic control was performed in 53 patients (total of 204 anastomoses: 3.8 anastomoses per patients; range, 3 to 5); all Y anastomoses were patent and the 204 ITA-coronary anastomoses were patent; moderate stenosis was found in 2 side to side anastomoses between the right ITA and marginal arteries, and competitive flow related to moderately stenosed right coronary artery was found in 4 patients, without clinical consequences.
Conclusions: In diabetic multiple vessel disease patients this method of myocardial revascularisation can be performed safely, with good early postoperative results. In terms of angiographic control the patency of all the anastomoses is excellent.

P5344 | BENCH
Increased circulating betatrophin concentrations in patients with coronary heart disease

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Objective: Betatrophin has recently been described as a key hormone to stimulate beta-cell mass expansion in response to insulin resistance and obesity in mice. It is reported that betatrophin can regulate the plasma levels of triglyceride. Triglyceride elevations are a highly significant independent risk factor for coronary heart disease (CHD). However, the circulating levels of betatrophin in patients with CHD are not known. This study measured serum betatrophin levels in patients with CHD and explored the correlations between its serum levels and various parameters in CHD.
Methods and results: We analyzed the concentrations of betatrophin by ELISA

in blood samples of 40 diagnosed patients with CHD by coronary angiography and 40 health controls. Routine anthropometric and serologic data were collected. Serum betatrophin, fasting glucose, lipid protein profiles, homocysteine and high-sensitivity C-reactive protein were measured. Serum betatrophin levels were significantly higher in CHD patients than in healthy control subjects (569.09 (444.52–798.85) versus 410.46 (339.02–526.41) pg/ml; $p<0.01$). Importantly, serum betatrophin associated positively with the severity of coronary branch luminal narrowings (R=0.304, $p<0.05$), homocysteine (R=0.278, $p<0.01$) and high-sensitivity C-reactive protein (R=0.179, $p<0.05$) in CHD patients, whereas there was no significant connection with blood lipids and glucose. In CHD subjects, multivariate regression analyses showed that the homocysteine was independent factors influencing serum betatrophin levels.
Conclusions: Serum betatrophin levels are significantly increased and associated positively with the severity of coronary branch luminal narrowings in patients with CHD. Our results suggest that betatrophin may play a role in the pathogenesis of CHD.

P5345 | BEDSIDE
Does iron deficiency have any prognostic impact in acute coronary syndromes?

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Background: Iron homeostasis has a central role in aerobic metabolism and is particularly important for cells with high energy demand, like cardiomyocytes. Iron deficiency (ID) is associated with a poor outcome in heart failure patients (P) and studies have demonstrated favourable effects of i.v. iron on the functional status and exercise capacity in these P. Little is known about ID prognosis value in P with Acute Coronary Syndromes (ACS).
Purpose: To determine the prevalence and prognostic value of ID in P with ACS.
Methods: Prospective, unicentric study including 543 P admitted with ACS over 1 year and a minimal 6 months follow-up. Serum iron, ferritin, total iron binding capacity and transferrin saturation were evaluated in the first 24 hours of hospitalization. ID was defined as a transferrin saturation $\leq$20% and was further classified as absolute (ferritin $<$100ug/L), when iron stores were depleted; or functional (ferritin $>$100ug/L), when iron delivery to cells was restricted. The clinical event studied was 6 months mortality (6M).
Results: ID was diagnosed in 37,9% (n=189) of P and was more often functional (n=144). P with ID had a higher prevalence of anemia (p=0,001). P with ID had more often history of diabetes (p=0,001) and surgical coronary revascularization (p=0,006). At admission, they presented more frequently with non ST elevation ACS (p=0,028) and heart failure ($p<0,001$). They had lower mean levels of glomerular filtration rate ($p<0,001$) and higher mean levels of RDW ($p<0,001$), C reactive protein ($p<0,001$) and type B natriuretic peptide ($p<0,001$). At echocardiographic evaluation, they had more often moderate/severe left ventricular systolic dysfunction ($p<0,001$), biventricular systolic dysfunction ($p<0,001$) and mitral regurgitation grade $>$II/IV (p=0,023). P with ID had higher prevalence of coronary multivessel disease ($p<0,001$), but revascularization were less often performed in these P (p=0,032). During hospitalization, they had higher incidence of major adverse cardiovascular events (41% vs 18%;$p<0,001$), however, ID was not associated with a higher incidence of bleeding complications or mortality. 6M was higher in P with ID (9,5% vs 3,1%;p=0,004), however, only when ID was functional it persisted as an independent predictor of 6M (HR 2,9; IC 95%;p=0,023), in P with or without anemia.
Conclusion: ID was diagnosed in almost a 1/3 of the P with ACS. Only functional ID persisted as an independent predictor of 6M, irrespective of the presence of anemia.

P5346 | BEDSIDE
Prognostic value of the product between creatinine and urea nitrogen in the admission of patients with acute coronary syndrome

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Introduction: Chronic renal disease is related with higher cardiovascular morbidity and mortality and is associated with more severe coronary disease. Opposed to cystatin-C, creatinine hasn't related with mortality in acute coronary syndromes (ACS).
Objective: Determine if a new variable – product of creatinine and urea nitrogen (UC) during admission – has intra-hospital mortality (IHM) prognosis compared with cystatin-C.
Methods: Retrospective study with 1039 patients (P) admitted with an ACS. Our variable was calculated multiplying the value of creatinine (μmol/L) and urea (mmol/L) on admission. With the ROC curve we established the cut-off of 1200 (Sensibility 81,6% e Specificity 67,3%) and created two groups: group A (GA) $\leq$1200 and group B $>$1200.
Results: Our population was mainly male 68,2% with a mean age of 68±15 years. Patients were admitted with: NSTEMI/UA 56,8% and STEMI 43,2%.
First we analyzed the ROC curve and concluded that UC (AUC 0,811) was more correlated with IMH than cystatin C (AUC 0,755).
Patients from both were groups were mainly male (79,5%vs 64,8%, p=0,075). P from GB were older (76±9 vs 64±13A, $p<0,001$) and with more diabetes (46,9% vs 26,6%, $p<0,001$), hypertension (90,2% vs 71,4%, $p<0,001$) and chronic renal disease (58,9% vs 4,8%, $p<0,001$). They had higher values of maximum troponin (69±154 vs 44±91ngr/ml, $p<0,001$) and Nt pro BNP (15284 vs 2367 pmol/L, $p<0,001$). They were admitted less frequently because of STEMI (36% vs 39,8%, $p<0,049$) but in a higher Killip class (KK$>$2 23,6% vs 3,7%, $p<0,001$) and developed more frequently cardiorenal syndrome (64% vs 14,6%, $p<0,001$). GB had higher IHM (13,8% vs 2,3%, $p<0,001$), mortality during follow-up (41,8% vs 12,7%, $p<0,049$) but not MACE (26,2,% vs 54,7%, p=0,011).
In multivariate analysis UC was a better IHM (CI 95%, OR 8,6, $p<0,001$) compared with cystatin C (p=0,079).
Conclusions: When compared with cystatin-C our variable was a better predictor of IHM.

P5347 | BEDSIDE
Non-invasive identification of impaired coronary flow reserve in coronary artery disease patients with intermediate coronary stenosis by assessment of digital reactive hyperemia

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Impaired coronary flow reserve (CFR) has a prognostic value in CAD patients with intermediate coronary stenosis (50–70%). Peripheral arterial tonometry after reactive hyperemia (RH-PAT) is a method to assess peripheral microvascular endothelial function and is linked to coronary microvascular endothelial dysfunction. We investigated the value of RH-PAT as a noninvasive tool to identify CAD patients with reduced coronary flow reserve (CFR).
Methods: Using RH-PAT (EndoPat, Itamar), digital pulse volume changes during reactive hyperemia were assessed in 89 patients with angiographically documented CAD and $<$70% stenosis of LAD. The PAT device consists of two finger-mounted probes, which include a system of inflatable latex air-cushions within a rigid external case. A blood pressure cuff is placed on one upper arm (study arm), while the contralateral arm serves as a control (control arm) RH-PAT index was calculated as the ratio of the digital pulse volume during reactive hyperemia divided by that at baseline using the Endo-PAT apparatus. Coronary flow reserve (CFR) of the LAD after adenosine infusion was assessed using Doppler echocardiography Patients were categorised to those with either normal ($\geq$2.5) or impaired ($<$2.5) CFR.
Results: A decreasing CFR was related with decreasing RH-PAT index (r=0.45 p=0.003). RH-PAT index was lower in patients with CFR$<$2.5 compared with those with CFR$>$2.5 (1.4±0.3 vs. 1.85±0.4, p=0.006). By ROC analysis, an RH-PAT index $>$1.5 was found to have a sensitivity of 75% and a specificity of 77% to identify patients with CFR$<$2.5.
Conclusions: Digital hyperemic response, as measured by RH-PAT, is attenuated in patients with impaired CFR suggesting a role for RH-PAT as a noninvasive test to identify CAD patients with significant coronary endothelial dysfunction and thus adverse prognosis.

P5348 | BEDSIDE
Accuracy of the GRACE score for the estimation of hospital and 1-year mortality of elderly patients with acute coronary syndromes

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Background: The GRACE score has been accepted as the gold-standard estimation for in-hospital mortality risk-stratification of acute coronary syndrome (ACS) patients. Elderly patients usually have more comorbidities and higher mortality. We aimed to assess the accuracy of the GRACE score in elderly ACS patients.
Methods: We included all ACS patients in a single centre in a 4 years time period. Patients were classified according to the GRACE score in low ($>$108), intermediate (109–140) or high ($>$141) risk. Patients $>$75 years were considered elderly.
Results: We included 1237 patients and 438 (35.4%) age $>$75 years old. Elderly patients were more frequently females (40.9% vs. 20.9%; $p<0.01$), had higher prevalence of risk factors but presented less frequently as ST-elevation ACS (27.6% vs. 35.2%; p=0.01). Mean GRACE score was also higher in elderly patients: 155.8±35.3 vs. 120.0±31.7 ($p<0.01$). Revascularization was performed more frequently in non-elderly patients (83.2% vs. 69.4%; $p<0.01$) even in the setting of ST-elevation ACS (97.2% vs. 80.2%; $p<0.01$). Hospital mortality was almost 4-fold higher in elderly patients (9.1% vs. 2.4%; $p<0,01$) but when analyzed by GRACE score risk categories, elderly patients had significantly higher mortality only in low risk category (3.9% vs. 0.1%; $p<0.01$); no differences was observed in intermediate risk patients (2.7% vs. 2.7%; p=0.99) and event a trend towards lower mortality in high-risk category (24.7% vs. 42.3%; p=0.08) was observed. One-year follow up was achieved in 93% of the cohort, median time 360.0 days. Mortality rate was 6.4% and it was much higher in elderly patients: 13.3% vs. 2.8% ($p<0.01$). According to GRACE score risk categories, elderly patients had higher mortality only in the low-risk subgroup (11.0% vs. 1.5%; log-rank $<$0.01) and no differences were observed in intermediate (12.8% vs. 8.3%;

log-rank=0.21) or high-risk (18.8% vs. 13.0%; log-rank=0.24) categories. Multivariate analysis, performed by Cox-regression, showed that age >75 years was independently associated to higher 1-year mortality (HR: 2.51 95% CI 1.38–4.58; p<0.01) as well the GRACE score (1.01 95% CI 1.01–1.02). When divided in GRACE score risk categories, age >75 year was associated to mortality only in low-risk patients (HR: 3.70 95% CI 1.42–9.61; p<0.01).
Conclusions: The GRACE risk score is useful for risk prediction in elderly patients admitted for ACS although it might underestimate the risk in low-risk category.

P5349 | BEDSIDE
The role of acute kidney injury in acute myocardial infarction

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Myocardial infarction (MI) and renal pathology - two serious diseases. Even moderate acute kidney injury (AKI) may lead to increased mortality.
Aim of the work: To study the influence of systemic inflammatory on the course of MI, accompanied by AKI in patients without chronic kidney disease.
Materials and methods: The study included 343 people with MI without chronic kidney pathology, but in the hospital they had developed their AKI. The patients were divided into 3 groups: I-136 people, they have the AKI did not reduce glomerular filtration rate (GFR) less than 60 ml/min/1.73 m^2, II - 81 patient with AKI and reduced GFR from 59 to 30 ml/min/1.73 m^2, III - 126 people without the development of the AKI in the hospital. The group was dominated by men, the average age of patients 63,5±5.6 years. Evaluated laboratory data and clinical course.
Results: QMI was from 74.6% in group III to 79.2% in I. Leukocytosis at admission was observed in all patients. Between the II and III groups: 12,35±0,28*109/l vs 10,14±0,15*109/l, P<0.01.Respiratory rate at admission in all groups were above normal: 20,29±0,85, 23,57±1,08, 18,60±0,90 per minute. Between II and III groups P<0.01. Heart rate: 92,56±3,25, 94,30±3,30, 86,70±2.50 beats per minute. P>0,05. Cystatin C was significantly increased in patients of group II vs III: 989,23±51,34 vs 721,37±12,78 ng/ml. Neutrophilic lipocalin was elevated in all groups but between I and III: 164,69±9,74 vs 103,40±5,69 ng/ml, P<0.01.Epidermal growth factor (EGF) and interleukin 6 (IL-6) has undergone a rapid surge. EGF: 1613,42±54,9, 1960,23±85,11, 993,47±63,58 pg/ml and IL-6: 29,78±2,05, 34,59±2,45, 26,58±2,33 ng/ml. C-reactive protein: 35,83±2,15, 89,56±4,63, 28,68±2,02. P<0.01 between II and III. The development of acute and chronic heart failure significantly more in group II compared to III: Killip II-IV:71,6% vs 23,0%, NYHA-IV:87,8% vs 45.7%. Recurrence MI and stent thrombosis in 2 times and 4 times in group II more than in III. Postpunctional hematomas in group II 11,1% vs 3.2% in III and 6.6% in I. Gastrointestinal bleeding was in 2 patients of group II. Mortality: I - 7,4%, II - 21,0%, III - 6.3%.
Conclusions: During the development of the AKI on the background of MI especially with at low GFR there is an increase in systemic inflammatory response against which indicated a more severe clinical course and increased mortality.

P5350 | BEDSIDE
Impaired glucose tolerance and coronary artery spasm in non-diabetic patients underwent acetylcholine provocation test

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Background: Impaired glucose tolerance (IGT) is known to be a risk factor of significant coronary artery disease (CAD) and endothelial dysfunction. However, currently there is no enough available data regarding the impact of newly-diagnosed IGT on coronary artery spasm (CAS) in real world clinical practice.
Methods: A total of eligible 4,745 consecutive non-diabetic patients (pts) without significant CAD underwent acetylcholine (Ach) provocation test were enrolled. IGT was defined as follows; [fasting glucose, 100–125 md/dL; or Hb A1c%, 5.7–6.4%]. Significant CAS was defined as >70% of narrowing by incremental intracoronary Ach injection of 20, 50 and 100 μg into left coronary artery. Pts were divided into two groups based on the presence of IGT: the IGT group (n=1,345) and the control group (n=3,400). To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model.
Results: After PSM analysis, 2 propensity-matched groups (1,337 pairs, n=2,674, C-statistic=0.654) were generated and the baseline characteristics of the two groups were balanced. Major angiographic and clinical parameters during Ach provocation test were not different between the two groups. IGT was not an independent predictor of Ach-induced CAS (58% vs.59%, p=0.609; HR=0.960; 95% C.I, 0.823 - 1.120).
Conclusions: In this study, despite the expected endothelial dysfunction, IGT was not associated with Ach induced CAS, suggesting that the mechanisms and risk factors of CAS may be different from those of atherosclerotic CAD.

Table. Angiographic and clinical characteristics during Acetylcholine Provocation Test: Propensity Score Matched Analysis

Variables, N (%)	IGT (n=1337)	Control (n=1337)	Hazard Ratio [95% C.I]	p Value
Coronary artery spasm (Visible narrowing >70%)	787 (58.8)	800 (59.8)	0.960 [0.823 - 1.120]	0.609
EKG Change	57 (4.2)	61 (4.5)	0.931 [0.643 - 1.347]	0.706
ST-segment elevation	18 (1.3)	17 (1.2)	1.059 [0.543 - 2.065]	0.865
ST-segment depression	14 (1.0)	20 (1.4)	0.696 [0.350 - 1.385]	0.300
T-inversion	10 (0.7)	15 (1.1)	0.664 [0.297 - 1.483]	0.315
Chest pain	604 (45.1)	609 (45.5)	0.985 [0.845 - 1.147]	0.846
AV Block	339 (25.3)	359 (26.8)	0.925 [0.778 - 1.099]	0.379

P5351 | BEDSIDE
Long term mortality and risk of myocardial infarction associated with presence and extent of coronary artery disease

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Introduction: Coronary angiography (CAG) is the current state-of-the-art in determining presence and extent of obstructive coronary artery disease (CAD) to assess risk of future myocardial infarction (MI). Atherosclerosis is one of several potential causes of ischemic stroke but studies comparing the extent of CAD and the risk of ischemic stroke is lacking.
Purpose: To examine the potential association between severity of CAD and long-term clinical outcomes: death, MI and ischemic stroke.
Methods: We performed a population-based cohort study of every CAG registered at our institutions from January 1st 2003 to December 31st 2012. In case of multiple CAG examinations during the period, only the first CAG was included. Patients were divided into sub-cohorts according to number of afflicted vessels with obstructive CAD (lumen narrowing ≥50%) at the time of examination: 0-, 1-, 2- and 3-vessel disease (VD), and finally diffuse CAD. Left main stenosis was defined as 2-VD. Patients were followed for a maximum of 7 years. End-points were all-cause mortality, ischemic stroke and MI. Crude and adjusted hazard ratios were estimated using Cox proportional hazards model. Subgroup analyses were performed according to level of comorbidity and procedural priority.
Results: A total of 84,025 patients were eligible for analyses, 31,734 had 0-VD, 21,490 had 1-VD, 11,435 had 2-VD, 9,871 had 3-VD, and finally 6,173 had diffuse CAD. Mean follow up was 4.4 years. Patients with 3-VD had the highest accumulated all-cause mortality risk during follow-up, followed by patients with 2-VD, diffuse CAD and 1-VD, while patients without obstructive CAD had the lowest mortality risk. Risk of MI was highest among patients with 3-VD followed by 2-VD and 1-VD, while patients with 0-VD or diffuse CAD had the lowest MI rates. Patients with diffuse CAD and 3 VD had the highest risk of ischemic stroke followed by 2 VD, 1 VD and lastly 0 VD. Death, MI and ischemic stroke rates all increased with increasing level of comorbidity and higher procedural priority.
Conclusions: Presence and extent of CAD were associated with increasing risk of death, MI and ischemic stroke. Diffuse CAD (alongside 3-VD) was found to be associated with the highest risk of future ischemic stroke, despite remaining in lower risk of future MI.

P5352 | BEDSIDE
Are there differences on prognosis among patients with previous ischemic heart disease versus cerebrovascular disease admitted with acute coronary syndrome?

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Background: It is known that patients with previous vascular disease (PVD) have a poorer outcome than those without and prognosis worsens as the number of affected vascular beds increases.
Aim: To evaluate if there are differences in in-hospital and 6-month mortality among patients admitted with acute coronary syndromes with previous ischemic heart disease (IHD) versus cerebrovascular disease (CVD).
Methods: We analysed 4871 patients (pts) admitted consecutively in our coronary care unit with a diagnosis of acute coronary syndrome and included in a prospective registry, from January 2002 to October 2013. Patients were divided in 3 groups: group 1 - pts without PVD (n=3718, 76.3%); group 2 – pts with previous IHD (n=825, 16.9%); group 3 - pts with previous CVD (n=257, 5.3%). We excluded pts with previous IHD plus CVD (n=71, 1.5%). For each group we compared clinical features and adverse events. Primary endpoint was the occurrence of death at 6 months; follow-up was completed in 98% of patients.
Results: Pts in group 3 were older (63±13 vs 67±12 vs 71±11 years;p<0.001), had higher proportion of women (25% vs 21.9% vs 32.3%;p<0.001) and hypertension (58% vs 73.1% vs 83.7%;p<0.001). Group 2 had more often body mass index >25kg/m^2 (47.1% vs 52.5% vs 50.8%; p=0.016), dyslipidaemia (46% vs 69.3% vs 52.1%;p<0.001) and diabetes (23.5% vs 38.8% vs 36.6%;p<0.001). Group 1 had more frequently history of smoking (29.5% vs 19.0% vs 12.8%;p<0.001) and absence of conventional risk factors (8.7% vs 4.0% vs 3.9%;p<0.001). On admission, those with previous CVD (group 3) presented more often Killip >1 (19.6% vs 29.6% vs 34.2%;p<0.001), anaemia (19.8% vs 28.6% vs 33.9%;p<0.001) and renal insufficiency (eGFR <60 ml/min) (19.2% vs 31% vs 40.9%;p<0,001). Group 2 presented more severe coronary artery disease (11.7% vs 22.2% vs 16.7%;p<0.001) and higher prevalence of left ventricular dysfunction (56.2% vs 61.8% vs 58.4%;p=0.03). ST-segment el-

evation myocardial infarction was more prevalent in Group 1 (54.5% vs 25.6% vs 51%;p<0.001), while myocardial infarction without ST-elevation was more frequent in group 2 (41.2% vs 65% vs 45.5%;p<0.001). In-hospital (4.5% vs 4.7% vs 7.0%;p<0.001) and 6-month mortality (8.7% vs 10.6% vs 16.5%;p<0.001) were higher in patients with previous CVD. In multivariate analysis and after adjusting for different baseline characteristics, pts with previous CVD had higher risk of 6-month mortality compared to those without PVD [OR 1.67, 95% CI (1.06–2.63),p=0.026].
Conclusion: Previous CVD remained as a strong predictor of 6-month mortality in patients admitted with acute coronary syndrome.

P5353 | BEDSIDE
Major adverse cardiac and cerebrovascular events in chronic kidney disease patients undergoing cardiac catheterization: a 7-year follow-up

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Background: Chronic Kidney Disease (CKD) is an independent risk factor for coronary artery disease affecting almost one-third of patients (pts) admitted to coronary care units. Coronary angiography (CA) or percutaneous intervention (PCI) is challenging in this setting, because of an increased risk of contrast-induced acute kidney injury (CIAKI).
Purpose: Between January and December 2007, 243 consecutive pts with indication to CA/PCI and an estimated glomerular filtration rate (eGFR) <60 cc/min were enrolled in this prospective cohort study to evaluate if post-procedural CIAKI was associated with major-adverse-cardiac-and-cerebrovascular-events (MACCE) occurrence during a 7-year follow up (FUP).
Methods: All pts were given appropriate CIAKI prophylaxis. CIAKI was defined as a serum creatinine (sCR) increase of +0.5 mg/dl in 48 hours or +50% in 7 days. The primary endpoint was MACCE incidence during the FUP, defined as: acute coronary syndrome, PCI, coronary artery bypass grafting surgery, acute pulmonary oedema, cardiogenic shock, transient ischemic attack, stroke, cardiovascular or cerebrovascular death. The secondary endpoints were post-procedural CIAKI and 5-year eGFR.
Results: On admission the 243 pts were 73±8 years old with a Mehran risk score of 7.9±3.4, a sCR of 1.88±1.68 and an eGFR of 43±14 cc/min. There were 89 (37%) women, 204 (84%) hypertensive, 74 (30%) diabetics. Forty-nine (20%) pts developed CIAKI after CA/PCI. During the 7-year FUP, 47 (19%) MACCE were observed. Five-year eGFR was 40±18 cc/min. The pts who suffered CIAKI after the index procedure not only had a lower freedom from MACCE during the 7-year FUP (46% vs. 74%, p<0.01), but also a worse 5-year eGFR (25±16 vs. 42±17 cc/min, p<0.01).
Conclusions: CKD pts undergoing CA/PCI have an increased risk of CIAKI. Post-procedural CIAKI was associated with a higher MACCE rate within 7 years after discharge. CIAKI pts showed an accelerated progression of their renal dysfunction during the first five years following discharge. A single CIAKI episode might increase MACCE risk at FUP by enhancing vascular, endothelial and atherosclerotic damage typical of CKD. CIAKI prevention in high-risk pts is then highly recommended.

P5354 | BEDSIDE
Prognostic impact of chronic total coronary occlusion on implantable cardioverter-defibrillator recipients with ischemic heart diseases

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Background: The prognostic impact of chronic total coronary occlusion (CTO) on implantable cardioveter-defibrillator (ICD) recipients remains unclear.
Methods: Consecutive 84 patients with ischemic heart disease receiving ICD therapy for primary or secondary prevention were initially enrolled. 2 patients were excluded because of lost follow-up. During a median 3.8 years follow-up period, we investigated major adverse cardiac events (MACE) including cardiac death, appropriate device therapy, hospitalization due to heart failure and implantation of ventricular assisted devices.
Results: Of 84 study patients (mean age, 70±8 years; 86% men), 34 (40%) patients had CTO. Between the groups of patients with CTO (+CTO) and without CTO (-CTO), there is no significant difference in age, left ventricular ejection fraction (LVEF), NYHA functional class III or IV, rate of receiving cardiac resynchronization therapy, and percentage of secondary prevention. +CTO tended to have higher MACE rate (log-rank, p=0.054). Among +CTO, there was no difference of MACE rate between patients with and without viability. When analysis was limited to the patients with ICD for secondary prevention (n=47), 16 patients (34%) with CTO had higher MACE rate compared to –CTO (log-rank, p<0.01). Cox proportional hazards regression analysis showed presence of CTO was a significant factor for higher MACE rate, but LVEF was not. Multivariate analysis showed the presence of CTO was one of predictors of MACE (p<0.05).
Conclusions: In patients with ischemic heart disease receiving ICD implantation, the presence of CTO had an adverse impact on long-term prognosis especially in secondary prevention.

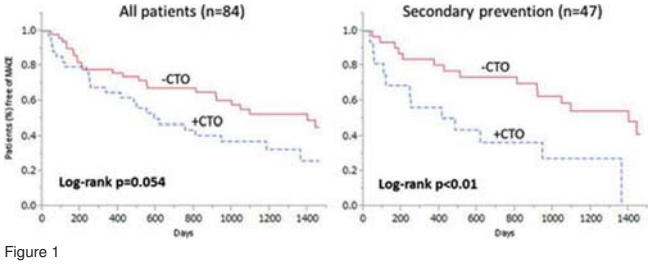

Figure 1

CORONARY ARTERY DISEASE AND COMORBIDITIES III

P5355 | BEDSIDE
Impact of drug-eluting stent-associated coronary artery spasm on 3-year clinical outcomes: a propensity score matching analysis

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Background: It has been reported that significant endothelial dysfunction or clinically evident vasospasm can be associated with drug-eluting stents (DESs). However, the impact of DES associated coronary artery spasm (CAS) on 3-year clinical outcomes in patients (pts) with vasospastic angina has not been fully elucidated.
Methods: A total of 2,797 consecutive pts without significant coronary artery lesion (<70%) who underwent the Acetylcholine (Ach) provocation test were enrolled between Nov 2004 and Oct 2010. DES-associated spasm was defined as significant CAS in proximal or distal to previously implanted DES site at follow-up angiography with Ach provocation test. Patients were divided into two groups: (DES-CAS; n=108, CAS; n=1,878). For baseline adjustment, propensity score matching (PSM) was performed and 102 pairs were generated (C-statistics=0.766, DES-CAS; n=102, CAS; n=102).
Results: Baseline characteristics were worse in the DES-CAS group. However, after PSM, both baseline characteristics and the Ach test results were balanced except higher incidence of diffuse CAS and ECG change in the DES-CAS group. At 3 years, after baseline adjustment, the DES-CAS group showed a higher incidence of coronary revascularization, recurrent chest pain and major adverse cardiac events (MACEs) compared with the CAS alone group (Table).

Table. Three-year cumulative clinical outcomes

	Entire Patients				Propensity Score-Matched Patients			
Variable, N (%)	Total (n=1986)	DES-CAS (n=108)	CAS (n=1878)	p Value	Total (n=204)	DES-CAS (n=102)	CAS (n=102)	p Value
Outcomes at 3yr								
Mortality	7 (0.3)	2 (1.8)	5 (0.2)	0.051	2 (0.9)	1 (0.9)	1 (0.9)	ns
Cardiac death	5 (0.2)	1 (0.9)	4 (0.2)	0.244	1 (0.4)	1 (0.9)	0 (0.0)	ns
Myocardial infarction	8 (0.4)	2 (1.8)	6 (0.3)	0.066	2 (0.9)	2 (1.9)	0 (0.0)	0.498
PCI	19 (0.9)	10 (9.2)	9 (0.4)	<0.001	10 (4.9)	10 (9.8)	0 (0.0)	0.001
Cerebrovascular accidents	5 (0.2)	1 (0.9)	4 (0.2)	0.244	1 (0.4)	0 (0.0)	1 (0.9)	ns
Repeat CAG	194 (9.7)	27 (25.0)	167 (8.8)	<0.001	33 (16.1)	25 (24.5)	8 (7.8)	0.001
MACE : Mortality, PTCA, MI	28 (1.4)	11 (10.1)	17 (0.9)	<0.001	11 (5.3)	10 (9.8)	1 (0.9)	0.005
	HR:12.4 (95%C.I: 5.66-27.2)			<0.001	HR: 10.9 (95%C.I: 1.37-87.4)			0.024

DES-CAS, drug eluting stent coronary artery spasm, CAS, coronary artery spasm, MI; myocardial infarction, PCI; percutaneous coronary intervention, CAG; coronary angiography, MACE, major adverse cardiovascular events,

Conclusion: In this study, DES associated CAS was related to higher incidence of adverse 3-year clinical outcomes. Special caution should be exercised in significant CAS pts who underwent PCI with DESs.

P5356 | BEDSIDE
Impact of acute hyperglycemia after angioplasty for acute myocardial infarction

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Introduction: Hyperglycemia (HG) has been shown to be a powerful predictor of worse outcome after ST segment-elevation myocardial infarction (STEMI).
Aim: Investigate the relationship between acute HG and angiographic and clinical outcome after primary or rescue angioplasty for STEMI.
Methods: We prospectively included 399 patients who underwent revascularization for STEMI. We compared intrahospital outcomes between the groups of patients with HG (HG+) and without HG (HG-) and outcomes between diabetic and non diabetic in the HG+ group. Plasma glucose was measured at hospital admission. HG was defined as plasma glucose >11mmol/l (198mg/dl).
Results: Among the overall population, 150 (37.6%) patients had HG. They were more frequently women with a more frequent history of diabetes and dyslipidemia. They presented with lower blood pressure and more right ventricular heart failure. Procedural success was significantly lower in the HG+ group (86% vs 92%, p=0.05) with lower rates of ST segment resolution at 24 hours (47.3% vs 61.4%, p=0.006). Intrahospital outcomes were worse in the HG+ group as attested by a higher mortality (20% vs 10.4%, 0.008), higher late heart failure (32% vs 18.1%,

p=0.001), more frequent ventricular arrhythmias (16% vs 6.8%, 0.01) and atrial fibrillation (9.3% vs 4.4%, p=0.05). Those outcomes were similar in the HG+ group regardless to the diabetic status.
Predictive factors for intrahospital mortality in the overall cohort were: procedural failure (OR: 4.76, 95% CI [1.65; 13.7] p=0.004), heart failure at presentation (OR: 9.75, 95% CI [4.14; 22.87], p<0.001], non ST regression at 24 hours (OR: 2.19, 95% CI [1.08, 4.445], p=0.029), anemia (OR: 4.22, 95% CI [2.06; 8.63], p<0.001), high creatinine levels (OR: 1.09, 95% CI [1.03; 1.14], p: 0.001) high glycemia (OR: 2.66, 95% CI [1.2, 5.9], p: 0.016). Diabetic did not predict intrahospital mortality (p: 0.64) even in the group of patients with hyperglycemia.
In non diabetic patients (n=260), HG was associated with larger infarct size (p=0.001) and more adverse outcome (p=0.009). In the same group, HbA1c was associated with one year mortality (p=0.02).
Conclusion: HG in patients with STEMI is an important predictor of worse outcomes with an increasing mortality risk even beyond 11mmol/l. In non diabetic patients, both elevated admission glucose and HbA1c levels were associated with adverse outcome. These results suggest the usefulness of glycemia assessment in the setting of STEMI even in non diabetic and the beneficial effect of strict glycemic control.

P5357 | BEDSIDE
Relation of resistin to PCSK9 levels in CAD patients with varying degree of obesity

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Objectives: To investigate the association of resistin levels with proprotein convertase subtilisin-kexin type 9 (PCSK9), another novel regulator of atherosclerosis, in the condition of coronary artery disease (CAD).
Methods: We prospectively enrolled a total of 356 consecutive stable CAD patients who were not treated with lipid-lowering drugs in the present study. The baseline clinical characteristics were collected. Plasma PCSK9 and resistin levels were determined by ELISA. The relationship between plasma PCSK9 and resistin levels was investigated.
Results: Overall, resistin levels exhibited a positive nonparametric correlation with PCSK9 (r=0.123, p<0.05). When the patients classified into groups based on degree of obesity, the resistin correlated significantly to PCSK9 levels in Non-obese patients (r=0.162, p<0.05) but not in obese patients (r=0.087, p=0.205).Contrasted with the PCSK9 levels, resistin showed no significant associations with metabolic parameters including lipid profile. The PCSK9 and resistin levels related differently to inflammatory markers in both obese and non-obese patients. Multivariate regression analysis corroborated the relation between PCSK9 and an elevated resistin level in non-obese patients independently of traditional cardiometabolic and inflammatory parameters (p<0.05, all).
Conclusions: The plasma resistin levels were positively related to the PCSK9 levels in CAD patients with normal weight, suggesting that the circulating resistin might represent a link with PCSK9 level variations in CAD progression of non-obese condition.

P5358 | BEDSIDE
Prevalence of coronary artery disease in end-stage liver disease transplantation candidates

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Introduction: Orthotopic liver transplantation (OLT) is the only effective treatment in patients with end-stage liver disease (ESLD). Evidences suggest that coronary artery disease (CAD) is associated with increased peri-operative OLT mortality. Thus, identification of CAD is crucial in pre-OLT evaluation. There is no widely accepted diagnostic algorithm to detect CAD because of the lack of specific guidelines and unclear data on predictive value of non invasive stress tests in ESLD patients.
Purpose: of the present study was a) to assess CAD prevalence in OLT candidates and b) to record cardiac events in 3 years follow-up after OLT.
Methods: From 2007 to 2014 OLT candidates have been evaluated by cardiologic physical examination, electrocardiography and echocardiography. Stress echo was systematically performed in asymptomatic patients aged >50 years with diabetes and/or two or more of the following risk factors: active smoking, CAD family history, peripheral vascular disease. If stress-echo was not feasible, patients underwent coronary computerized tomography (CT) or coronary angiography (CGF) according to the cardiologist decision. Direct CGF was scheduled in patients with CAD history and/or typical symptoms of angina. A 3 years follow-up (1 visit/year) was scheduled only for post-OLT patients.
Results: Patients considered for OLT were 633, 367 (58.2%, age 57±5.7 years, males 74%) underwent OLT (45 excluded for pre-existent cardiac comorbidity, 7.2%). Stress Echo was performed in 139 (22.3%) and positivity was found in 12 pz (0.2%). Coronary CT was performed in 10 (1.5%). CGF was performed in 75 patients (11.8%,) but only in 38 (6%) for known CAD and/or symptoms. Critical coronary lesions were found in 12 patients (1,8%): 7 revascularized by PTCA, 1 by CABG and 4 medically managed. Not-critical coronary lesion were found in 25 patients (3.9%). 31 patients (4.8%) referred to CGF were subsequently removed by transplant list, none for coronary lesions, whereas OLT was successfully performed in all revascularized patients (n=8). During follow-up (35±20 months) 38 patients died (10.3%), 5 with symptoms of congestive heart failure, but no ischemic cardiac events were observed in the overall OLT population.
Conclusions: CAD detection remains a clinical challenge in ESLD patients candidates to OLT. The large number of normal stress echoes and normal CGF, even in presence of cardiovascular risk factors, demonstrates that CAD prevalence in ESLD is no higher than in general population and that the gold method to detect CAD in that patients is still unclear.

P5359 | BEDSIDE
The influence of comorbidity on the prognosis following coronary computed tomography angiography in patients suspected of coronary artery disease

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Background: Coronary CT angiography (CTA) testing in patients suspected of coronary artery disease (CAD) carries prognostic information. With an ageing population, the burden of comorbidity in patients undergoing coronary CTA increases. Comorbidity may interfere with the prognostic value of coronary CTA.
Purpose: To evaluate the influence of comorbidity on the prognostic information derived by coronary CTA testing.
Methods: A total, of 17,020 consecutive symptomatic patients with suspected CAD, who underwent coronary CTA (≥64-detector row) between January 2007 and December 2012 in 10 centers, were included. The coronary CTA result was defined as normal (0% luminal stenosis), non-obstructive CAD (1%-49% luminal stenosis) or obstructive CAD (≥50% luminal stenosis). Comorbidity was assessed using the Charlson Comorbidity Index (CCI) scores and categorized as low (score=0), moderate (score=1) or severe (score≥2). During a mean follow-up time of 2.7 (SD: 1.1, range: 1–6) years the composite end-point comprising all-cause death and myocardial infarction was registered. Cox regression was used to compute hazard ratios (HR) with 95% confidence intervals (CI) as measures of relative risk for the occurrence of the combined end-point, adjusting for age, sex, established cardiac risk factors, individual comorbidities and concurrent cardiovascular medical treatment.
Results: Mean (SD) age was 57 (11) years. 56% were women. Comorbidity burden was low in 76.0%, moderate in 14.7%, and severe in 9.3% of the patients. During follow-up 297 patients reached the composite endpoint. Compared to patients without CAD, both patients with non-obstructive CAD (HR=1.12, 95% CI: 1.02–1.23) and obstructive CAD (HR: 2.06, 95% CI: 1.88–2.26) exhibited an increased relative risk of the composite endpoint. Comorbidity influenced the prognostic value of coronary CTA with HRs (95% CI) in patients with non-obstructive disease of 1.05 (0.94–1.20), 1.14 (0.92–1.41) and 1.31 (1.11–1.56) in patients with low, moderate or severe comorbidity, whereas in patients with obstructive CAD figures were 2.13 (1.88–2.43), 1.65 (1.31–2.06) and 2.41 (2.05–2.85), respectively.
Conclusion: Obstructive CAD as identified by coronary CTA predicts cardiovascular risk regardless of comorbidity burden. However, in the presence of non-obstructive CAD, prognosis is influenced by comorbidity.

P5360 | BEDSIDE
Triglycerides-to-HDL-cholesterol ratio predicts atherosclerosis severity and major adverse cardiovascular events after acute coronary syndrome

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Background and introduction: Prognosis in acute coronary syndrome (ACS) is a major issue in clinical practice; most cardiovascular events are associated to coronary atherosclerosis. Insulin resistance is one of the most important factors that promote endothelium lipid accumulation, however plasmatic insulin measurement is not available in most medical care units and it is expensive. Triglyceride-to-HDL-cholesterol (TGL/HDL) ratio is a less expensive test and is available in most hospitals, also has proven excellent correlation with insulin resistance, hence could be used as a surrogate marker, and indirectly could show association with atherosclerosis clinical phenomena.
Purpose: To assess the association between TGL/HDL ratio and the atherosclerosis severity and major adverse cardiovascular events (MACE) in acute coronary syndromes.
Methods: A prospective cohort of 550 patients was analyzed, inclusion criteria was any gender, >18 years-old, ACS diagnosis (according to international standards) and coronariography at the event. All patients had complete blood-lipid test and 30 day follow-up, three-vessel disease, acute heart failure, cardiogenic shock and death were recorded, as well as composite endpoint (MACE). Chi-sqaured, Student-t test and logistic regression were used for association study.
Results: Mean age was 68±11.39 years, 74% male, 68.4% had diabetes and

78.2% arterial hypertension; body mass index (BMI) was 29.35±4.4 kg/m^2 and glucose at hospital admission 209.2±104.6 mg/dL. ST-elevation ACS was in 52.4%. Three-vessel disease was in 51.5% (TGL/HDL ratio 8.5±4.1 vs. 6.4±4.0 in ≤2 vessel disease, p<0.001). During the follow-up period 36.1% subjects developed acute heart failure, 14.5% cardiogenic shock, and 6.5% death and MACE (any of these) in 39.6%. TGL/HDL ratio was significantly higher in subjects with any adverse event (p<0.001). Mean TGL/HDL ratio in MACE group was 8.7±5.5 vs. 6.7±2.8 in non-MACE group (p<0.001). For 30-day MACE, TGL/HDL ratio cut-off point was 6.8 (64% sensibility and 52% specificity, AUC 0.61, 0<0.001); whereas TGL/HDL ratio cut-off point for 3-vessel disease was 6.9 (67% sensibility, 61% specificity, AUC 0.68,p<0.001). MACE significant independent predictors were: age, diabetes, TGL/HDL ratio and BMI (p<0.01 all).
Conclusions: TGL/HDL ratio is a surrogate insuline resistance marker strongly associated to atherosclerosis severity and major adverse cardiovascular events in patients with acute coronary syndrome, and may be useful for routine use since it's lower cost.

P5361 | BEDSIDE
In-Hospital impact of anemia at admission in patients with acute coronary syndromes

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Background and introduction: There is a continuous search for prognostic markers to identify patients with acute coronary syndrome (ACS) who are at high risk for adverse events. Anemia has been reported in 15–30% of patients with acute coronary syndrome. It is known that anemia is associated with increased risk of mortality and has the potential to worsen myocardial ischemia; however, few studies have investigated the in-hospital impact of anemia at admission in the patients admitted by ACS.
Purpose: To evaluate the in-hospital prognosis of the presence of anemia at admission in the patients with ACS.
Methods: A total number of 10107 patients included in the national registry of ACS, from 1st of October 2010 and until 20th October 2014 were divided in two groups: Group A – patients with anemia (Hb<12 g/dL in women and; Hb<13 g/dL in men) and Group B – patients without anemia. We evaluate the relationship between anemia on admission with cardiovascular events and in-hospital mortality.
Results: After compared the Group A (n=7532) with Group B (n=2576) we found that the Group B had a higher prevalence of AMI without elevation of the ST segment (53,5 vs 46%, p<0,001),and higher mean age (73 vs 64, p<0,001) and time to balloon (398 vs 362 min, p<0,001). The was also more co-morbilits (in particular hipertension, diabetes mellitus and familiar history of cardiovascular disease) and a higher prevalence of dispneia as the dominant sympton (8,4% vs 3,1%). The Group B had also a higher Killip Class at admission (prevalence of classe II-IV of 27,5 vs 11,6%, p<0,001), a worse left ventricular function (mean ejection fraction of 50 vs 55%, p<0,001), a higher incidence of heart failure (27,6 vs 13,2%, p<0,001), cardiogenic shock (6,5 vs 3%, p<0,001), atrial fibrillation (7,9 vs 4,5%, p<0,001) and a higher mortality (6,9 vs 2,6%, p<0,001).
Conclusion: The presence of anemia at admission is predictor of a worse in-hospital curse, with this patients having more heart failure, atrial fibrillation and mortality.

P5362 | BEDSIDE
Association of vitamin D receptor genetic polymorphisms with coronary artery disease in Russian population

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Vitamin D appears to be implicated in different stages of atherosclerosis. Vitamin D protective effects against immune inflammation are performed via vitamin D receptors in vascular wall.
Purpose: To assess the association of FokI and TagI vitamin D receptor (VDR) gene polymorphisms and vitamin D insufficiency with incidence of coronary artery disease (CAD) in Russian population.
Methods: The VDR FF, Ff, ff genotypes (FokI polymorphism) and the VDR TT, Tt, tt genotypes (TagI polymorphism) were determined in a sample of 193 Russian men with CAD and 140 healthy men by a polymerase chain reaction-restriction length polymorphism (PCR-RFLP)-based method. 25(OH)D 3 plasma concentration was estimated by ELISA (DRG). Coronary angiography was performed. ANOVa analysis, exact Fisher test and Odds-Ratio calculation were performed.
Results: The frequency of F allele was lower in CAD patients than in healthy people (0,55 and 0,59 respectively, p<0,05). The frequency of FF VDR genotype was lower in patients with incidence of myocardial infarction in the debut of CAD than in patients with incidence of angina in the debut of CAD (15 from 84 patients (18%) and 40 (37%) from 109 patients respectively; p=0,01, OR=0,38 (0,19–0,75). The frequency of t allele (TagI VDR gene polymorphism)was higher in CAD patients than in healthy people (0,39 and 0,31 respectively, p=0,02, OR=1,28 (1,01–1,81). Traditional risk factors were similar in patients-carriers of different VDR gene genotypes.
25(OH)D 3 plasma concentration was lower in CAD patients, than in healthy people: 35,6±1,25 nmol/l and 49,0±3,19 nmol/l respectively, p<0,001. In patients with multi-vessel coronary artery stenosis 25(OH)D 3 plasma concentration was lower than in patients with one-vessel stenosis (31,1±2,04 nmol/l and 43,07±3,34 nmol/l respectively, p<0.01).
Conclusions: t allele of VDR gene (TagI polymorphism) correlates with increased risk of CAD, FF genotype of VDR gene (FokI polymorphism) correlates with lower risk of myocardial infarction incidence in Russian population. Vitamin D insufficiency is associated with multi-vessel coronary arteriosclerosis.

P5363 | BEDSIDE
Association of carotid wall shear stress, carotid atherosclerosis, and coronary artery disease in patients with chest pain

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Background: Wall shear stress (WSS) is critically important in both vascular remodeling and atherosclerosis and can be assessed by ultrasound (US) as well as carotid intima-media thickness (IMT) and plaque burden. This study aimed to investigate the relationships between carotid WSS and the parameters of carotid atherosclerosis in the common carotid artery (CCA) in patients with suspected coronary artery disease (CAD).
Methods: Carotid artery US was performed in 950 patients with suspected CAD, and mean IMT, total plaque area (TPA), and hemodynamic parameters of CCA, including peak and mean WSS, were measured. Carotid parameters were analyzed according to the presence of CAD, and the predictive values of WSS and TPA for the presence of significant CAD were analyzed.
Results: Compared to patients without CAD (n=667), patients with CAD (n=283) showed significantly higher mean CCA IMT (0.66±0.15 mm vs. 0.74±0.27, p<0.001), TPA (0.13±0.24 vs. 0.20±0.42 cm^2, p=0.002), and beta stiffness index (5.12±3.11 vs. 5.60±2.66, p=0.045) and lower mean WSS (2.59±0.82 vs. 2.23±0.90 dyne/cm^2, p<0.001). Mean carotid WSS showed significant negative correlations with the beta stiffness index (r=–0.116, p<0.001), mean IMT (r=–0.193, p=0.007), and TPA (r=–0.296, p<0.001). Binary logistic regression analysis showed that age (Odds ratio [OR] 1.038, 95% confidence interval [CI] 1.010–1.066), presence of diabetes mellitus (OR 1.606, 95% CI 1.194–1.807), current smoking (OR 1.758, 95% CI 1.564–1.866), carotid TPA (OR 2.615, CI 1.320–5.183), and mean WSS (OR 0.554, CI 0.371–0.838) were significant predictors of CAD.
Conclusion: In patients with chest pain, low local shear stress and high plaque burden in the carotid arteries were significant predictors of CAD. This finding is further strengthened by the significant association between IMT/TPA of the carotid arteries and WSS. These findings indicate that carotid WSS has a role as an index of atherosclerosis and serves as a predictor of significant coronary atherosclerosis.

P5364 | BEDSIDE
Evolution of high sensitivity troponin-T in patients undergoing high efficiency on-line hemodiafiltration versus conventional low-flux hemodialysis

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Introduction and aims: On-line hemodiafiltration (HDF) has been associated with better atherosclerosis-related inflammatory markers profile than conventional low-flux hemodialysis (HD). Recent large randomized clinical trials suggested that HDF had a beneficial effect on survival when higher convection volumes are provided. High-sensitivity troponin T (hs-TnT) has been related to all-cause and cardiovascular mortality in end-stage renal disease patients. The aim of this study was to determine the effect HDF vs HD on hs-TnT evolution at one year follow-up.
Methods: Patients were randomized from 2007 to 2013 to HD or post-dilution online HDF in accordance with the CONvective TRAnsport STudy (CONTRAST) protocol initially as part of the Montreal CONTRAST cohort (until 2010) and subsequently as part of the local cohort (2010–2013). Hs-TnT were obtained before dialysis at baseline and at 1-year follow-up. Comparison of the evolution of hs-TnT values between groups was performed with an appropriate non-parametric test.
Results: 54 HDF patients and 59 HD patients were included. Mean age was 60±16 years in the HDF group and 64±12 years in the HD group, (p=0.170). Prior to randomization, all patients were treated with conventional hemodialysis. Mean dialysis time was similar between groups. Median dialysis vintage was 21 (interquartile range 7–66) months in the HDF vs. 27 (12–53) months in HD (p=0.769). Patients with a myocardial infarction within 2 months before randomization were excluded. At baseline, median hs-TnT value was 49 (31–89) umol/L in the HDF group vs. 60 (36–96) umol/L in the HD group (p=0.370). During the following year, dialysis was provided according to randomization with comparable dialysis session time and frequency. Mean Kt/V was 1.9±0.4 in HDF vs. 1.6±0.2 in HD (p<0.001). Mean convection volume was 27.9±0.9L in the HDF group. At one year follow-up, median hs-TnT remained stable at 47 (32–86) umol/L in the HDF group (p=0.508 vs. baseline) but significantly increased to 62 (40–104) umol/L in the HD group (p=0.021 vs. baseline). The median change in hs-TnT values was –3 (–7 to+7) umol/L in the HDF group vs. +8 (–5 to +25) umol/L in the HD group (p=0.024).

Conclusions: Treatment with high-efficiency HDF is associated with stable hs-TnT values whereas low-flux HD is associated with significant increase in hs-TnT levels at one-year follow-up. Future studies are needed to establish whether stability of hs-TnT values is linked to better outcome in HDF patients.

CORONARY ARTERY DISEASE AND COMORBIDITIES IV

P5365 | BEDSIDE
Analysis of new score of risk in a population of diabetic patients with acute coronary syndrome undergoing coronary revascularization by percutaneous angioplasty

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Background: The Syntax score (SX) is a tool proposed for the analysis of the anatomy coronary and cardiovascular risk stratification in patients with lesions of the left main and/or multivessel. The ACEF score (age/left ventricular ejection fraction + 1 if creatinine>2.0 mg/dL) is a risk score based on the clinical characteristics of patients, can predict the prognosis of patients undergoing surgical revascularization.The Clinical Syntax (CSS) integrating elements of the coronary anatomy to clinical parameters, so it could be a new and more comprehensive prognostic tool for patients undergoing percutaneous revascularization.
Methods: We therefore conducted a retrospective observational study analyzing the characteristics of 111 patients with acute coronary syndrome undergoing angioplasty in the last 6 months of 2013 and then followed-up after at least 12 months. For these patients were calculated Syntax score, ACEF and Clinical Syntax score and was correlated these indices with cardiovascular outcomes.The objective of this study was to evaluate the prognostic ability of individual score mentioned in predicting cardiovascular events. Were considered as events: sudden death, MI, revascularization new TLF. Based on the values of SX, ACEF and CSS patients were divided into 3 groups, low (SX <9, ACEF <1.022, CSS <15.6), medium (SX 9–17, ACEF 1.022 to 1.277, CSS 15.6 to 27.5) and high risk (SX>17 ACEF>1.277, CSS>27.5).
Results: In our sample events occurred in 29 patients (incidence 26%) The incidence of AMI in our sample was 23%, while that of restenosis was 18%.In our follow-up no patient experienced a death.Calculating ACEF, SX and CSS, events are distributed as appeared in three risk categories of each score: ACEF low risk 12% (2 events), medium risk 17% (6 events), high risk 36% (21eventi); SX: low risk 23% (8 events), medium risk 20% (8 events), high risk 35% (13 events); CSS: low risk 20% (12eventi), medium risk 9% (2 events), 48 high-risk % (15 events).Therefore the incidence of MACE was significantly higher in patients with ACEF high compared to patients with ACEF intermediate and ACEF low (36% vs. 17% vs. 12% p=0.03), as well as for the Clinical Syntax, the group of high shows a significant difference in risk of events compared with medium and low risk (48% vs 9% vs 20%, p=0.04). While there are no significant differences between the medium and low risk for both the ACEF score (p=0.06).
Conclusion: The ACEF score and Clinical Syntax score are valuable tools for risk stratification of cardiovascular events in diabetic patients undergoing percutaneous angioplasty.

P5366 | BEDSIDE
Association between serum thyroid stimulating hormone (TSH) levels and coronary collateral development

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Introduction: Coronary collaterals are an alternative source of blood supply to the myocardium. Studies have shown that thyroid hormones are pro-angiogenic for the development of blood vessels. In the study, we aimed to analyze the effects of the serum thyroid stimulating hormone (TSH) levels and different thyroid clinics on the development of coronary collaterals.
Materials and methods: 561 consecutive patients who have undergone coronary angiography and had at least one major coronary artery stenosis of ≥90% were enrolled in the study. Collateral development was graded according to the Cohen-Rentrop method. Grades were divided into two subgroups; patients with grade 0–1 collateral were defined as having poor, and patients with grade 2–3 collateral were defined as having good collateral. Then, association between the serum thyroid hormones and the coronary collateral was assessed. Subsequently, participants were divided into three subgroups according to the thyroid hormone levels; euthyroidism, subclinical hyperthyroidism, and subclinical hypothyroidism. Then, the effect of different thyroid clinics on the coronary collateral formation was investigated.
Results: Mean age of the patients was 63.5±10.7 years. 425 of the cases (75.8%) were men. Serum triglyceride (153.0±78.6 mg/dL vs. 176.9±74.3 mg/dL, p=0.03) and TSH (1.99 μIU/ml vs. 2.30 μIU/ml, p=0.02) levels were lower in patients with good collaterals compared to those with poor collaterals. Subjects with good collaterals were significantly more likely to have severe lesion location on the right coronary artery (RCA) (72.4% vs. 52.2%, p<0.01). Other demographic characteristics, laboratory data and cardiovascular medications were similar among the groups. Then, the effect of different thyroid clinics on the development of coronary collaterals was investigated, and found that good collateral formation was statistically higher in the subclinical hypothyroidism group (21.1% vs. 8.2%, p<0.001). After that, the association between the various clinical characteristics and the extent of the collaterals was assessed by using univariate and multivariate regression models. Analysis of data has revealed that lesion location on the RCA and presence of subclinical hyperthyroidism were independent predictors of better collateral development [(OR: 1.87, 95% CI 1.15–3.03, p=0.01 for the RCA), and (OR: 2.35, 95% CI 1.05–5.29, p=0.04 for subclinical hyperthyroidism)].
Conclusion: We demonstrated that subclinical hyperthyroidism is associated with better coronary collateral formation.

P5367 | BEDSIDE
Admission hemoglobin levels and Killip class in acute coronary syndrome patients: insights from the cohort EPIHeart

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Background: In the setting of an acute coronary syndrome (ACS) hemoglobin levels have the potential to worsen the myocardial ischemic insult. Killip classification is a simple clinical tool that has previously shown good prognostic value in patients with myocardial infarction. Data relating hemoglobin levels to clinical outcomes during patients' in-hospital stay remains limited.
Purpose: Our aim was to examine the association between baseline hemoglobin values and Killip classification during the index hospitalization in patients with ACS.
Methods: The data were obtained in the framework of an ongoing cohort of ACS, consecutively admitted at the Cardiology department of two tertiary hospitals of different regions, between August 2013 and April 2014. We analyzed data regarding demographic and clinical characteristics, as well as laboratory data. Patients were categorized according to Killip classification regarding their evolution during the hospitalization (Classes I, II, III, and IV), as registered in medical records. The association of admission hemoglobin (continuous variable) and the dependent variable Killip class was quantified using odds ratios (OR) and their 95% confidence interval (95% CI) estimated by multinomial logistic regression.
Results: Among 332 patients admitted for ACS (50.3% ST-elevation ACS and 49.7% non-ST-elevation ACS), the mean age was 64±14 years and 72.6% were male. Hemoglobin admission values ranged between 5.5 and 18.3 g/dL (median 14.3). Two hundred and fifty four patients evolved in Killip I, 49 in Killip II, 19 in Killip III and 10 in Killip IV, and their median (interquartile range) admission hemoglobin was 14.5 (13.3–15.4), 13.5 (12.2–15.3), 13.1 (11.2–14.3) and 12.6 (11.0–16.1), respectively (p<0.001). After adjustment for differences in baseline characteristics (sex, age, creatinine at admission, ACS type and previous heart failure), for each 1 g/dL higher hemoglobin at admission the probability of evolving in Killip class III decreased by 27% (OR=0.73, 95% CI 0.55–0.97, p=0.028), and that of evolving in class IV decreased by 34% (OR=0.66, 95% CI 0.47–0.92, p=0.015) with no effect seen for Killip II (OR=1.06, 95% CI 0.85–1.32, p=0.592).
Conclusions: In ACS patients, admission hemoglobin values independently predict Killip class. So, our results reinforce the fact that in the setting of ACS, lower hemoglobin levels at admission are related with worse clinical evolution, namely regarding severe heart failure.

P5368 | BENCH
Fibrinogen high levels, but not fibrinogen genetic variability is a risk factor coronary artery disease in patients with essential hypertension and diabetes mellitus type 2

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Purpose: It is well established that hypertension (HTN) and diabetes mellitus (DM) are important risk factors for coronary artery disease (CAD). In addition, controversial data exist related to the role of fibrinogen genetic variants in atherosclerosis-CAD. Therefore, we examined the effects of the rs180070 and rs2070011 fibrinogen polymorphisms on the risk for CAD/myocardial infarction (MI) in patients with DM and HTN admitted with stable angina pectoris symptoms.
Methods: A total of 744 subjects were enrolled in 3-year period. Fibrinogen polymorphisms were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Fibrinogen plasma level were measured by the Clauss method.
Results: The AA homozygosity of rs180070 was associated with significantly higher levels of fibrinogen in both HTN and DM (p=0.05, p=0.04 respectively). The presence of AA genotype (rs180070) was also significantly associated with increased risk of CAD in the general population [OR: 3.2, 95% CI, (1.01–10.1, p=0.049)]. Interestingly, multivariate logistic regression analysis showed that fibrinogen levels >443 mg/dl were associated with higher risk for CAD [OR: 3.9, 95% CI, (1.7–9.4, p=0.002)] compared to levels <347 mg/dl in the general population. Similar associations were observed in HTN and DM patients. In hypertensive patients, higher fibrinogen levels >443 mg/dl [OR: 3.5, 95% CI (1.14–10.9, p=0.029), but not the AA genotype of rs180070 [OR: 3, 95% CI (0.78–11.9,

p=0.11)] were independent predictors of CAD. Similarly, in DM only fibrinogen remained an independent predictor of CAD [OR 5.86, 95% CI (1.1–31.2, p=0.038)]. Finally, neither the AA homozygosity of the rs180070 nor the AA homozygosity of the rs2070011 was associated with the occurrence of MI in the overall cohort [OR: 1.87, 95% CI (0.37–8.9), p=0.46 and OR: 0.75, 95% CI (0.39–1.43), p=0.378 respectively]. No association between the AA homozygotes (rs180070) and MI was detected in DM or HTN subjects.
Conclusions: Our results indicate that elevated fibrinogen levels may be an independent predictor of CAD risk in both HTN and DM subjects. Although, the presence of the AA homozygostiy (rs180070) resulted in higher fibrinogen levels and risk of CAD in the overall cohort, no significant effect was found in the subgroups of HTN and DM. This finding suggest that the AA genotype does not raise CAD risk independently of fibrinogen levels and major risk factors. Interestingly, fibrinogen levels were not associated with the incidence of MI, which could be attributed to the low event rate.

P5369 | BENCH
miRNA-197 and miRNA-223 predict cardiovascular death in a cohort of patients with symptomatic coronary artery disease

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Background: Circulating microRNAs (miRNAs) have been described as potential diagnostic biomarkers in cardiovascular disease and in particular, coronary artery disease (CAD). Few studies were undertaken to perform analyses with regard to risk stratification of future cardiovascular events. So far, only one large-scale prospective study involving miRNA screening has been performed identifying miR-126, miR-197 and miR-223 as related to future myocardial infarction.
Purpose: The aim of our prospective study was to further evaluate these miRNAs in a large prospective cohort of patients with invasively diagnosed CAD.
Methods: We prospectively evaluated baseline levels of 3 miRNAs (miR-126, miR-197 and miR-223) in serum samples of 1,112 CAD patients with respect to the endpoint cardiovascular death (n=21; 1.9%). Patients enrolled had symptoms of suspected coronary artery stenosis and CAD was diagnosed via coronary angiography. miRNA quantification was performed using real time polymerase chain reaction (RT-qPCR). Cycle threshold (Ct) values were normalized to C. elegans miR-39 (cel-miR-39). The formula $2^{[-(Ct[miRNA]-Ct[cel\text{-}miRNA\text{-}39])]}$ was used for Ct <40. In the case of Ct ≥ 40 the Ct value was considered as undetermined.
Results: The median follow-up period was 4 years [25th; 75th percentile: 2.78; 5.04]. The median age was 63.5 years [57; 69] with 80.4% males. 38.7% of the patients presented with acute coronary syndrome (ACS) and 61.3% were diagnosed with stable angina pectoris (SAP).
Elevated levels of miRNA-197 and miRNA-223 reliably predicted future cardiovascular death in the overall group (miRNA-197: Hazard Ratio (HR) 1.594 per one standard deviation (SD) increase (95% confidence interval (CI) 1.078; 2.358), p=0.02, concordance index (c-index) 0.786; miRNA-223: HR 1.923 per one SD increase (1.098; 3.397), p=0.024, c-index 0.801). In ACS patients the predictive power of these two miRNAs was even higher (miRNA-197: HR 2.05 per one SD increase (1.162; 3.618), p=0.013, c-index 0.887); miRA-223: HR 3.488 per one SD increase (1.254; 9.708), p=0.017, c-index 0.849).
Conclusion: Elevated levels of serum-derived circulating miRNA-197 and miRNA-223 were identified as predictors for cardiovascular death in patients with CAD. These results are based on the largest study so far investigating the applicability of miRNAs as biomarkers in cardiovascular disease. Our results suggest circulating miRNAs as promising biomarkers not only with diagnostic but also with prognostic and predictive value with respect to future cardiovascular events.

P5370 | BEDSIDE
Association between sex hormone-binding globulin and coronary artery disease in males

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Background: Low concentration of testosterone in men is found to be associated with coronary artery disease (CAD) and its risk factors. Major portion of testosterone is bound to sex hormone-binding globulin (SHBG). The link between SHBG and coronary artery disease is not well established.
Purpose: The objective was to evaluate the association between sex hormone-binding globulin (SHBG), sex hormones and coronary artery disease among men.
Methods: A hospital-based case-control study used patients with angiographically proven coronary artery disease (n=84) and acute myocardial infarction (n=84) as cases and controls (n=84) from the surgical wards. Serum samples were used to assess the levels of high sensitivity C-reactive protein (hs-CRP), total cholesterol, HDL-cholesterol (high density lipoprotein), triglycerides, SHBG and total testosterone (TT). The levels of LDL-cholesterol (low density lipoprotein) were calculated using Friedewald's formula and free testosterone (FT) and bioavailable testosterone (BT) levels were calculated using Vermeulen's formula. Free androgen index (FAI) was calculated. Data were analysed using appropriate statistical tests.
Results: Total testosterone (TT) (11.58±2.9 vs. 18.64±7.4 nmol/L, p=0.001), free testosterone (FT) (0.183±0.056 vs. 0.388±0.256 nmol/L, p=0.001), bioavailable testosterone (BT) (4.31±1.32 vs. 9.10±6.02 nmol/L, p=0.001), free androgen index (24.6±7.65 vs. 54.3±40.8, p=0.001) were significantly lower in patients compared to controls, but SHBG (48.4±7.16 vs. 42.8±12.1 nmol/L, p=0.001) and hs-CRP (3.55±1.23 vs. 1.69+0.57 mg/L, p=0.001) were significantly higher in patients compared to controls. SHBG (p=0.040, OR=0.040, 95% CI: 0.78–2.78), TT (p=0.017, OR=3.10, 95% CI: 0.75–12.72), hs-CRP (p=0.001, OR=10.54, 95% CI: 4.57–15.63), smoking (p=0.009, OR=3.99, 95% CI: 1.41–11.32) were found to be significant independent predictors of CAD, but not BT (p=0.826, OR=0.354, 95% CI: 0.042–2.80) and FT (p=0.659, OR=0.651, 95% CI: 0.025–1.26).
Conclusion: Serum low TT, high SHBG and hs-CRP are associated with CAD and are independent predictors of CAD in men.
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P5371 | BEDSIDE
Differential adipose tissue bradykinin receptors gene expression profiles in obese patients with and without coronary artery disease

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Purpose: Adipose tissue is an inflammatory source of coronary artery disease (CAD). Kinin receptors may be an important determinant of the impact of adiposity on endothelial function and cardiovascular function. The aim of this study was to examine kinin receptors gene expression levels in the adipose tissue in obese patients with and without CAD.
Methods: Obese patients (BMI $>30 kg/m^2$) undergoing coronary angiogram were participated in the study. We included 10 patients with CAD (6 male, 61±8 years old) and 9 patients without CAD (6 male, 63±8 years old). Subcutaneous white adipose tissue biopsies were obtained from the site of paracentesis before the procedure and analyzed for bradykinin receptor type 1 (BR1) and 2 (BR2) gene expression by RT-quantitative PCR.
Results: Adipose tissue analysis revealed increased BR1 and BR2 gene expression levels in obese patients with CAD compared to those without CAD. More specifically, BR1 gene expression levels were 654±345 in patients with CAD versus 107±99 in patients without CAD and BR2 gene expression levels were 452±145 in patients with CAD versus 133±107 in patients without CAD ($p<0.05$ for both). No statistical significant correlation were found between BR1 and BR2 gene expression levels and patients' BMI.
Conclusions: There is a divergence in BR1 and BR2 gene expression in adipose tissue between obese patients who exhibit or do not exhibit CAD. Our findings may have implications in the pathophysiology and treatment of atherosclerosis and should be further investigated.

P5372 | BEDSIDE
A prognostic value of aortic annulus displacement assessed by contrast left ventriculography in cardiac catheter laboratory

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Background: Left ventricular (LV) longitudinal strain has been a novel index of LV systolic function commonly used in echocardiography. We developed the estimation of aortic annulus displacement (AAD) from conventional left ventriculography (LVG) in cardiac catheter laboratory.
Purpose: The purpose of this study was to evaluate whether AAD obtained by LVG was associated with the incidence of adverse events.
Methods: Nine hundred and ninety eight consecutive non-atrial fibrillation patients who had undergone conventional catheters containing LVG based on clinical indications were enrolled and followed retrospectively from our clinical chart. End diastole length (EDL) and end systole length (ESL) were assessed from the

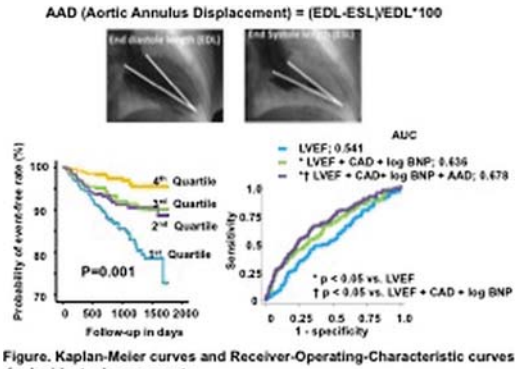

Figure. Kaplan-Meier curves and Receiver-Operating-Characteristic curves for incident adverse events

apex to the aortic valve insertion on the LVG. AAD was calculated as 100*(EDL-ESL)/EDL. The Cox regression analysis was used to predict the endpoints of adverse events.
Results: Ninety six outcomes (all-cause death; 39, congestive heart failure; 21, late revascularization; 34, myocardial infarction; 2) were observed during the follow-up period for median 3.1 years. In multivariate analysis, adverse events were significantly associated with lower AAD (hazard ratio 0.852; 95% confidence interval 0.791–0.918, $p<0.01$) after adjustment for traditional risk factors and coronary artery disease (CAD). The area under the curve (AUC) of AAD was greater than that of LV ejection fraction (LVEF) (0.656 vs. 0.541, $p<0.05$). AAD improved AUC compared with traditional risk factors, and AAD combined with LVEF, CAD and brain natriuretic peptide had the largest AUC (0.678).
Conclusion: Lower AAD was related to incidence of adverse events in patients who underwent coronary angiography for clinical indications. AAD is superior predictor to conventional LVEF as a predictor of adverse events.

P5373 | BEDSIDE
Background characteristics and prognosis in non-invasively treated patients with type 1 and type 2 myocardial infarction. Data from the SWEDEHEART registry

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Purpose: To assess differences in demographic, clinical characteristics and long-term survival between non-invasively treated patients with type 1 and type 2 myocardial infarction (MI).
Methods and results: A total of 59394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry and followed up for a mean of 1.87 years. The majority of cases presented with type 1 MI (n=53342; 89.8%) while 6.9% (n=4083) with type 2 MI; 66.8% (n=2726) of patients with type 2 MI and 20.6% (n=10978) with type 1 MI did not undergo coronary angiography during hospitalization. For backgroud characteristics see table. Type 2 MI patients developed smaller myocardial necrosis (max troponin T 735±1213 vs. 965±1798ng/L, $p<0.001$) as compared to those with type 1 MI. Tachycardia (6.7 vs. 2.5%), acute anemia/bleeding (9.4 vs. 1.5%) or acute respiratory failure (5.5 vs. 2.0%) could be more often identified in type 2 MI patients.
The crude long-term mortality risk was lower in patients with type 2 MI (HR 0.92, 95% CI 0.87–0.98) as compared to type 1 MI and remained significantly lower after adjustment for age, sex, co-morbidities, treatments and triggering mechanisms (HR 0.81, 95% CI 0.73–0.89).

	Type 1 MI w/o coronary angiography (n=10,978)	Type 2 MI w/o coronary angiography (n=2,726)	p
Age, y (±SD)	83.5±9.0	80.5±9.8	<0.001
Women, %	50.0	50.2	ns
Smoking, %	42.8	51.2	<0.001
Hypertension, %	62.5	59.8	0.008
Diabetes, %	31.2	32.6	ns
History of MI, %	49.3	44.5	<0.001
History of CHF, %	24.9	24.3	ns

Conclusions: Among the selected group of conservatively managed MI patients in this real life study, those classified as type 2 MI had lower age, lower proportion of hypertension and previous cardiovascular events, smaller myocardial necrosis, but higher prevalence of identifiable triggering mechanisms. Both crude and adjusted long-term mortality risk were significantly lower in conservatively managed patients with type 2 MI compared with type 1 MI.

P5374 | BEDSIDE
Identification and characterization of heterozygous familial hypercholesterolemia patients using the Vanderbilt University Medical Center Synthetic Derivative database

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Background: Despite an estimated prevalence of 1:300–1:500, and an associated high risk of premature cardiovascular disease (CVD), few contemporary studies have characterized the heterozygous familial hypercholesterolemia (FH) population with respect to demographics, clinical characteristics, or treatment patterns.
Purpose: To leverage structured and unstructured longitudinal clinical data and bioinformatics expertise to identify and characterize FH patients within the Vanderbilt University Medical Center de-identified electronic medical records (EMR) database (Synthetic Derivative) from 1996 to 2014.
Methods: Using diagnostic and procedure codes, narrative text from clinical care, laboratory values, and inpatient and outpatient medication histories, adult FH patients were identified using Dutch Lipid Network (DLN) criteria components and classified as "probable" or "definite" FH. Demographics, clinical characteristics, laboratory measures, and use of lipid lowering therapies were described.
Results: Out of a population of 218,652 individuals with at least one low-density lipoprotein cholesterol (LDL-C) measure, we identified 622 probable and 430 definite FH patients. Herein results are limited to definite FH patients, among whom 40% were male, 68% white, 39% ever-smokers, and 35% obese (body mass index $>30 kg/m^2$). Median number of clinic visits and hospital admissions over the cumulative EMR were 47 [interquartile range (IQR) 15–132] and 2 (IQR 0–9), respectively, over a median duration of 9 (IQR 3–14) years. Median number of LDL-C measures was 6 (IQR 3–15); 83% and 16% had a recorded LDL-C value >330 or 250–329 mg/dl, respectively, and maximum LDL-C had a median value of 340 (IQR 309–386). Median value (mg/dl) for high-density lipoprotein cholesterol and triglycerides were 47 (IQR 39.5–58) and 164 (IQR 115–241), respectively. Prevalence of CVD was 8% for myocardial infarction, 11% peripheral arterial disease, non-hemorrhagic stroke or unstable angina, 13% heart failure, 15% revascularization, 24% type 2 diabetes, and 87% hypertension. The prevalence of statin use was 84%, with 45% taking a high-dose statin and 48%, 37% and 27% also taking ezetimibe, fibrate or niacin, respectively. None of the patients had evidence in any clinical document indicating LDL receptor mutation testing, and only five were found to have narrative keyword strings explicitly noting the presence or suspicion of familial or inherited hypercholesterolemia.
Conclusion: Rigorous EMR characterization in a tertiary medical center population suggests that FH may be under-recognized and inadequately treated.
Acknowledgement/Funding: EpidStat Institute, Ann Arbor, MI

P5375 | SPOTLIGHT
Impact of coronary calcification in female patients undergoing PCI: Results from a pooled analysis of 26 randomized trials

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Background: Previous studies, in which the majority of patients were male, have shown that percutaneous coronary intervention (PCI) of moderately and severely calcified coronary lesions is an independent predictor of death, myocardial infarction (MI), stent thrombosis (ST), and restenosis after PCI. Whether or not similar associations exist for female patients undergoing PCI remains unclear.
Methods: We pooled patient level data of female participants from 26 randomized trials of drug eluting stents. Calcification was evaluated by qualitative coronary angiography in central core laboratories or sites. We divided the study population into two groups according to calcification grade: none/mild vs. moderate/severe. Subsequently, we sought to evaluate the frequency and impact of coronary calcification on future ischemic outcomes.
Results: Of 11,557 women included in the primary pooled analysis, coronary calcification status was available for 7156 patients. Compared to none/mild calcification (n=5343, 75%), patients with moderate/severe calcification (n=1813; 25%) were older, were more likely to have diabetes, hypertension, hypercholesterolemia, previous history of CABG, lower ejection fraction, more multivessel disease, greater number of lesions and more commonly at least one B2/C lesion. At 3-year follow-up, women undergoing PCI of lesions with moderate/severe calcification had higher rates of mortality (7.2% vs. 5%, p=0.0005), cardiac death (4% vs 2.5%, p=0.002), myocardial infarction (MI; 6.8% vs. 4.5%, p=0.003) and target lesion revascularization (TLR; 9.1% vs. 7.5%, p=0.025) compared to those with only none/mildly calcified lesions. Stent thrombosis (ST) did not reach statistical significance (p=0.17). After adjustment for baseline differences, calcification status remained independently associated with 3-year all-cause mortality (HR: 1.69, 95% CI 1.15–2.49, p=0.0078) and TLR (HR; 1.39, 95% CI 1.14–1.68, p=0.0009) but not cardiac death, MI, or ST.
Conclusion: Moderate to severe coronary artery calcification is present in one of four women undergoing PCI and is a powerful independent predictor of late mortality and TLR.

P5376 | BEDSIDE

Prognostic value of coronary artery calcium score for major perioperative cardiovascular complications in type 2 diabetic patients undergoing trans-femoral amputation

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Perioperative risk for major perioperative cardiovascular complications is particularly high in patients with type 2 diabetes undergoing trans-femoral amputation and contrast application for angiography is often contraindicated due to nephropathy. The aim of this study was to identify prognostic value of coronary computed tomographic angiography (CCTA) and coronary artery calcium (CAC) score for major perioperative cardiovascular complications in these patients.

Materials and methods: In this prospective single center interventional cohort study, we evaluated 331 consecutive pts with diabetes and without history of coronary intervention or myocardial infarction (MI) undergoing trans-femoral amputation during the year 2013. 179/331 pts (54%) had no contraindications for contrast application and were included in the study cohort. CCTA and CAC-scoring were performed using a 64 detector rows CT scanner GE USA "Light speed" VCT cardiac 72013287YA 2008.

Results: Female in our study were significantly older than male (68.1±5.9 vs. 57.2±6.2, p=0.0017). All women and 65% of men had clinical coronary artery disease (CAD). Increasing CAC was associated with significant increasing severity of CAD and incidence of cardiovascular complications (Table). Perioperative period of 26 (14.5%) of pts was complicated by acute MI (19 Q-wave and 7 non Q-wave), 3-vessel obstructive CAD was in 85.7%, 2-vessel in 4.8%.

CAC compared with severity of CAD

n (%)	CAC=0 n=6	CAC=1–99 n=20	CAC=100–399 n=44	CAC=400–999 n=84	CAC ≥1000 n=25
No CAD	4 (66.7)	3 (15)	–	–	–
Non-obstructive CAD	2 (33.3)	17 (85)	21 (47.7)	6 (7.1)	–
1-vessel obstructive CAD	–	–	16 (36.4)	41 (48.8)	–
2-vessel obstructive CAD	–	–	5 (11.4)	29 (34.5)	7 (28)
3-vessel obstructive CAD	–	–	2 (4.5)	8 (9.5)	18 (72)
Perioperative MI, n=26	–	–	2 (4.5)	8 (9.5)	16 (64)
Death, n=10	–	–	–	1 (1.2)	9 (36)

CAC, coronary artery calcium; CAD, coronary artery disease.

Conclusion: Predicative value of CAC for perioperative MI and death is high in pts with type 2 diabetes undergoing trans-femoral amputation. Whereas pts with a CAC<99 had only a small prevalence of potentially obstructive CAD, the incidence of MI or death increased from 4.5% to 64% with increasing CAC score from 400 to 1000 indicating increasing need for coronary revascularization before surgery.

CORONARY ARTERY DISEASE AND COMORBIDITIES V

P5377 | BEDSIDE

Acute coronary syndrome in patients without cardiovascular risk factors: in-hospital morbidity and mortality

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Background: Although it is less frequent, a fraction of patients admitted with Acute Coronary Syndrome (ACS) does not have known cardiovascular risk factors (CVRF).

Purpose: We aimed to evaluate the impact of the absence of known CVRF on the in-hospital morbidity and mortality in a population with ACS.

Methods: Prospective study of 1294 consecutive patients admitted for ACS in a single coronary unit (CCU), from October 2009 to September 2014. We defined CVRF as previous ACS, percutaneous coronary intervention, coronary artery bypass graft, stroke, systemic hypertension, diabetes mellitus, dyslipidemia, smoking, peripheral vascular disease and family history. We compared 2 groups, according to the presence of CVRF: group I) patients without CVRF and group II) patients with at least one CVRF. We compared them regarding the primary composite endpoint (EPC)-cardiovascular death, non-fatal myocardial infarction or stroke- and the in-hospital mortality.

Results: In our study, 7,50% of patients presented with no known CVFR and there were no statistical differences regarding sex or age between the two groups [I: n=97; 7,50%; 75,3% men; 67,65 years (interq (iq)= 21,29) vs II: n=1197; 92,5%; 69,4% men; 66,55 years (iq=21,60)]. At admission, group I presented higher rate of ST-segment elevation myocardial infarction [I: 66,0% vs II: 40,2%, p<0,01]and shorter door-to-angiography time [I: 85,0 minutes (iq=639,25) vs II: 158,0 minutes (iq= 393,00), p<0,001]. Group I had more one-vessel disease [I: 46,5 vs II: 33,1, p<0,02] in contrast with group II, who had more multivessel disease. There was no difference referring to Killip class or to analytic parameters (glycaemia, creatinine, troponin, CK and BNP) between both groups. During hospitalization, group I was less prescribed with beta-blockers [I: 39,2% vs II: 51,7%, p<0,03], calcium antagonists [I: 5,2% vs II: 12,6%, p<0,03] or nitrates [I: 42,3% vs II: 53,8%, p<0,05]. There was no difference regarding neither invasive stratification nor reperfusion therapy. Group I experienced more cardiogenic shock [I: 16,5% vs II: 5,8%, p<0,001] and cardio-respiratory arrest [I: 13,4% vs II: 5.4%, p<0,03]. In-hospital age-adjusted mortality was superior in group I [I: 31,0% vs II: 12,2%, p<0,01] as was EPC [I: 15,5% vs II: 7,0%, p<0,01].

Conclusion: The absence of known CVRF did not reflect a better in-hospital prognosis. On the opposite, these patients had worse clinical outcome and, thus, even in the absence of CVRF we should keep a close monitoring and the recommended therapeutics.

P5378 | BEDSIDE

Percutaneous coronary revascularization reduces risk of acute renal failure when compared to coronary artery bypass graft: a meta-analysis of 8 studies and 257980 patients

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Introduction: Incidence of acute renal failure after PCI (Percutaneous Coronary Intervention) and CABG (Coronary Artery Bypass Graft) remains to be determined.

Methods: Pubmed, Google Scholar and Cochrane Collaboration were searched for randomized controlled trials or studied with multivariable analysis comparing incidence of acute renal failure after PCI and CABG. Metaregression analysis was also performed for baseline features.

Results: Four randomized controlled trials with four hundred and thirty five patients and for observational studies with two hundred fifty-seven thousand and five hundred forty-five patients were included. Three vessels revascularization was performed in 54.0% (23.0–78.3) of patients, and acute renal failure was significantly reduced by PCI when compared to CABG with an Odds Ratio (OR) of (0.76 [0.58–0.99] I2 99%): this result was mainly driven by data derived from observational studies adjusted with multivariable analysis (OR of 0.67 ([0.65–0.68] I2 0%), while it did not reach significance for RCTs only (OR of 0.83 [0.42–1.61] I2 99%). At meta regression analysis, the benefit of PCI in reducing renal failure compared to CABG was significantly increased in patients with diabetes mellitus (B –0.01; [–0.02; –0.01], p=0.01) and with congestive heart failure (B –0.09 [–0.16; –0.03]; p=0.01).

Conclusion: Risk of acute renal failure is significantly reduced by PCI when compared to CABG: this benefit, although derived mainly from observational studies, is significantly increased in patients with diabetes mellitus and congestive heart failure.

P5379 | BEDSIDE

Routine SYNTAX scoring correctly identifies suitability for PCI in high-risk surgical patients

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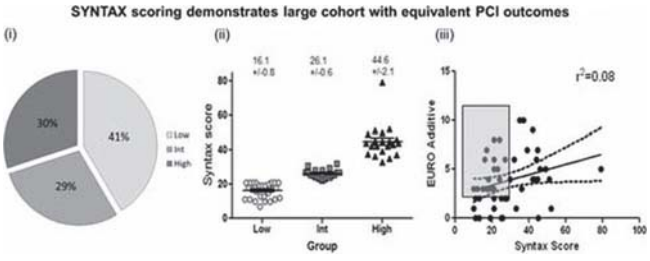
Introduction - European guidelines recommend SYNTAX scoring to direct optimal revascularisation strategies in non-diabetics with multi-vessel disease. Data suggest equivalent outcomes between CABG and PCI in low and intermediate risk tertiles. However, the impact of increased SYNTAX scoring upon rates of referral for surgical revascularisation in clinical practice in these groups remains unclear

Methods: A prospectively collected database of 3896 patients at a single UK tertiary centre was interrogated for referrals for CABG, between Jan and Dec 2013. To ensure equivalence, diabetics and those undergoing concomitant valve surgery or other procedures were excluded. All others were SYNTAX scored and demographic data acquired.

Results: A total of 189 patients were referred for surgery. 83% were male, mean age was 65.3±1.0 yrs, 37% were smokers, 24% diabetic and 60% hypertensive. 71% presented with an acute coronary syndrome. After exclusions, 81 patients remained and underwent SYNTAX scoring. Of these, 41% were found to be in the low tertile, 29% were in the intermediate and 30% were in the high tertile (i) and (ii). When plotted against additive EUROscore, it was possible to identify patients with favourable anatomy for PCI with a high predicted surgical jeopardy (iii).



Conclusions: Routine use of SYNTAX scoring suggests a high percentage of in-

dividuals with multi-vessel coronary disease referred for surgery are in low or intermediate tertiles and would have equivalent outcomes with PCI. SYNTAX scoring allows for more nuanced decision making regarding options for coronary revascularisation and increases patient choice. In particular, when combined with EUROscore, it identifies patients with high surgical risk and favourable anatomy for PCI.

P5380 | BEDSIDE

Impact of albuminuria on contrast-induced acute kidney injury and in-hospital adverse cardiac events in patients who underwent emergency coronary intervention

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Purpose: The aim of this study was to evaluate the predictive value of albuminuria for risk of contrast-induced acute kidney injury (CI-AKI) and in-hospital adverse events (AE) in patients with ACS who underwent emergency PCI.
Methods: A total of 215 consecutive ACS patients undergoing emergency PCI were enrolled. Urinary albumin to creatinin ratio (ACR; mg/gCr) was measured and patients were divided into three groups as follows; normoalbuminuria (ACR <30 mg/gCr, 126 patients), microalbuminuria (30≤ ACR <300mg/gCr, 72 patients) and macroalbuminuria (300≤ ACR mg/gCR, 17 patients).CI-AKI was defined as a greater than 25% increase in creatinine from the baseline or an absolute increase of ≥0.5mg/dl within 72h after the procedure. In-hospital AE was defined as the composite of cardiovascular death, pulmonary edema, unplanned PCI or CABG, fatal arrhythmias.
Results: Incidence of CI-AKI (p<0.0001) and in-hospital AE (p=0.001) were gradually increased among three groups (Figure).Length of stay in ICU was significantly longer in macroalbuminuria group than the other group (p=0.008). Multivariate logistic regression analysis, adjusting for potential confounding factors, resulted in an odds ratio (OR) for CI-AKI in macroalbuminuria group was 6.58 (95% CI, 1.364–31.736; p=0.019) and 3.96 (95% CI 1.457–10.774, p=0.007) in microalbuminuria group when compared with normoalbuminuria group. OR for in-hospital AE in macroalbuminuria group was 5.80 (95% CI 1.347–24.936; p=0.018) and 3.59 in microalbuminuria group (95% CI 1.674–7.697, p=0.001) when compared with normoalbuminuria group.
Conclusions: The elevated urinary albumin excretion rate is an independent predictor of CI-AKI and in-hospital AE in patients with ACS and graded increase in the incidence across microalbuminuria to macroalbuminuria were observed.

P5381 | BEDSIDE

Impact of lipoprotein(a) on long-term major cardiovascular events in patients with chronic kidney disease after percutaneous coronary intervention

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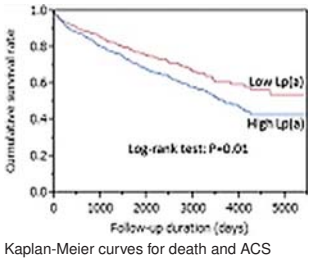
Background: Chronic kidney disease (CKD) is associated with a tremendously increased risk for cardiovascular disease. Traditional risk factors for cardiovascular disease show diminished predictive power in these patients compared with non CKD patients. Serum levels of lipoprotein (a) [Lp(a)] can be risk factors for adverse events. However, the clinical implications of Lp(a) in patients with CKD who underwent percutaneous coronary intervention (PCI) remains uncertain.
Objectives: We ained to determine the role of Lp(a) in patients with CKD who underwent PCI.
Methods: A total of 3,508 patients were treated by first PCI between 1997 and 2011 at our institution. Of these patients, 1,079 patients with CKD were analyzed. Patients were divided into median groups according to individual log Lp(a) [high Lp(a) (n=529) vs low Lp(a) (n=550)]. The primary outcome was a composite of all-cause death and acute coronary syndrome (ACS).
Results: Baseline characteristics of two groups were similar. The median follow-up period was 4.7 years. Cumulative event-free survival was significantly worse for the group with high Lp(a) than with low Lp(a) group (P=0.01). Multivariable analysis selected a log Lp(a) level as an independent predictor of primary outcomes (hazard ratio, 1.25; 95% CI, 1.01–1.55; P=0.04).



Kaplan-Meier curves for death and ACS

Conclusions: A high Lp(a) value could be associated with a poor prognosis after PCI for patients with CKD.

P5382 | BEDSIDE

The validation of CHA2DS2-VASc-CKD2 score for risk stratification in patients with coronary heart disease undergoing PCI without known atrial fibrillation

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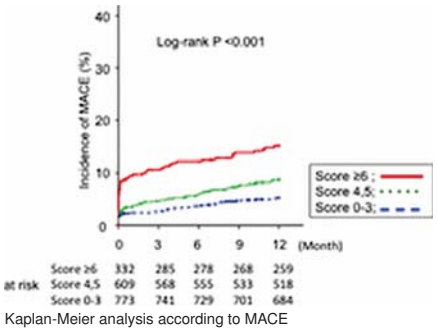
Introduction: Few simple risk stratification schemes assessing adverse events in patients with coronary heart disease (CHD) has been studied. CHA2DS2-VASc score is simple system to add each component if it was present, and its validation for patients in CHD has not been evaluated. Kidney function associates with adverse events, however, it doesn't include CHA2DS2-VASc score.
Purpose: In this study, we proposed CHA2DS2-VASc-CKD2 score and evaluated its clinical validation to predict clinical outcome in CHD without AF.
Methods: Of 1,923 consecutive patients with CHD from SHINANO registry, 1,714 patients without AF were evaluated (age 70±11 years, 394 women). CHA2DS2-VASc-CKD2 was calculated by CHA2DS2-VASc score added 2 in patients with estimated glomerular filtration rate (eGFR) <30 ml/min/1.73m^2, or 1 in patients with eGFR 30 to 59 ml/min/1.73m^2. The primary endpoint was MACE including cardiac death, myocardial infarction, stroke, and hemorrhagic events at 1-year.
Results: The mean CHA2DS2-VASc score 3.4±1.5. One-year follow-up was completed in 1,632 patients (95.2%). Cumulative incidence of MACE was 139 cases. Figure 1 indicated higher CHA2DS2-VASc score associated with higher incidence of MACE (P<0.001).
The incidence of MACE was significantly associated with CHA2DS2-VASc-CKD2 score (hazard ratio 1.25, 95% confidence interval 1.13–1.38, p<0.001).



Kaplan-Meier analysis according to MACE

Conclusions: The CHA2DS2-VASc-CKD2 score could predict future adverse events in CHD without known AF.

P5383 | BEDSIDE

Genetic variation in ADAMTS7 is associated with severity of coronary artery disease

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Purpose: Genome-wide association studies have identified ADAMTS7 as a risk locus for coronary artery disease (CAD) and myocardial infarction (MI). Functional studies suggest ADAMTS7 may promote cellular processes in atherosclerosis. We studied if risk variant carriers exhibit a greater burden of angiographic CAD.
Methods: We genotyped ADAMTS7 in the Southampton Atherosclerosis Study (SAS, n=1359), and replicated in the Emory Genebank (Emory GB, n=2684). Angiographic CAD was phenotyped in both cohorts, as presence of >50% stenosis in any epicardial vessel and semi-quantitative scores including the Gensini Score (GS), Sullivan Extent Score (SES) and the Duke Severity Index (DSI).
Results: We confirmed an association between ADAMTS7 genotype and presence of CAD under an additive genotype model in SAS (p=0.05) and Emory GB (p=0.017), but found no association with MI in the presence of CAD. ADAMTS genotypes were associated with all of the angiographic severity scores in SAS (GS p=0.017, SES p=0.045, DSI p=0.029), and independently replicated in

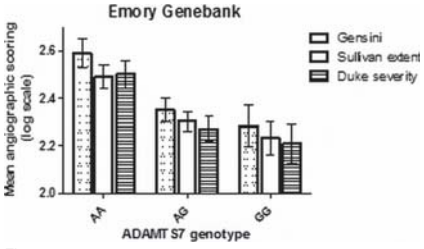

Figure 1

Emory GB (GS p<0.001, SES p<0.001, DSI p=0.001). Meta-analysis demonstrated that homozygous carriers of the risk allele had greater odds of multi-vessel disease [OR 1.36 (95% CI 1.13–1.63)] and proximal stenoses [OR 1.41 (95% CI 1.15–1.72)], compared to non-risk allele carriers. Additionally, the risk genotype was associated with greater fibrous cap thickness (p=0.013) and % area of α-actin (smooth muscle cell marker) in the intima (p=0.029), following ex-vivo immunohistochemical analysis of human coronary atherosclerotic plaque (n=48).
Conclusions: The ADAMTS7 risk variant is associated with multiple angiographic measures of CAD burden and plaque remodeling, further supporting the role of this protease in promoting atherosclerosis.

P5384 | BEDSIDE
Background characteristics, treatment and long-term prognosis in patients with significant coronary artery stenosis classified as type 1 or type 2 myocardial infarction. Data from SWEDEHEART registry

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Aim: To assess differences in incidence, demographic and clinical characteristics, treatment and long-term prognosis between patients with type 1 and type 2 myocardial infarction (MI) and significant coronary artery disease.
Methods and results: A total of 59.394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies registry and followed until 2014 (mean follow-up 1.9 y). The vast majority of cases were classified as type 1 MI (n=53.342; 89.8%) while 6.9% (n=4.083) as type 2 MI. Coronary angiography was performed in 43.721 patients and the presence of significant CAD was confirmed in 92.8% (n=37.589) of patients with type 1 MI and 52.8% (n=695) with type 2 MI.
As compared to type 1 MI patients with significant CAD, type 2 MI patients were older (71.8±10.5 vs. 68.9±11.5y), had higher proportion of hypertension (78.4 vs. 65.0%), diabetes (31.4 vs. 23.7%), previous MI (40.5 vs. 24.8%) and coronary interventions (36.0 vs. 22.0%), history of cardiac (16.4 vs. 7.5%) and renal failure (32.6 vs. 20.1%; p<0.001 for all). Type 2 MI patients developed smaller extent of myocardial damage (max troponin T 972±1860 vs. 1774±3077ng/L) and less frequently received cardioprotective treatment (betablockers 85.5 vs. 89.9%; statins 84.6 vs. 93.7%; aspirin 85.6 vs. 95.1%, other antiplatelets 70.2 vs. 89.3%; p<0.001 for all) as compared to type 1 MI patients. Tachycardia (10.1 vs. 1,3%), acute anemia/bleeding (3.6 vs. 0.6%) or infection (5.0 vs. 1.7%; p<0.001 for all) could be more often identified in type 2 MI group as compared to type 1.
The patients with significant CAD and type 2 MI diagnosis showed significantly higher crude long-term mortality as compared with type 1 MI patients (HR 1.71, 95% CI 1.45–2.03). However, after adjustment for age, sex, co-morbidities, treatments, triggers and troponins, the long-term mortality risk was lower in type 2 MI group (HR 0.71, 95% CI 0.56–0.88).
Conclusions: The majority of patients with type 1 MI and half of the patients with type 2 MI, who underwent invasive management showed presence of significant coronary artery disease. Among them, type 2 MI patients as compared with type 1 MI patients, were characterized by having more risk factors, co-morbidities and triggering mechanisms; and receiving less cardioprotective treatments. Despite having higher crude long-term mortality, patients with type 2 MI showed an approximately 30% lower adjusted long-term mortality risk compared to type 1 MI patients.

P5385 | BEDSIDE
Copeptin, a marker of vasopressin, predicts coronary artery disease, cardiovascular and total mortality

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Background: We recently showed in a middle-aged population that the stable vasopressin marker plasma copeptin (copeptin) predicts development of diabetes mellitus. Furthermore, copeptin significantly interacted with diabetes on cardiovascular morbidity and mortality. Thus, in middle age copeptin specifically predicted diabetic heart disease and death.
Purpose: Here, we tested if copeptin predicts a risk of coronary artery disease (CAD), cardiovascular mortality and death in an older population.
Methods: Between the years of 2002–2006, we examined and measured fasting plasma copeptin in 5386 participants of a population-based longitudinal study (mean age 69.4±6.2 years, 69.8% males) and related copeptin to risk of CAD (first myocardial infarction or coronary revascularization), cardiovascular and total mortality during a mean follow-up time of 6.5 years using multivariate adjusted (age, gender, systolic blood pressure, antihypertensive therapy, smoking, diabetes, LDL and HDL cholesterol) Cox proportional hazards models.
Results: Among subjects free from CAD at baseline, the multivariate adjusted hazard ratio (HR) (95% confidence interval) per 1 standard deviation (SD) increment of log-transformed copeptin for risk of CAD development was 1.20 (1.08–1.33) (P=0.001). There was a borderline significant interaction between diabetes and copeptin on CAD risk (P=0.08) with higher copeptin associated risk in subjects with diabetes [1.49 (1.14–1.95); P=0.004] than in non-diabetic subjects [1.15 (1.02–1.50); P=0.02]. Moreover, each SD increment of copeptin independently predicted total mortality [1.31 (1.21–1.41); P<0.001], an effect driven by the copeptin association with cardiovascular mortality [1.36 (1.21–1.53); P<0.001]. Subjects belonging to the top versus the bottom quartile of copeptin had a more than 70% increased risk of dying from cardiovascular disease [1.75 (1.19–2.57); P=0.004].
Conclusion: In contrast to our previous findings in middle-aged subjects, copeptin predicts development of CAD both in diabetic and non-diabetic individuals in an older population free from coronary artery disease. However the predictive ability is more pronounced among diabetics. Furthermore, copeptin strongly predicts cardiovascular mortality both in diabetics and non-diabetics. If these associations are causal, pharmacological vasopressin receptor blockade, or suppression of vasopressin by increased water intake, appears as interesting candidates for primary prevention of CAD.

P5386 | BEDSIDE
Proprotein convertase subtilisin-kexin type 9 as a biomarker for the development and severity of coronary artery disease in general population

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Objectives: To evaluate the relation of circulating proprotein convertase subtilisin-kexin type 9 (PCSK9) levels to the development and severity of coronary artery disease (CAD).
Methods: A total of 1031 consecutive individuals (552 CAD and 479 controls) were prospectively enrolled with angiography and lipid-lowering-therapy being parts of the screening process. The associations of plasma PCSK9 levels with the incidence and severity of CAD were investigated. Further, a mediator analysis was performed to detect the potential mechanisms underlying the associations.
Results: No difference in PCSK9 levels between CAD cases/controls status was detected. Considering many variables differed between cases/controls might mask the truth, we further investigated it when adjusting for confounding factors. Significantly, after adjustment these factors, patients with CAD presented a higher PCSK9 level than the controls (all p<0.05), and the PCSK9 levels positively associated with CAD severity (all p for trend <0.05). Moreover, logistic regression analysis showed positive associations of PCSK9 levels with CAD. Importantly, mediator analysis indicated that the effect of PCSK9 levels on CAD was mediated significantly by increased lipid (around 20%) and severe inflammation (around 15%).
Conclusions: PCSK9 levels associated positively with CAD susceptibility, the relative important mechanisms including lipid and inflammation pathway involved partly in this association.

CORONARY ARTERY DISEASE AND COMORBIDITIES VI

P5387 | BEDSIDE
A clinical conundrum: is nitrate still safe and effective in coronary artery spasm when combined with myocardial bridge?

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Background: Coronary artery spasm (CAS) often combined with myocardial bridge (MB), as it increases the risk of CAS at the tunneled segment by damaging intima and endothelium. Nitrates have been widely used as anti-ischemic drugs in CAS patients (pts), while it is not recommended in MB pts. Thus, we investigated the long-term impact of nitrate on clinical outcomes in pts with CAS and MB.
Method: A total of 729 consecutive MB pts with positive acetylcholine (Ach) provocation test were enrolled. Significant CAS was defined as >70% of narrowing by incremental intracoronary injection of 20, 50 and 100 μg into left coronary artery. Patients were divided into two groups according to the chronic nitrate

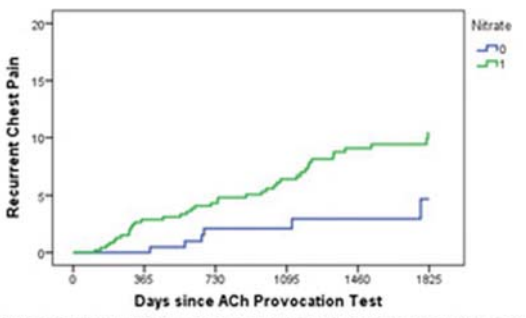

Figure 1. Cumulative incidence of recurrent ischemic chest pain requiring follow-up coronary angiography

administration (Nitrate group: n=483, No nitrate group; n=243). Patients who received any regular nitrate drug were included into the nitrate group. To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model, and clinical outcomes were compared between the two groups up to 5 years.
Results: Baseline characteristics were well-matched between the two groups following propensity score matching. There was no significant difference in mortality or major adverse cardiac & cerebrovascular events (MACCE) between the two groups. However, Nitrate group showed significant higher rate of recurrent chest pain which subsequently needed re-evaluation of coronary artery by follow-up angiography (p=0.009, Figure 1) compared with No Nitrate group.
Conclusion: Chronic Nitrate administration in myocardial bridge patients with CAS was associated with higher incidence of recurrent ischemic chest pain requiring follow up coronary angiography.

P5388 | BEDSIDE
Thyroid function and proprotein convertase subtilisin/kexin type 9 levels in euthyroid subjects with coronary artery disease

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Objectives: Both thyroid hormone and proprotein convertase subtilisin/kexin type 9 (PCSK9) are key regulators of lipid metabolism. Their respective impacts on dylipidemia and associated coronary artery disease (CAD) development have been receiving continued interest. We sought to examine whether plasma PCSK9 correlates with thyroid hormones in euthyroid subjects with stable CAD.
Methods: A total of 447 euthyroid subjects with stable CAD were prospectively enrolled with angiography and lipid-lowering-therapy being parts of the screening process. Baseline clinical characteristics were collected. Fasting free triiodothyronine (FT3), free thyroxine (FT4), thyrotropin (TSH), glucose, and lipid profile were measured. Plasma PCSK9 levels were determined by ELISA.
Results: Plasma PCSK9 levels exhibited an inverse correlation with FT3 ($r=-0.182$, $p<0.001$) and a positive correlation with TSH ($r=-0.100$, $p=0.035$). After adjustment for cardiometabolic risk factors, patients with higher PCSK9 differed from that with lower PCSK9 in FT3, FT4, and TSH levels ($p<0.05$, all). When Logistic analysis was performed with PCSK9 tertiles as the dependent variable, FT3 (OR=0.430, 95% CI: 0.206–0.897), FT4 (OR=0.863, 95% CI: 0.708–0.995) and TSH (OR=2.114, 95% CI: 1.003–4.457) exhibited independent associations with an elevated PCSK9 level (tertile 3). Finally, multiple linear analysis revealed that PCSK9 levels related significantly and independently only to FT3 ($\beta= -0.110$, $p=0.019$) but not FT4 ($\beta= -0.073$, $p=0.110$) and TSH ($\beta= -0.087$, $p=0.060$).
Conclusions: We showed a negative association between thyroid function and PCSK9 levels in euthyroid subjects with stable CAD, suggesting a potential interaction between PCSK9 and lower levels of thyroid hormones in patients with CAD.

P5389 | BEDSIDE
Impact of uric acid and cystatin c on long-term clinical outcomes in patients undergoing percutaneous coronary intervention with drug-eluting stents

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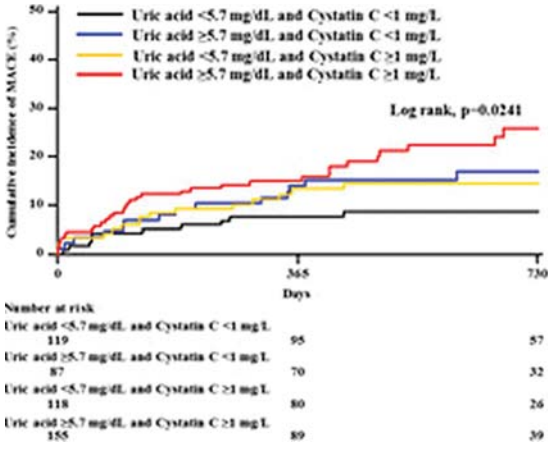
Background: Cystatin C is a surrogate marker for estimate glomerular renal function and an independent predictor of mortality and cardiovascular disease. Hyperuricemia is associated with poor outcome in patients with cardiovascular disease. The aim of this study was to evaluate the incremental effect of uric acid and cystatin C on long-term clinical outcomes among patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DES).
Methods: A total of 1,463 patients undergoing PCI with DES were consecutively enrolled from January 2009 to December 2013. Among 1,463 patients, both of uric acid and cystatin C was available in 480 patients. We divided into four groups based on the median value of uric acid and cystatin C. A major adverse cardiovascular event (MACE) was defined as a composite of death, non-fatal myocardial infarction, stroke, and revascularization. We compared MACE according to uric acid and cystatin C level.
Results: During 2-year follow-up, MACE developed 72 (15.0%). In multivariate analysis, high uric acid and cystatin C was an independent predictor for 2-year MACE (adjusted hazard ratio 2.559, 95% confidence interval 1.227–5.338, p=0.012).
Conclusions: Combining of high uric acid and cystatin C was associated with increased long-term adverse clinical outcomes in patients undergoing PCI in DES era.



P5390 | BEDSIDE
Do patients with acute coronary syndromes without conventional risk factors have a better prognosis?

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Introduction: The great majority of patients (pts) with acute coronary syndromes (ACS) have at least 1 conventional cardiovascular risk factor (CCRF). The relationship between each one of these factors and atherosclerosis is well established but less is known about pts without any of these. The aims of this study were to establish the profile of the pt with ACS without conventional cardiovascular risk factors (WOCCRF) and compare its prognosis to the pt with at least 1 conventional cardiovascular risk factor (WCCRF).
Methods: We retrospectively analyzed the registries of ACS's included in the National Registry of ACS's, between October of 2010 and October 2014. We compared pts WOCCRF to pts WCCRF (hypertension, dyslipidemia, diabetes, active smoking or family history of heart disease) regarding demographic data, previous history, admission data, coronary angiography results, treatment and complications during hospitalization. We performed multivariate analysis to evaluate the impact of having at least 1 CCRF on cardiovascular adverse events. We also compared the mortality and readmission for cardiovascular disease at one year follow-up between the two groups.
Results: A total of 10756 ACS's were considered, 332 (3.1%) WOCCRF. The pts were mostly males (72.3%) with a mean age of 67±15 years, similar to the ones WCCRF. Previous dementia and neoplasia were more frequent in the group WOCCRF (3.8% vs 1.8%; p=0.011 and 6.1% vs 4.4%; p=0.155 respectively) unlike cardiovascular diseases, heart failure (HF), renal failure and pulmonary diseases. Pts WOCCRF most commonly presented ST-segment elevation myocardial infarction (STEMI) (47.3% vs 40.6%; p=0.014) compared to pts WCCRF who more frequently presented non-STEMI (48.1% vs 44.3%; p=0.175). There were no differences regarding the symptoms being chest pain the main complaint (90.7% average). 2–3 vessel disease was less common in pts WOCCRF (33.6% vs 51.1%; $p<0.001$). The groups were similar regarding total ischemic time, infarct location, percentage of reperfusion therapy and complications during hospitalization, including in-hospital mortality (IHM), HF or re-infarction (rMI). In multivariate analysis having at least 1 CCRF was neither an independent predictor of IHM nor the composite endpoint of IHM, HF or rMI. At one year follow-up, cox regressions for cardiovascular death and hospital readmission showed similar results between groups.
Discussion and conclusions: In this analysis the absence of CCRF was not a protective factor as these pts didn't have a better in-hospital or one year follow-up prognosis compared to those WCCRF.

P5391 | BEDSIDE
Impact of anemia at admission in a one year prognostic of patients with acute coronary syndromes

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Background and introduction: There is a continuous search for prognostic markers to identify patients with acute coronary syndrome (ACS) who are at high risk for adverse events. Anemia has been reported in 15–30% of patients with acute coronary syndrome. It is known that anemia is associated with increased risk of mortality and has the potential to worsen myocardial ischemia. However, data relating anemia at admission to clinical long term outcomes in ACS remain limited.
Purpose: We sought to evaluate the impact of the presence of anemia at admission of patients with ACS for a follow up of one year.
Methods: A total number of 10 107 patients included in the national registry of ACS, from 1st of October 2010 and until 30th October 2014, with complete information and data about the haemoglobin value at admission were divided in two groups: Group A – patients with anemia ($Hb<12$ g/dL in women and $Hb<13$ g/dL in man) and Group B – patients without anemia. The one year survival and readmission rate regarding cardiovascular events was evaluated.
Results: We compared the Group A (n=908) with Group B (n=2721) after discharge for hospital readmissions and mortality through one year. Although more hospital readmissions were registered in the Group B (290 vs. 168, $p<0,001$)

for cardiovascular reasons, cardiovascular mortality was higher in Group A (139 events vs 121 events, p<0,001). Analysing the correlation between anemia at admission and mortality using proportional hazards regression we found that the presence of anemia at admission is associated to a 1,72% (HR 1,72; 95% CI 1.12 to 2,64, P<0.05) increase in mortality. On the other hand, no linear correlation was found between the presence of anemia and hospital admissions in a one year period (HR 1,23; 95% CI 0,91 to 1,67, P>0.05).
Conclusion: The presence of anemia at admission is a predictor of cardiovascular events and mortality in patients across the spectrum of ACS.

P5392 | BEDSIDE
Predictive value of routine cardiovascular screening for myocardial ischemia in kidney transplantation candidates: a single center prospective study (MONICARD study group)

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Cardiovascular disease is the first cause of death in end stage renal disease (ESRD) patients. The presence of significant coronary artery disease in kidney transplantation candidates (KTC) is predictive of major adverse cardiac events (MACE). Our study investigated the predictive value of a systematic cardiovascular workup in KTC, with the objectives 1) to assess long term cardiovascular mortality and morbidity, 2) to identify baseline characteristics associated with cardiovascular outcomes and 3) to test the incremental predictive value of different tests included in our routine risk assessment.
KTC referred to our cardiology outpatient clinic for routine cardiovascular risk evaluation were prospectively enrolled. Patients were classified using the following risk assessment method.
1. Practice Guidelines Assessment (PGL)+ if they had one of the following: age >50, diabetes, cardiac symptom, known cardiac disease, resting ECG abnormalities. 2. Independently of their PGL status, they were Clinical Evaluation (CE)+ if they had one of the following: cardiac symptom, cardiac disease, physical examination abnormality, ECG abnormality. 3. On top of CE, they were re-categorized Integrative Doppler Assessment (IDA)+ if they had at least one abnormality on resting echocardiography or echo-Doppler evidence of peripheral arterial disease. 4. On top of IDA they were re-categorized Integrative stress Assessment (ISA)+ if they had a positive myocardial stress test. We recorded all-cause mortality, cardiovascular mortality, and non-fatal MACE.
188 patients were enrolled in the study between July 2010 and March 2013. Etiologies of ESRD were diabetes, hypertension and polycystic kidney disease for 50% of patients. 144 (79%) patients were PGL+, and 92 (49%) were CE+. Among 96 CE- patients 52 (54%) were IDA+ raising the number of abnormal screening status to 144 patients. Adding myocardial stress test didn't reclassify any IDA- patients to ISA+. During a median follow-up of 2.2 years we recorded 6 death (3.2%), 5 NSTEMI, 4 strokes and 5 new onset of heart failure. PGL+ and CE+ status were not significantly associated with these outcomes (χ^2; p=0.6 and p=0.2). IDA+ and ISA+ status were significantly associated with these outcomes (χ^2; p=0.05 and p=0.05) but ISA added no significant prediction value to IDA.
In our high risk ESRD population normal clinical cardiovascular routine evaluation with normal echocardiography and normal peripheral arterial echo-Doppler had an excellent negative predictive value for future death or MACE. Routine myocardial stress tests added no significant prognostic value regarding death or MACE.

P5393 | BEDSIDE
Major bleeding in acute myocardial infarction: population characterization, predictors and impact in prognosis

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Introduction: The presence of major bleeding (MB) is a feared complication in patients (P) with Acute Myocardial Infarction (AMI) and may have impact in the therapeutic strategy and prognosis of these P.
Purpose: To characterize the population of P with AMI and MB (defined by Gusto criteria) and assess their impact on therapeutic approach and in-hospital complications and mortality. We evaluate possible predictors of the onset of MB.
Methods: We studied 9513 D with AMI included in a multicenter national register. We considered two groups: P with MB and P without MB. We registered age, sex, co-morbidities, in-hospital therapy, results of coronary angiography, angioplasty performed and ejection fraction (EF). The following in-hospital complications were defined: heart failure (HF), cardiogenic shock, stroke, use of mechanical ventilation and need of blood transfusion. We compared the in-hospital mortality and multivariate analysis was performed to identify the predictors of MB predictors.
Results: Major bleeding was found in 1,5% of P with AMI (141 P). These P were older (72±12 vs 66±14 years, p<0,001), had higher prevalence of females (37,6 vs 27,6%, p=0,009), hypertension (81,9 vs 68,5%, p<0,001), previous HF (12,1 vs 5,5%, p<0,001), chronic renal failure (11,5% vs 5,9%; p=0,005) and previous bleeding history (9,4% vs. 1,6% p<0,001). At admission, P with MB received less therapy with aspirin (95,0% vs 98,4%, p=0,01), more therapy with glycoprotein IIb/IIIa inhibitors (28,8% vs. 21,5%, p=0,039) and unfractionated heparin (37,9% vs. 29,0%, p=0,022). Patients with MB received the same rate of coronary angiographies and angioplasties, but were more often submitted to more than one coronary angiography (13,8% vs. 7,1%, p=0.006), more coronary angiography performed by femoral artery (45,2% vs. 27,5%, p<0,001) and showed more multivessel disease (63,6% vs 50,4%, p=0,006). MB was associated with lower EF (EF<50%: 46,2% vs 36,8%, p=0,029), greater need of invasive mechanical ventilation (5,7% vs 1,3%, p=0,001) and blood transfusions (41,8% vs. 1,4%, p<0,001), but with no differences in the other complications. In-hospital mortality was higher in P with MB (12,1% vs. 3,2%, p<0,001). By multivariate analysis, were identified as predictors of MB: age, previous history of bleeding, therapy with glycoprotein IIb/IIIa inhibitors and heparin.
Conclusions: The presence of MB is present in 1,5% of P with AMI and is associated with an increased in-hospital mortality. There were identified as MB predictors: age, previous history of bleeding and therapy with glycoprotein IIb/IIIa inhibitors and unfractionated heparin.

P5394 | BEDSIDE
Impact of Triglyceride Levels on cardiovascular event in T-SPARCLE registry in Taiwan

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Background: The association between fasting triglyceride (TG) and the occurrence of major adverse cardiovascular event (MACE) remains elusive. The objectives of the present study were to analyze the magnitude of the association between TG and MACE in the Taiwanese Secondary Prevention for Patients with AtheRosCLErotic Disease (T- SPARCLE) registry.
Methods and results: Two-year follow-up data from a nationwide cohort study of 3434 patients with atherosclerotic cardiovascular disease (aged 65.6 years, 68.6% men) were used to identify risk factors for the occurrence of MACE, defined as cardiovascular death, nonfatal myocardial infarction (MI), and non-fatal stroke. Seventy cases of MACE occurred during the follow up. The Cox proportional hazard model was applied to detect the independent risk factors for MACE. Adjustment was made for variables including age, sex, history of stroke, heart failure, MI/coronary artery disease, hypertension, diabetes, lipid-lowering agents except statin, and statin. Compared with TG <150mg/dL, multivariate-adjusted HRs for MACE ranged from 1.42 (95% confidence interval (CI): 0.75–2.67) for TG of 150–199 mg/dL, 1.49 (95% CI: 0.62–3.60) for TG of 200–249 mg/dL, to 2.50 (95% CI: 1.17–5.37) for TG ≥250 mg/dL.
Conclusions: By using the 2-year follow-up data of T- SPARCLE registry, we provide evidence that TG is an independent risk factor for MACE in subjects with higher TG levels (≥250 mg/dL).

Abstract P5394 – Table 1. Hazard Ratios for MACE

	Crude	Model 1	Model 2	Model 3	Model 4	Model 5
<150 mg/dL	Reference	Reference	Reference	Reference	Reference	Reference
150–200 mg/dL	1.48 (0.79–2.77)	1.49 (0.79–2.80)	1.43 (0.76–2.69)	1.42 (0.75–2.67)	1.42 (0.75–2.67)	1.42 (0.75–2.67)
201–250 mg/dL	1.53 (0.0.64–3.63)	1.60 (0.67–3.81)	1.47 (0.62–3.52)	1.48 (0.62–3.57)	1.48 (0.62–3.57)	1.49 (0.62–3.60)
>250 mg/dL	2.84* (1.40–5.77)	2.57* (1.26–5.24)	2.54# (1.24–5.19)	2.49# (1.16–5.33)	2.49# (1.16–5.33)	2.50# (1.17–5.37)

*p<0.001; #p<0.05. Hazard ratio (95% confidence interval). Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, history of stroke, HF and MI/CAD; Model 3: adjusted for age, sex, history of stroke, HF, MI/CAD, HTN and DM; Model 4: adjusted for age, sex, history of stroke, HF, MI/CAD, HTN, DM, statin and other lipid lowering agents (except statin); Model 5: adjusted for age, sex, history of stroke, HF, MI/CAD, HTN, DM, statin, other lipid lowering agents (except statin) and LDL-C.

P5395 | BEDSIDE

Impact of new-onset dyslipidemia on coronary artery spasm as assessed by acetylcholine provocation test

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Background: Dyslipidemia is known to be a risk factor of coronary artery disease (CAD) and endothelial dysfunction. However, there are limited data regarding the impact of new-onset dyslipidemia (NODL) on significant coronary artery spasm (CAS) in real world clinical practice.
Methods: A total of 4,520 consecutive patients (pts) without the history of dyslipidemia and statin medication and the coronary fixed lesion of less than 50% underwent acetylcholine (Ach) provocation test were enrolled. Significant CAS was defined as >70% of narrowing by incremental intracoronary injection of 20, 50 and 100 μg into left coronary artery. New onset dyslipidemia (NODL) was defined as newly recognized dyslipidemia on admission lipid profile in pts who denied history of dyslipidemia or statin administration history. Pts were divided into two groups based on the presence of NODL: the NODL group (n=478), the control group (n=4,042). To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model.
Results: After PSM analysis, 2 propensity-matched groups (476 pairs, n=952, C-statistic=0.651) were generated and the baseline characteristics of the two groups were balanced. NODL group showed higher incidence of (+) Ach provocation test results and higher incidence of ischemic chest pain during the Ach provocation test (Table). Presence of NODL was an independent predictor of Ach-induced CAS (62.1% vs. 52.9%, p=0.004; hazard ratio = 1.461, 95% CI [1.128 - 1.892]).

Table. Angiographic and clinical characteristics during Acetylcholine Provocation Test

	Post PSM			
Varia bles, N (%)	NODL (n=476)	Control (n=476)	p Value	HR [95% C.I]
Coronary artery spasm (Visible narrowing >70%)	296 (62.1)	252 (52.9)	0.004	1.461 [1.128 - 1.892]
EKG Change	16 (3.3)	23 (4.8)	0.252	0.685 [0.357 - 1.313]
ST-segment elevation	5 (1.0)	6 (1.2)	0.762	0.831 [0.252 - 2.743]
ST-segment depression	7 (1.4)	8 (1.6)	0.795	0.873 [0.314 - 2.427]
T-inversion	3 (0.6)	8 (1.6)	0.129	0.371 [0.097 - 1.407]
Chest pain	250 (52.5)	200 (42.0)	0.001	1.526 [1.181 - 1.971]
AV Block	118 (24.7)	134 (28.1)	0.240	0.841 [0.630 - 1.122]

Conclusions: In this study, NODL was an independent predictor of Ach-induced CAS and associated with higher incidence of ischemic chest pain during Ach provocation test, suggesting possible causal relationship between NODL and endothelial dysfunction

P5396 | BEDSIDE

Association of progression or regression of coronary artery atherosclerosis with long-term prognosis

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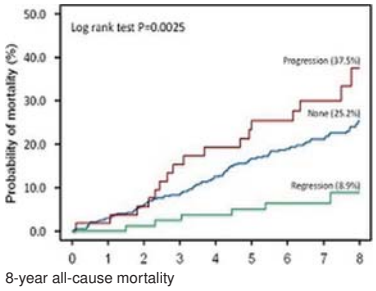
Background: The association between coronary atherosclerosis progression or regression with long-term prognosis remains poorly investigated. We assessed the association of atherosclerosis progression or regression with long-term mortality.
Methods and results: The study included patients with coronary artery disease (CAD) who underwent coronary angiography at baseline and at 2 years thereafter. Coronary segments with ≥25% and <50% diameter stenosis at baseline were included into the analysis. Atherosclerosis progression or regression was defined as a change in minimal lumen diameter (MLD) of non-treated segments of 0.2 mm and –0.2 mm, respectively. The primary outcome was all-cause mortality. Quantitative coronary angiographic evaluation was performed in 6259 coronary segments. Of them, 1790 non-stented segments with ≥25% diameter stenosis at baseline angiogram and 806 stented segments were analyzed. Based on the change in MLD between baseline and 2-year angiography, patients were divided into 3 groups:progression (8.8%); regression (13.2%); no progression or regression of atherosclerosis (78.0%). There were 126 deaths over 8-year follow-up: 17 deaths among patients with progression, 6 deaths among patients with regression and 103 deaths occurred among patients with no progression/regression (Kaplan-Meier estimates of 8-year mortality, 37.5%, 8.9% and 25.2%, respectively; adjusted hazard ratio=1.16, 95% confidence interval 1.05 to 1.29, P=0.004 for 0.1 mm reduction in MLD).
Conclusions: In patients with CAD regression or progression of atherosclerosis in non-treated coronary segments with mild atherosclerosis was significantly associated with 8-year mortality. Atherosclerosis regression may be used as an intermediate end point in anti-atherosclerotic interventional studies.



8-year all-cause mortality

CORONARY ARTERY DISEASE AND COMORBIDITIES VII

P5397 | BEDSIDE

Prognostic value of automatically measured ST-segment deviation in patients undergoing exercise ECG

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Background: Conventional exercise ECG is done frequently in evaluation of patients with suspected stress induced myocardial ischemia, due to its wide availability. Therefore it is an interesting tool to not only gain diagnostic, but also prognostic information. We wanted to evaluate whether an automatically measured, easy to use single value could provide this information.
Methods: 813 consecutive patients referred to exercise stress myocardial perfusion imaging were recruited. Prognostic endpoints (death, myocardial infarction, revascularization) were determined by 2 year follow up. To find the best prognostic values we included ST-deviations for all 12 leads, at different timepoints (baseline, maximum ST-depression, maximum workload, 2 minutes into recovery), at J-point +40ms, +60ms, and +80ms. All single values as well as delta change between timepoints were evaluated by univariate and, if significant, multivariate Cox proportional hazards analysis.
Results: Median duration of follow up was 756 days and at 720 days the combined endpoint was reached in 153 (18.8%) of patients. From all measured leads, timepoints and changes, absolute ST-depression in lead I, at the time of maximum ST-depression, provided the best prognostic value for the combined endpoint (see figure). Multivariate analysis showed the prognostic performance to be independent of other important clinical (age, sex, cardiovascular comorbidities) or test parameters (e.g. achieved heart rate or workload).

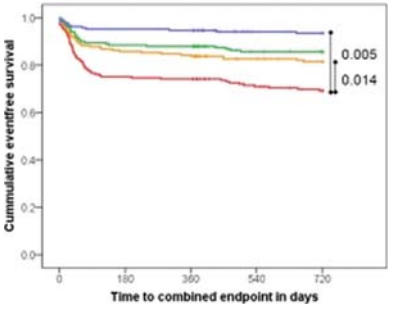

Figure 1. Kaplan-Meier curves according to quartiles of ST-depression in lead I showing ability to predict the combined endpoint; comparisons were done with log-rank test.

Conclusion: In patients referred for evaluation of suspected stress induced myocardial ischemia, an automatically measured single value exercise ECG can provide good prognostic utility. The best single value is the absolute ST-depression at J-point + 80ms in lead I at the time of maximal ST-depression.

P5398 | BEDSIDE

Premature myocardial infarction is strongly associated with increased levels of remnant cholesterol

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Background: Elevated levels of remnant cholesterol have been associated with increased cardiovascular risk. The aim of this study was to investigate the role of remnant cholesterol in premature myocardial infarction (MI).
Methods and results: We prospectively enrolled 302 patients into our multicenter case-control study comprising 102 consecutive MI survivors (≤40 years) and 200 hospital controls. MI Patients were frequency-matched for age, gender, and center. Remnant cholesterol was calculated from standard lipid parameters. Remnant cholesterol was 1.7-fold higher in premature AMI patients compared to controls (61.1±36.8 vs. 35.8±16.8 mg/dL;p<0.001). Remnant cholesterol was the lipid fraction most strongly associated with premature myocardial infarction (OR 3.94; 95% CI 2.61–5.96;p<0.001; table 1) for an increase of 1-SD. This observa-

Table 1. Logistic regression analysis assessing the association of different lipid parameters with premature myocardial infarction

	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Remnant cholesterol	3.94 (2.61–5.96)	<0.001	3.34 (2.17–5.14)	<0.001
Non-HDL cholesterol	3.01 (2.16–4.20)	<0.001	2.78 (1.95–3.95)	<0.001
Triglycerides	2.56 (1.60–4.08)	<0.001	2.09 (1.29–3.37)	0.003
Remnant/HDL cholesterol ratio	2.41 (1.75–3.31)	<0.001	1.99 (1.45–2.75)	<0.001
Total cholesterol	2.21 (1.66–2.96)	<0.001	2.14 (1.56–2.93)	<0.001
LDL/HDL cholesterol ratio	2.03 (1.54–2.68)	<0.001	1.77 (1.30–2.41)	<0.001
LDL cholesterol	1.56 (1.20–2.02)	0.001	1.62 (1.21–2.16)	0.001
Apo B_{100}	1.54 (1.18–2.02)	0.001	1.36 (1.03–1.81)	0.03
HDL cholesterol	0.63 (0.48–0.83)	0.001	0.77 (0.57–1.05)	0.09
Lp(a)	1.16 (0.89–1.50)	0.28	1.09 (0.82–1.45)	0.54
Apo A_1	0.79 (0.59–2.05)	0.12	0.92 (0.67–1.26)	0.59

Odds ratios refer to a change of 1-SD in continuous variables. Multivariate model is adjusted for age, body-mass index, hypertension, diabetes and center.

tion was independent from clinical risk factors and plasma lipid levels. This association persisted when adding triglycerides, LDL cholesterol and HDL cholesterol to the multivariate model (OR 3.37; 95% CI 2.05–5.55).
Conclusion: Remnant cholesterol is strongly associated with premature myocardial infarction, can be easily calculated and might serve as a new potent risk marker in this young patient population.

P5399 | BEDSIDE
Type 1 or type 2 myocardial infarction in patients without significant coronary artery disease - do we choose clinical type by chance? Data from the SWEDEHEART registry

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Purpose: To compare the background characteristics, triggering mechanisms, treatments and long-term prognosis in a large real-life cohort of invasively managed patients without significant stenosis diagnosed on discharge with type 2 and type 1 MI.
Methods and results: A total of 59.394 patients with MI were registered between 2011–2013 in our Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies registry and followed until 2014 (mean follow-up 1.9 years). In accordance with the universal definition of MI from 2007 patients were classified in the registry as type 1 and type 2 MI, respectively. In 43.721 patients coronary angiography was performed during hospitalization and no significant stenosis were found in 47.2% (n=621) of type 2 MI and 7.2% (n=2.912) of type 1 MI patients. Except for higher proportion of women (65.9 vs. 57.6%,p<0.001) and lower incidence of previous MI and coronary interventions (16.0 vs. 23.2% and 10.5 vs. 18.8%, respectively; p<0.001 for both) in type 2 MI group, no significant difference in prevalence of conventional risk factors as age, hypertension, diabetes, CHF nor extent of myocardial necrosis was observed between type 1 and type 2 MI patients. Triggering mechanisms such as tachycardia (8.9 vs. 1.4%), acute respiratory failure (4.7 vs. 2.3%), acute anemia/bleeding (1.6 vs. 0.4%), p<0.001 for all triggers, could be identified more often in type 2 MI as compared to type 1 MI patients. Cardioprotective and antiplatelet treatment were less frequently prescribed in type 2 AMI group (ACEI/ARB 66.6 vs. 71.5%,p=0.015; betablockers 78.1 vs. 83.1%,p=0.003; statins 69.7 vs. 90.6%,p<0.001). The long-term mortality did not differ significantly between patients without significant stenosis diagnosed with type 2 MI as compared to type 1 MI, neither the crude mortality (HR 1.14, 95% CI 0.84–1.55), nor the mortality adjusted for age, sex, co-morbidities, treatments, triggering mechanisms, troponins and treating center (HR 0.77, 95% CI 0.48–1.25).
Conclusions: Among patients without significant coronary artery stenosis, few differences in background risk factors and no difference in long-term prognosis between those classified as type 1 or type 2 MI could be found. Presence of triggering mechanisms seemed to favor type 2 MI diagnosis, although clear triggering mechanisms were lacking in the majority of cases. The classification seemed often to be done at random and leading to a probably inadequate difference in treatment between the two types of MI.

P5400 | BEDSIDE
Type 2 myocardial infarction - does the presence of stenosis matter? Data from the SWEDEHEART registry

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Purpose: To compare the background characteristic, triggering mechanisms; treatment and long-term prognosis in a large cohort of invasively managed patients with type 2 MI with and without significant coronary artery stenosis.
Methods and results: A total of 59.394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies registry and followed until 2014 (mean follow-up 1.9y). In accordance with the universal definition of MI from 2007 6.9% (n=4.083) of patients were classified as type 2 MI, out of whom 33% (n=1.357) underwent coronary angiography. In 52.8% (n=695) at least one significant coronary artery stenosis was found. Type 2 MI patients with significant stenosis were older (71.8±10.5 vs. 67.9±11.8y), more frequently men (69.2 vs. 34.1%) and smokers (63.4 vs 53.5%; p<0.001 for all) than those without significant stenosis. In comparison with type 2 MI patients without obstructive CAD, those with significant stenosis showed higher proportion of hypertension (78.4 vs. 67.6%), diabetes (31.4 vs. 14.3%), previous MI (40.5 vs. 16.0%) and coronary interventions (36.0 vs. 10.5%), history of cardiac (16.4 vs. 6.1%) and renal failure (32.6 vs. 20.9%; p<0.001 for all). Type 2 MI patients with significant stenosis developed larger myocardial necrosis (max troponin T 972±1860 vs. 400±717ng/L, p<0.001) and more frequently received cardioprotective and antiplatelet treatment (ACEI/ARB 79.6 vs. 66.6%; betablockers 85.5 vs. 78.1%; statins 84.6 vs. 69.7%; aspirin 85.6 vs. 71.8%, other antiplatelets 70.2 vs. 39.0%; p<0.001 for all) as compared to those without significant stenosis. The crude long-term mortality risk was significantly higher in type 2 MI patients with significant coronary stenosis (HR 2.56, 95% CI 1.85–3.53) and remained highly significant also after adjustment for age, sex, co-morbidities, triggers, treatments, troponin and treating center (HR 2.22, 95% CI 1.23–4.02).
Conclusions: Of the one third of the type 2 MI patients undergoing invasive coronary angiography in this real life study, almost half had no significant coronary stenosis. Patients with significant coronary artery disease were older and had more traditional risk factors. Both crude and adjusted long term mortality was more than two times higher in type 2 MI patients with significant stenosis as compared to those without significant stenosis. The results indicate that type 2 MI patients with and without significant coronary artery disease should be regarded as two separate entities.

P5401 | BEDSIDE
The epicardial adipose tissue is related with coronary spasm as well as coronary aterosclerosis in female patients presented with chest pain: from the KoRean wOmenS chest pain rEgistry (koROSE)

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Background: Epicardial adipose tissue (EAT) is a cardiometabolic risk factor by secreting several pro-atherosclerotic and pro-inflammatory adipokines and related with the coronary atherosclerosis. But the relation of EAT with coronary vasospasm (CS) has not been evaluated. This study was done to investigate the relation of EAT and CS from the KoRean wOmen'S chest pain multicenter rEgistry (koROSE) data.
Methods: 344 female patients (60.7±10.4 years) who presented with chest pain in outpatient clinic and who underwent echocardiography (ECHO) and coronary angiography were included for the study. Significant coronary artery stenosis (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing of at least one coronary artery. In remained 251 patients, provocation test was done in 128 patients (58.8±9.5 years) if they have minimal lesion in coronary artery (<30% narrowing). CS was defined as >90% narrowing induced by intracoronary acetylcholine injection. EAT thickness was measured by ECHO as ASE guideline.
Results: In whole 344 patients, mean EAT was higher in patients with CAS than patients without CAS (7.8±2.9 vs 7.0±2.7, P=0.012). Among 128 patients, CS was detected in 48 patients (14%). EAT thickness of patients with spasm was higher than that of patients without spasm (7.9±2.5 vs 6.9±2.6, P=0.04) and was similar to patients with CAS (7.9±2.5 vs 7.8±2.9, P=0.98). The incidence of dyslipidemia was higher in patients with CS than in patients without CS (29.2% vs 11.3%, P=0.016) but there was no difference in other classical cardiovascular factors (age, diabetes, hypertension, and body mass index) between two groups. In multivariate regression analysis corrected with these cardiovascular risk factors, EAT was independently related with CS (OR: 1.154, 95% CI: 1.02–1.33) as well as dyslipidemia (OR: 2.797, 95% CI: 1.06–7.38).

	Minimal stenosis (<30% narrowing) Provocation test		Moderate stenosis (30–50% narrowing) (n=123)	Significant stenosis (>50% narrowing) (n=93)
	Negative (n=80)	Positive (n=48)		
EAT thickness (mm)	6.9±2.6	7.9±2.5	6.6±2.3	7.8±2.9

Conclusion: EAT thickness was associated with the presence of coronary vasospasm as well as coronary atherosclerosis. From these findings, coronary spam may have a similar pathophysiology with coronary atherosclerosis and could be a harbinger of coronary stenosis.

P5402 | BEDSIDE
Characteristics of coronary artery ectasia in patients with ST-segment elevated myocardial infarction

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Background: The characteristics of patients with coronary artery ectasia (CAE) who suffered from ST-segment elevated myocardial infarction (STEMI) are little known. We assessed the differences in the backgrounds and prognoses between CAE and non-CAE patients with STEMI.
Methods: A total of 2364 patients with STEMI underwent primary percutaneous coronary intervention in our hospital between January 2004 and September 2014. We investigated 2305 patients excluding stent thrombosis and Kawasaki disease. CAE patients were defined as patients whose coronary artery was ectatic and inappropriate for stent implantation. We compared the differences in the backgrounds and clinical prognoses between CAE and non-CAE patients with STEMI by retrospectively assessing the coronary risk factors and angiographies from the medical records.
Results: CAE was obsereved in 15 (0.65%) of the 2305 patients. The median diameter of the culprit lesions was 4.3±1.2 mm in CAE patients and 3.0±0.6 mm in non-CAE patients ($p<0.0001$). Younger age and higher body mass index (BMI) were more related to CAE patients (55.7±13.0 years vs. 68.8±12.7 years, $p<0.0001$; 26.6±3.3 vs. 23.7±3.6, p=0.0022), while diabetes was less related (6.7% vs. 31.1%, p=0.048). Culprit lesions tended to appear in the right coronary artery of CAE patients (86.7% vs. 41.3%, p=0.0007), whereas max creatinine kinase and in-hospital mortality did not differ between CAE and non-CAE patients. One CAE patient had a past history of acute aortic dissection (AAD) on admission for STEMI and two CAE patients acquired AAD after admission for STEMI. A significant difference was observed in the incidence of AAD between CAE and non-CAE patients (20.0% vs. 3.8%, p=0.018).
Conclusion: Younger age, higher BMI, and non-diabetes characterized CAE patients who acquired STEMI. Culprit lesions tended to appear in the right coronary artery of CAE patient. CAE patients might be associated with AAD.

P5403 | BEDSIDE
Is chronic obstructive pulmonary disease a predictor of poor one-year outcome after myocardial infarction?

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Rationale: The prognosis of myocardial infarction (MI) outcomes, especially in patients with comorbidities, is one of the relevant issues of present-day medicine.
Objective: To determine predictors of one-year outcome after ST segment elevation myocardial infarction (STEMI).
Materials and methods: 529 STEMI patients admitted in 2008–2009 including 373 men (64.8%) were enrolled in the study; the mean age was 63 years. The in-hospital mortality rate was 10.9% (58 deaths). One-year outcome was assessed at discharge with the following endpoints: death, recurrent MI, stroke, decompensated congestive heart failure, repeat emergency coronary revascularization and unstable angina. Occurrence of any endpoint within one year was considered as a poor one-year outcome.
Results: In one year, the outcome was assessed in 384 (81.5%) patients (as contact was lost with 23 patients (4.9%) and information on 64 patients (13.6%) was insufficient). A poor one-year outcome was registered in 139 patients (36.2%), with 46 fatal outcomes (12%) within the year. According to the univariate logistic regression analysis, independent predictors of a poor one-year STEMI outcome included: age ($p<0.001$), male gender (p=0.0023), Killip II-IV (p=0.0001), anterior MI (p=0.0069), increased body mass index (BMI) ($p<0.001$), ejection fraction (EF) reduced to less than 40% (p=0.0001), the number of affected coronary arteries ($p<0.001$), increase in NT-proBNP levels ($p<0.001$), no percutaneous coronary interventions ($p<0.001$) as well as the history of diabetes mellitus (p=0.0362), COPD (p=0.0451) and stroke (p=0.0367). Multivariate logistic regression determined a group of predictors that significantly affected the poor one-year STEMI outcome: COPD 6.05 (95% CI 1.91–19.18, p=0.002), number of affected coronary arteries 3.14 (95% CI 1.77–5.57, $p<0.001$), NT-proBNP 1.03 (95% CI 1.02–1.04), MIT 0.87 (95% CI 0.79–0.96, p=0.008). ROC analysis confirmed the quality of the model (AUC=0.89, 95% CI 0.84–0.94, $p<0.001$).
Conclusions: Significant predictors of a poor one-year outcome are COPD, number of affected coronary arteries, NT-proBNP levels and body mass index.

P5404 | BEDSIDE
The cardiovascular disease risk factor profile in a young woman (under the age of 45) with acute coronary syndrome (ACS)

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Background: The coronary arter disease (CAD) mainly affects elderly people, but also more and more young people get sick. It is estimated that every 20th person with CAD is under the age of 45, and only 20% of them are women. The literature concerning this matter is rather limited.
The aim of this study was to determine the profile of risk factors predisposing to ACS in young women under the age of 45 years.
Methods: The study group includes 1941 women aged ≤45 years with ACS, hospitalized in Polish hospitals pursuing register PL – ACS from 2007 to 2014. The control group are young women, without CAD in history – data collected in NATPOL and WOBASZ registry (n=1170).
Results: In young women with ACS in comparison to control group significantly ($p<0,0001$) more common occurrence of hypertension (48.8% vs. 16.7%); hypercholesterolemia (36.1% vs.12.5%); obesity (22.3% vs. 15.3%); diabetes mellitus (10.6% vs.1.4%); smoking [currently] (48.7% vs. 40.0%). About 16.5% (n=320) of the women were not burdened with any of the above factors, while 12% had a family history of CAD. Woman with ACS had a higher number of risk factors in comparison to control group (1,7±1,2 vs. 1,1±1,0 $p<0,0001$). The independent predictors of risk ACS were: hypertension (OR - 4,22 [3,429–5,387][95% CI]); hypercholesterolemia (OR - 3,346 [2,605–4,299] [95% CI]); diabetes mellitus (OR - 6,657 [3,478–1,274][95% CI]); smoking (OR - 1,631 [1,340–1,987] [95% CI]) – for all $p<0,001$. There was no significance of obesity expressed by BMI (OR - 0,996 [0,975–1,017] [95% CI]).
Conclusions: Diabetes mellitus, hypertension, hypercholesterolemia and smoking increase the risk of ACS in young women, where the strongest factor is diabetes mellitus. Obesity and positive family history of CAD did not increase the risk of heart attack within tested population.

P5405 | BEDSIDE
Breast arterial calcification as an independent predictor of coronary atherosclerotic disease in a female cohort of African descent

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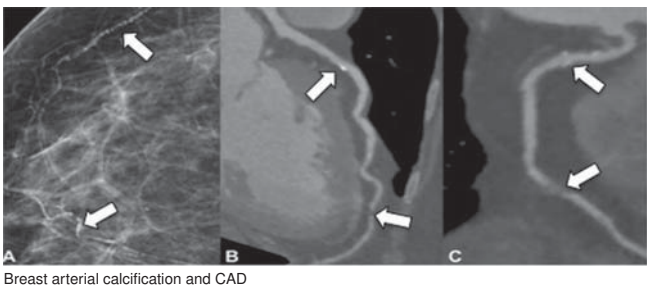
Background: Breast arterial calcification (BAC) is a common incidental finding on screening mammograms. Accumulating data on predominantly Caucasian women suggest an association between BAC and coronary artery disease (CAD). However, little is known about this association in other ethnic populations.
Purpose: We sought to comprehensively examine the correlation between BAC on digital mammography and CAD endpoints detected by cardiac computed tomography (CCT) in a female cohort of African descent.
Methods: Women with African ancestry who underwent digital screening mammography and CCT within 24 months were identified. Women with known CAD were excluded to avoid selection bias. Mammographic and CCT results were reviewed in a blinded fashion. Patient-related pertinent covariates were assessed (age, body mass index, diabetes, hyperlipidaemia, hypertension, smoking, and renal insufficiency).
Results: Two hundred women of African descent (median age 52.5 years) were eligible for inclusion. The median inter-procedural time was 8 months. BAC was present in 41 women (20.5%). Based on univariate analysis, covariates with discriminatory power were identified and adjusted for. Subsequently, multivariate regression analyses determined BAC to be significantly associated with coronary artery calcium score >100 (odds ratio [OR], 6.8; 95% confidence interval [CI], 2.4–19.5; $P<0.001$), atherosclerotic luminal narrowing (OR, 11.1; CI, 3.9–31.6; $P<0.001$), and coronary artery stenosis ≥50% (OR, 5.6; CI, 2.0–15.5; $P<0.001$) by CCT.



Breast arterial calcification and CAD

Conclusion: BAC on mammography is associated with increased probability of coronary calcification, coronary atherosclerosis, and obstructive CAD on CCT in women with African ancestry. Our data suggest that BAC is an easily assessable surrogate marker for CAD risk within this population.

P5406 | BEDSIDE

Relation between coronary arterial lesion location and major adverse cardiac events 6- months after an acute coronary syndrome

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Background: Anatomic heterogeneity in patients with coronary artery disease might expectedly lead to differences in short term outcomes. Several small follow-up studies have documented that lesion complexity is predictive of immediate results after percutaneous coronary intervention. However, it is unclear whether the coronary anatomy lesions continue to portend a worse prognosis. We sought to assess the impact of angiographic lesion location with 6-month clinical outcomes in patients presenting with acute coronary syndrome.
Methods: The data were obtained in the framework of an ongoing prospective cohort of ACS survivors consecutively recruited between August 2013 and April 2014, at the cardiology departments of two tertiary hospitals of different regions. Coronary arterial lesions location was based on the angiographic images obtained during catheterization. The extent of coronary artery disease was expressed as the presence of 1-, 2-, or 3-vessel disease ($\geq$70% luminal narrowing). We evaluated the relation between coronary arterial lesions location and the occurrence of major adverse cardiac events –MACE (defined by the composite endpoint -death, myocardial infarction or vessel revascularization) within 6-months after the index event (self-reported in a telephone interview).
Results: Among the 399 patients admitted due to ACS in the study period, 387 underwent catheterization, of whom 11.4% had significant disease of the left main coronary artery, 68.5% of the anterior descending artery, 44.1% of the circumflex artery and 50.9% of the right coronary artery. Overall, MACE were reported by 30 (7.8%) of patients, with no difference according to disease in the left main, anterior descending or circumflex artery, and a trend towards higher risk among patients with disease in the right coronary artery (9.8% vs 5.9%, p=0.156). Regarding the number of vessels with significant stenosis, 8.0% had no significant disease, 40.7% had 1-vessel, 30.8% 2-vessel and 20.5% 3-vessel disease, with a 6-month risk of MACE of 3.3%, 5.9%, 11.2% and 7.8%, p=0.32, respectively. After adjustment for differences in age and major cardiovascular risk factors, the odds ratio for MACE associated with disease of the right coronary artery was 1.82 (95% confidence interval: 0.80–4.14, p=0.15).
Conclusion: In our study, there was a trend for patients with right coronary artery disease to have a higher risk increase of MACE independently of other high-risk cardiovascular features after an ACS. The extension of coronary disease also seems associated with worse 6-month prognosis.

ROLE OF ECHO-IMAGING IN ISCHAEMIC HEART DISEASE

P5407 | BEDSIDE

Echocardiography, contractile reserve and magnetic resonance to predict left ventricular remodelling

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Background: The presence of adverse left ventricular remodeling (LVR) in STEMI patients is related to an increase in morbi-mortality at follow-up. Different parameters (assessed by magnetic resonance or echocardiography) have been associated, however, the main predictor of LVR remains still controversial.
Aims: We sought to know the incidence of LVR after an ST-segment elevation myocardial infarction (STEMI) and to identify a best image method to predict its occurrence.
Methods: One hundred and forty consecutive patients with an acute STEMI were studied after a successful primary angioplasty with CMR and low-dose dobutamine stress echo during the first week and at 6 months. Left ventricular volumes and ejection fraction (EF), myocardial area at risk (AAR), infarct size (IS), microvascular obstruction (MVO) and myocardial salvage index (MSI) were determined by CMR, and the global peak systolic strain (SS) basal and at low-dose by echocardiography. An increase in LV end-diastolic volume (LVEDV) $\geq$20% was defined as adverse LVR, a decrease $\leq$20% as reverse LVR and values in between as no LVR.
Results: Adverse LVR was observed in 29% and reverse LVR in 9% of patients. Derived CMR and echocardiographic variables among different groups are shown in table 1. In the univariate analysis only SS (P=0.023), IS (P=0.05) and the AAR (P=0.046) were predictors of adverse LVR. In the multivariate analysis, rest SS was the only predictor of adverse remodeling. A cut-off value of –15 (AUC: 0.8) predicted LVR with a Sensitivity of 75% and specificity of 70%.

	Basal EF (%)	IS (gr)	MVO (gr)	AAR (gr)	MSI (%)	Basal SS	DBT SS
No LVR (n=87)	51±7	27±12	2±2	43±15	18±10	14±3.2	15±4.2
Adverse LVR (n=41)	45±15	34±18	4±1.5	52±12	15±12	12±3.2	14±3.7
Reverse LVR (n=12)	47±10	23±13	0.9±1.8	41±18	25±8	15±3.2	16±3.9

Conclusions: LVR is a common process after an STEMI. Although CMR and echocardiographic derived parameters can predict its occurrence, a SS global strain higher than –15 seems to be the best predictor for LVR.

P5408 | BENCH

Prediction of adverse events after ST segment-elevation myocardial infarction by imaging techniques

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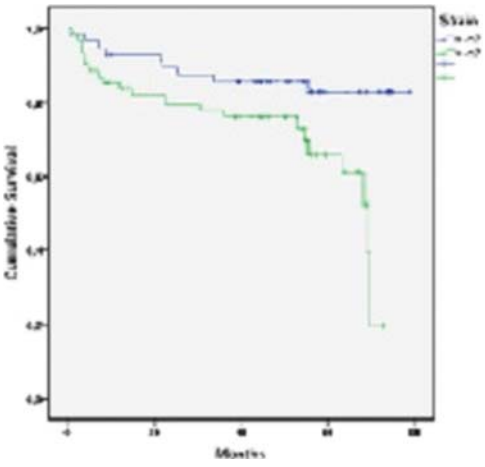
Background: After an ST-segment elevation myocardial infarction (STEMI), different magnetic resonance (CMR) and echocardiographic (TTE) variables have been proposed to predict adverse outcomes. However, no studies have been conducted to compare its prognostic value.
Objectives: To determine the value of CMR, rest TTE and at low-dose dobutamine to predict adverse events at long-term follow-up in STEMI patients.
Methods: One hundred and sixty-two consecutive patients with an STEMI were studied after a successful primary angioplasty with CMR and low-dose dobutamine stress echo during the first week and at 6 months. Left ventricular volumes and ejection fraction, myocardial area at risk, infarct size, microvascular obstruction and myocardial salvage index were determined by CMR. Global peak systolic strain (SS) was measured at rest and at low-dose dobutamine stress echo. Major adverse cardiac events (MACE) were determined at follow-up.
Results: Patients were followed by a median time of 45 months (11–79 months). MACE occurred in 43 patients (26%): stroke in 6, angina or re-infarction in 29, heart failure in 5, ventricular arrhythmia in 2, major bleeding in 2 and cardiovascular death in 5. In the univariate analysis, IS (Odds Ratio (OR): 1.8, P=0.045), SS at low-dose dobutamine (OR: 1.5, P=0.041) and SS at 6 months (OR: 1.9, P=0.038) were the strongest predictors for MACE. In the multivariate analysis, SS at 6 months was the only independent predictor of MACE (cut-off value: –17, area under the curve: 0.8, Sensitivity: 80% and Specificity: 75%) (Figure 1).



Conclusions: CMR and echocardiographic derived variables are excellent predictors of MACE in STEMI patients. Systolic strain at 6 months constitutes the strongest predictor of poor outcomes at long-term follow-up.

P5409 | BEDSIDE

Assessment of post-systolic shortening and early systolic lengthening by 2D speckle-tracking is useful to detect cad in patients with suspected NSTE-ACS

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Introduction - Post-systolic shortening (PSS) and early-systolic lengthening (ESL) assessed by speckle-tracking echocardiography (STE) are considered markers of myocardial ischemia.
Purpose: We aimed to examine the relation between the presence of PSS, ESL and coronary artery disease (CAD) in patients presenting with suspected non-ST-elevation acute coronary syndrome (NSTE-ACS) and no wall motion abnormalities in conventionnal echocardiography.
Methods: 58 patients with suspected NSTE-ACS, normal LVEF (i.e. LVEF $\geq$55%) and normal wall motion score index (i.e. WMSI=1) were prospectively enrolled. Echocardiography was performed on admission. Longitudinal strain was measured by 2D-STE using a 17 LV segment model. For each segment, peak positive early strain (representing maximum segmental systolic lengthening) and post-systolic shortening (defined as peak negative strain during diastole minus peak negative systolic strain) were recorded. Values for all segments were averaged to obtain global values, and territorial values (based on theoretical perfusion territories of the three major coronary arteries). Layer-specific longitudinal strains were

assessed from endocardium, mid-myocardium, and epicardium. All the patients underwent angio-coronarography. CAD was defined by the presence of coronary artery stenosis >50%.
Results: Global PSS and global ESL were able to detect CAD with good diagnostic performances (AUC=0.84, p<0.001 and AUC=0.68, p=0.02 respectively). Territorial PSS was able to detect the presence of significant stenosis in LAD (AUC=0,70, p=0.01), LCX (AUC=0,73, p=0.01) and RCA (AUC=0,86, p<0.001). Territorial ESL was able to detect presence of significant stenosis in LAD (AUC=0,69, p=0.02), LCX (AUC=0,71, p=0,02) but not in RCA (AUC=0,65, p=0.08). Layer-specific analysis did not show any difference in terms of diagnostic performance between the three layers.
Conclusion: Assessment of both PSS and ESL is useful to detect CAD in patients with NSTE-ACS and normal conventionnal echocardiography.

P5410 | BEDSIDE
How frequent are signs of left ventricular dysfunction in acute myocardial infarction patients with normal ejection fraction? Impact of the latest chamber quantification recommendations

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Aim: To study the prevalence of abnormal values of routine parameters of global left ventricular (LV) systolic function when LV ejection fraction (LVEF) remains normal in a large, unselected cohort of consecutive patients hospitalized for acute myocardial infarction (MI).
Materials and methods: A total of 421 consecutive patients with MI (with or without ST elevation) included in the REBUS (RElevance of Biomarkers for future risk of thromboembolic events in UnSelected post-myocardial infarction patients) study, underwent 2D- and Doppler echocardiography in the cardiac intensive care unit within 72 hours after admission to assess their LV function. Conventional parameters of LV systolic function were categorized to normal or abnormal due to the chamber quantification recommendations from 2015.
Results: Of the 356 patients finally enrolled to the study, normal LVEF was recognized in 236 (56.1%) or 262 (62.5%) patients, when using either the conventional or the new sex-specific LVEF cut-off, respectively. The new reference intervals for LVEF reclassified 26 (21.8%) patients from having abnormal to normal LVEF. The patients with abnormal LVEF were characterized by larger extent of myocardial necrosis (max cTn I 31.2±55.9 vs. 17.1±24.5 μg/L, p=0.001) and higher proportion of STEMI/LBBB (57.0 vs 39.5%, p=0.012), as compared to those with normal LVEF. No difference in age, sex and history of previous MI were observed. The patients with abnormal LVEF had significantly lower mean mitral annular plane systolic excursion (MAPSE) (0.96±0.20 vs. 1.18±0.21 cm, p<0.001), higher indexed LV end-systolic (LVESVi) (30.6±14.6 vs. 15.3±4.9 ml/m^2, p<0.001), end-diastolic (LVEDVi) (53.3±19.8 vs. 40.8±10.2 ml/m^2, p<0.001) and left atrial volume (LAVi) (37.9±11.9 vs. 31.6±11.0 ml/m^2, p<0.001). Using the new cut-off, among the patients with normal LVEF, an abnormal MAPSE (<1.1cm in women and <1.3cm in men) was observed in 64.4%. Elevated LVESVi (>24ml/m^2 in women and >31ml/m^2 in men) and LVEDVi (>61ml/m^2 in women and >74ml/m^2 in men) were found only in 0.4% of patients, while an enlarged LAVi (>34ml/m^2) in 33.8% of patients with normal LVEF.
Conclusions: Implementation of the latest recommendations on chamber quantification including sex-specific reference intervals resulted in the reclassification of ca 20% of patients from having abnormal to normal LVEF. A majority of patients classified as having normal LVEF on echocardiography within 72 h after MI had at least one marker of global systolic function outside the normal range. The prognostic significance of our observation is being investigated.

P5411

P5412 | BEDSIDE
New 3D echo-derived morphometric criteria for discriminating between ischemic and non-ischemic cardiomyopathy

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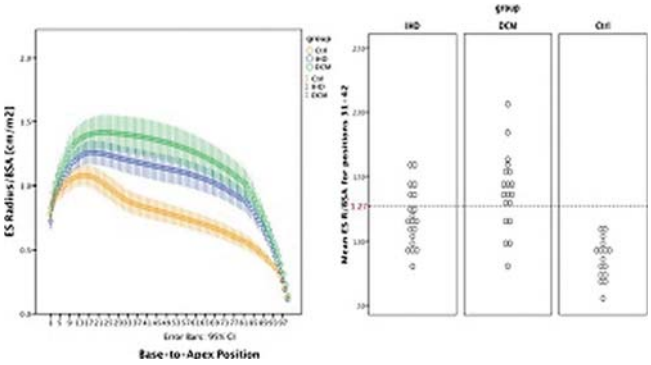
Background: Idiopathic dilated cardiomyopathy (DCM) is characterized by spherical reshaping of the left ventricle (LV). LV remodeling in ischemic heart disease (IHD) can render a similar appearance. We sought to identify novel morphometric criteria to discriminate between the two.
Methods: 3D echo was performed in patients with IHD (n=20), DCM (n=19) and controls (n=16), matching the first two groups for age, gender, LV volumes and ejection fraction. The LV endocardial surface was traced in 4 orthogonal planes in end-systole (ES) and end-diastole (ED) utilizing customized software (Omni4D). A mean radius normalized to body surface area (R/BSA) from edge of reconstructed LV to a centroid line axis was plotted from base to apex positions (#1–100 respectively). Point-by-point normalized radii were compared among groups and optimal cut-off values separating between the patients were validated in a separate group of DCM (n=5) and IHD (n=6) patients matched for LV volumes and ejection fraction.
Results: ES R/BSA values were significantly higher in DCM vs IHD patients at positions #19–77, and ED R/BSA values were higher at positions #36–57. ROC analysis showed ES R/BSA at positions #31–42 to hold the best discriminative capacity for DCM (AUC=0.72), with a sensitivity of 73.7%, specificity of 70% and accuracy of 71.8%. Multivariate analysis-based model including gender, HTN, and ES R/BSA improved accuracy to 76.9%, with a 68.4% sensitivity and 85% specificity. The application of the same model in the validation cohort yielded close discriminative capacity (72.7%, 60%, and 83.3% respective values).



ES R/BSA in DCM, IHD, and Ctrl patients

Conclusions: Applying a model incorporating ES standardized radii over the middle third region of the LV, hypertension, and gender distinguished successfully DCM vs IHD patients.

P5413 | BEDSIDE
Excellent discrimination ability of resting multilayer longitudinal strain using two-dimensional speckle tracking echocardiography for myocardial infarction and ischemic segments

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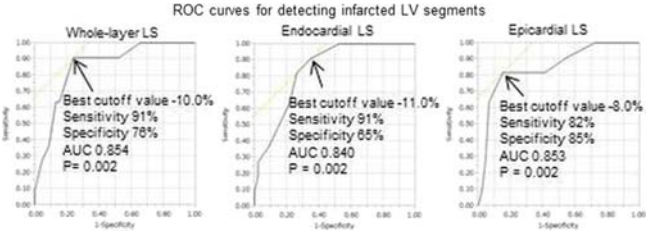
Background: Damage to left ventricular (LV) endocardial layers may occur at an early stage in myocardial infarction (MI) or ischaemia.
Purpose: To evaluate the ability of multi-layer longitudinal strain (LS) with 2D speckle tracking transthoracic echocardiography (TTE) to distinguish between MI, ischaemic, and non-ischaemic LV segments.

Methods: Retrospective data from 39 stable patients (32 males; 65.8±11.9 years), comprising 46 coronary arteries with ≥50% stenosis on invasive coronary angiogram (not related to MI), were assessed by invasive fractional flow reserve (FFR). All patients underwent TTE (Vivid E9) within 36 days of FFR, without clinical incident. Ischaemic and non-ischaemic segments were defined as those supplied by the stenotic vessels with FFR≤0.80 and FFR>0.80, respectively.
Results: Of the 39 patients, 10 had 11 coronary territories related to previous MI. FFR≤0.80 and FFR>0.80 was identified in 27 and 19 vessels, respectively. Using whole-layer, endocardial, and epicardial LS, no significant differences were detected between ischaemic and non-ischaemic segments, but the infarcted segments were significantly greater. According to receiver operating characteristic curves, the best cutoff values for whole-layer, endocardial and epicardial LS for infarcted segments were –10.0% (91% sensitivity, 76% specificity, area under the curve [AUC] =0.854, P=0.002), –11.0% (91%, 65%, AUC=0.840, P=0.002), and –8.0% (82%, 85%, AUC=0.853, P=0.002), respectively.



Conclusion: In stable patients with coronary artery disease, resting multi-layer LS is useful to detect infarcted LV segments. Furthermore, whole-layer, endocardial and epicardial LS were equally effective. However, it remains a diagnostic challenge to differentiate between ischaemic and non-ischaemic LV segments.

P5414 | BEDSIDE
Quantification of regional left ventricular function in patients with coronary artery disease by layer-specific strain

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Purpose: The study aimed to evaluate whether layer-specific myocardial strain performed by two-dimensional speckle tracking imaging (2D-STI) allows quantification of regional left ventricular function in patients with coronary artery disease (CAD).
Methods: 44 patients referred to selected coronary angiography (SCA) due to suspected CAD were prospectively included. All the patients had normal EF and no abnormal segmental wall motion of left ventricle. According to degree of coronary artery stenosis by SCA, there were 188 segments with >75% coronary artery stenosis (severe stenosis group), 76 segments with 50–75% coronary artery stenosis (moderate stenosis group), 132 segments with <50% coronary artery stenosis (mild stenosis group) and 240 segments without coronary artery stenosis (control group). Four-chamber, two-chamber and long-axis apical views were recorded in all the subjects. Layer-specific longitudinal strain indices including endocardium (LS-endo), mid-myocardium (LS-mid) and epicardium (LS-epi) were assessed by 2D-STI.
Results: In segments with or without coronary artery stenosis, the LS-endo, LS-mid, LS-epi of each segment decreased gradually (P<0.05). Compared with the control group, LS-endo, LS-mid, LS-epi of moderate stenosis group and severe stenosis group decreased significantly (P<0.05), however, there was no significant difference between moderate and severe group. Moreover, there was no significant difference between the control group and mild stenosis group (P>0.05). (Table 1)

Table 1. Comparison of Layer-specific longitudinal strain indices

Indices	Control group	Mild stenosis group	Moderate stenosis group	Severe stenosis group	F value	P value
LS-endo	24.92±8.84	22.26±9.11	22.93±10.36	22.76±9.63	4.56	0.004
LS-mid	20.83±6.23	21.60±6.15	18.63±8.23	18.28±6.83	9.02	0.0001
LS-epi	17.71±5.17	18.06±4.69	15.57±6.87	15.07±5.35	12.59	0.0001
F value	65.59	46.96	14.05	50.06		
P value	0.000	0.000	0.000	0.000		

Abbrivations: LS-endo, longitudinal endocardium strain; LS-mid, longitudinal mid-myocardium strain; LS-epi, longitudinal epicardium strain.

Conclusion: Layer-specific myocardial strain indices can recognize tiny changes of regional left ventricular systolic function in patients with CHD. In segments with normal wall motion, the regional systolic function of left ventricle has already been impaired.

P5415 | BEDSIDE
Routine manual thrombus aspiration has no impact on left ventricular remodeling: the echocardiographic substudy of the randomized physiologic assessment of thrombus aspiration in patients with ST-segment elevation myocardial infarction

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Background: It has been reported that index of microcirculatory resistance (IMR) is lower in STEMI patients who underwent thrombus aspiration before stent implantation compared to those treated with conventional primary PCI. The aim of this study was to evaluate impact of improved myocardial perfusion by manual thrombus aspiration assessed by IMR on left ventricular remodeling in STEMI patients at mid-term follow-up.
Methods: The total of 115 patients entered the echocardiography substudy of the PATA STEMI (randomized Physiologic Assessment of Thrombus Aspiration in patients with ST-segment Elevation Myocardial Infarction) trial which evaluated efficacy of manual thrombus aspiration using Eliminate3 catheter (Terumo Europe, Leuven, Belgium). Echocardiography was done within the first 24 hours after the index procedure and after 4 months. End-diastolic and end-systolic left ventricular (LV) volume indices, ejection fraction (EF), cardiac sphericity index (CSI) and regional wall motion score index (WMSI) were calculated.
Results: In baseline characteristics, in patients with thrombus aspiration compared to those with conventional primary PCI, total ischemic time tended to be longer (246,7±181,8 vs. 200,9±110,1 min, P=0,09) and AUC CK was smaller (40090±26158 U/L vs. 52676±32013 U/L, P=0,026, respectively). Also, corrected IMR was lower in thrombus aspiration group (27,5±16,8 vs. 39,9±32,7 U/L, p=0,0079), while CFR (1,68±0,81 vs. 1,61±0,67, P=0,6) and mean coronary wedge pressure in infarct related artery (20,4±6,6 vs. 21,4±7,8 mmHg, P=0,5) were similar. End-diastolic and end-systolic LV volumes per body surface area, EF, CSI volume and WMSI were similar between the thrombus aspiration and no aspiration group at baseline and at follow-up. At follow-up, percent change in WMSI tended to be greater in thrombus aspiration group (decrease in WMSI 8,2% vs. increase in WMSI 0,8%, P=0,094). The rate of LV remodelling and reverse LV remodelling was similar in thrombus aspiration and conventional primary PCI group (30,3 vs. 28,6%, p=0,84 and 42,4 vs. 28,6%, p=0,12, respectively).
Conclusions: Improved myocardial perfusion achieved by manual thrombus aspiration and assessed by index of microcirculatory resistance has no impact on left ventricular remodeling in STEMI patients at mid-term follow-up.

P5416 | BEDSIDE
Left ventricular global longitudinal strain rate is associated with changes in myocardial redox state in patients with ischaemic heart disease

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Background: Increased myocardial oxidative stress is directly involved in multiple cardiac abnormalities, but there is no non-invasive test to evaluate this in humans.
Purpose: We explored the ability of left ventricular global longitudinal strain (LS) and LS rate (LSR) to describe myocardial redox state in patients with coronary atherosclerosis.
Methods: Echocardiography was performed in 30 male, non-diabetic patients with no heart failure (good LV ejection fraction (LVEF=54.2±2.0%) and low B-natriuretic peptide level=75.7±15.5ng/mL) undergoing coronary bypass surgery, the day before surgery. Speckle-tracking echocardiography was used to calculate LS, LSR, LV end-systolic (ESV) and end-diastolic volumes (EDV) and LVEF. Myocardial tissue collected at the time of surgery (right atrial appendage) was used to determine myocardial NADPH oxidase-derived O2- radicals using ex-vivo bioassays and lucigenin chemiluminescence. Plasma malondialdehyde (MDA) was measured as an index of systemic oxidative stress.
Results: There was no association between LVEF and either plasma MDA or myocardial NADPH oxidase activity (p=NS for both). Systemic or myocardial oxidative stress were not associated with ESV, EDV or their respective indices adjusted for body surface area (p=NS for all). LS or LSR were not associated with plasma MDA (p=NS) but there was a positive association between myocardial NADPH oxidase activity and LSR (rho=0.380, p<0.05, but not with LS) indicating reduced LV longitudinal systolic deformation with higher myocardial oxidative stress.
Conclusions: Higher NADPH oxidase activity in human myocardium is linked with reduced left ventricular global strain rate before the development of systolic LV dysfunction. LSR appears to be a sensitive imaging biomarker for the characterization of myocardial redox state, and this finding may have major clinical implications for the prediction of ischaemic cardiomyopathy and the monitoring of treatments in patients with ischaemic heart disease.

P5417 | BEDSIDE

Prognostic assessment of myocardial viability after acute myocardial infarction: a clinical follow-up study by speckle tracking

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Purpose: We sought to use speckle tracking imaging (STI) for the assessment of myocardial viability and changes of left ventricular segmental function of the patients with acute myocardial infarction (AMI). Clinical incremental value of STI to identify viable segments through different time points was focused on in this study.
Methods: 54 patients with first onset AMI who underwent primary percutaneous coronary intervention (PCI) were enrolled in the study. The average age was 62.4±9.7 years. Dynamic images of left ventricle were acquired before, 3-month 1-year after PCI. Apical long-axis, four-chamber and two-chamber views, cross-sectional basal, mid and apical views were stored for 3 to 5 cardiac cycles. With the methods of standard 17 segments, longitudinal peak systolic strain (LPSS), radial peak systolic strain (RPSS) and circumferential peak systolic strain (CPSS) were analyzed for each segment in EchoPac workstation. According to the LPSS cut-off value of –5% as the determination of myocardial viability and recovery of segmental function, the percentage of infarcted area was calculated for the comparisons among infarcted area, infarcted site and segmental recovery.
Results: Before PCI, dysfunctional segments of AMI patients were 341 in total and it decreased to 207 at 3-month after PCI while 159 at 1-year follow-up. Between before and 3-month after PCI, the infarcted area percentage of early-recovery group (n=29) was decreased 18.9%, which was significantly higher ($p<0.05$, all) than both the decreases in late-recovery (n=15) (10.6%) and non-recovery group (n=10) (8.2%). The decreases of early-recovery and late recovery group had reached at 21.1% and 22.0% at 1-year after PCI, respectively. Both of them were significant different from non-recovery group (13.5%) ($p<0.05$, all). Compared to basal and mid segments, the apical infarcted area had recovered relatively earlier and more easily according to the statistical analysis of LPSS, RPSS and CPSS ($p<0.05$, all). CPSS of both early and late-recovery group were shown different compared to non-recovery group before PCI and 3-month after PCI ($p<0.05$, all), earlier suggesting the recovery of segmental function.
Conclusions: STI assessment was accurate for identifying viable myocardium and tracking the changes of left ventricular segmental function. After infarction, the segmental analysis of longitudinal and circumferential movements have suggested early and continuous recovery for patients. LPSS and CPSS from STI have provided clinical incremental value for the prognosis of AMI patients.

CARDIAC ECHO-IMAGING IN SYSTEMIC DISEASES

P5418 | BEDSIDE

Greater improvement of coronary artery function, left ventricular deformation and twisting by IL12/23 compared to TNF-a inhibition in psoriasis

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The role of treatment with anti-IL12/23 agents on left ventricular (LV) function, arterial stiffness and coronary microcirculation in psoriasis has not been fully clarified.
Methods: 114 psoriasis patients (52±13 yrs, 72men), (PASI disease activity score:11.8±8), were randomized to receive an anti-IL12/23 regimen (n=32), an anti-TNF (n=34) or cyclosporine (n=48). At baseline and after 4 months of treatment, we measured a) pulse wave velocity (PWV-m/sec), augmentation index (AI-%) and central systolic blood pressure (cSBP-mmHg) b) LV longitudinal strain (GLS-%) and LV torsion-deg using speckle tracking echocardiography c) coronary flow reserve (CFR) d) tumor necrosis factor (TNFa-pg/ml), interleukin-6 (IL-6-pg/ml), -10 (IL-10-pg/ml), -12 (IL-12-pg/ml), -17 (IL-17-pg/ml) and malondialdehyde (MDA-nM/L). Forty normal subjects served as controls.
Results: At baseline, patients had higher PWV, AI, and lower CFR, GLS and LV torsion than normals ($P<0.05$). After treatment, all patients had improved GLS (median values –18.2 [–15.4 to –21] vs. –19.6 [–16.3 to –21.4] P=0.04) and decreased IL-6 (2.26 [1,61–5.4] vs 2.01 [1.29–3.66], P=0.04). However, patients on anti-IL12/23 agents also reduced AI (31 [13–42] vs 27 [7.3–40] P=0.03), cSBP (131 [116–155] vs 123 [115–135] P=0.04), PWV (9.3 [7.5–13] vs 8.7 [7.4–10.3] P=0.04), MDA (1.41 [0.75–2,67] vs 1.03 [0.73–1.89] P=0.02), the TNFa/IL-10 ratio (4.1 [2.9–5.7] vs 3.4 [2.7–4.9] P=0.03) and improved CFR (2.8 [1.8–3.6] vs. 3.2 [2.5–4.3] P=0.03) post-treatment. In the anti-TNF group, CFR, GLS, LV torsion were improved and TNF/IL-10 was reduced post-treatment ($P<0.05$), whereas markers of arterial stiffness remained unchanged. Compared to baseline, patients on cyclosporine had unchanged CFR, GLS, LV torsion post-treatment (P=NS), but conversely increased AI (28.2 [13.3–33.5] vs 33.5 [16.9–37.1] P=0.04), cSBP (119 [110–134] vs 129 [113–139] P=0.04) and PWV (9.4 [7.9–12.7] vs 10.9 [8.7–13.9] P=0.03). Except IL-6, biomarkers remained unchanged. PASI similarly improved in all treatment arms. Compared to the anti-TNF and cyclosporine, anti-IL12/23 agents resulted in greater improvement of GLS (24% for IL-12/23 vs 10% for anti-TNF vs. 7% for cyclosporine), LV torsion (27% vs. 16% vs. 2%), CFR (14% vs. 11% vs. 5%) as well as in IL6 (12% vs. 5% vs. 11%), MDA (27% vs. 3% vs 2%) and TNFa/IL-10 (17% vs. 13% vs. 10%) $P<0.05$.
Conclusion: In psoriasis, IL12/23 inhibition improves vascular function and causes a greater improvement in coronary function and myocardial deformation than anti-TNF treatment, because of a greater reduction of the inflammatory and oxidative stress burden.

P5419 | BEDSIDE

Effect of liver transplant on the progression of cardiomyopathy in familial amyloid polyneuropathy

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In Transthyretin familial amyloid polyneuropathy (TTR-FAP) V30M, the cardiomyopathy is due to deposits of amyloid fibrils in the heart. In these patients (pts), the progression of cardiomyopathy is associated with increased risk of death. Liver transplantation suspends the hepatic production of amyloidogenic-mutated TTR protein. However the impact of this intervention on the progression of this cardiomyopathy is not completely known.
Purpose: To evaluate the impact of liver transplantation on the progression of infiltrative cardiomyopathy, by echocardiography.
Methods: Prospective study of consecutive pts with V30M TTR-FAP evaluated annually and performing an echocardiogram with conventional Doppler. Ecocardiographic evaluation of pts undergoing transplant was compared with that of non-transplanted. For that purpose, we conducted a nested case-control analysis with patient matching according to neurophysiological score measured prior to transplantation (<5% difference).
Results: From a total population of 284 TTR-FAP pts, 88 (44 transplanted, 44 non-transplanted), with a mean age of 47±15 years, 52% male, with identical median neurophysiological and clinical scores, 25 (IQR 8.75–51.25) and 24 (IQR 12–34), respectively, were selected for analysis. During a median follow-up of 96 months following the time of pairing, 233 echocardiograms were perfomed. Of these, 178 (76.4%) in the first 48 months. At the time of initial evaluation, the non-transplanted group exhibited greater thickness of the septal wall (12±3 vs. 10±2 mm; p=0.036), larger diameter of the left atrium (LA) (in apical 4-chamber; 49±9 vs. 45±6 mm; p=0.014) and lower E/A ratio (1.0±0.4 vs. 1.2±0.4;. p=0.035). In contrast, transplanted group showed the same ventricular thickness, E wave deceleration time (DT), pressure half-time (PHT), E/A ratio and the left atrial dimensions during follow-up. In pts not transplanted, there was an increase in myocardial thickness (10±2 to 17±3 mm; p=0.023) and progression of diastolic dysfunction parameters, including significant increase in E wave DT (Pearson R=0.22; p=0.042), PHT (Pearson R=0.26; p=0.021) and size of LA (Pearson R=0.22; p=0.032, significant at 48 months).
Conclusion: The FAP is accompanied by cardiac amyloid infiltration resulting in progressive worsening of ventricular thickening and diastolic dysfunction. Liver transplantation prevented the progression of cardiac amyloid infiltration, stabilizing the echocardiographic parameters at long-term.

P5420 | BEDSIDE

Subclinical abnormalities of two-dimensional speckle tracking echocardiography associate with early peripheral vascular disease in patients with chronic kidney disease

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Background: Very few studies have investigated the relationship between arterial stiffness and subclinical left ventricular (LV) dysfunction and none used two dimensional speckle tracking echocardiography (2DSTE).
Objectives: We sought to investigate the association between subclinical myocardial abnormalities assessed by 2DSTE and arterial stiffness in chronic kidney disease (CKD) patients with normal LV ejection fraction (LVEF) and no previous history of cardiovascular disease.
Methods: In this cross-sectional study we have enrolled 106 CKD patients. Pressure waveforms were recorded on radial, carotid and femoral arteries using applanation tonometry to estimate augmentation index (AIx) and aortic pulse wave velocity (aPWV). Conventional echocardiography and 2DSTE were used to determine LVEF, LV mass index (LVMI), global longitudinal and circumferential strain (GLS, GCS), number of segments with diastolic dysfunction (DD) and LV twist.
Results: Aortic PWV correlated crudely with the presence of diabetes ($r=0.58$, $p<0.001$), hypertension ($r=0.32$, $p<0.001$), LVMI ($r=0.29$, $p=0.01$), GLS ($r=0.300$, $p<0.003$), number of segments with DD ($r=0.416$, $p<0.001$), LV twist ($r=0.288$, $p<0.003$) while AIx was only associated with hypertension ($r=0.19$, $p=0.046$) and number of segments with DD ($r=0.317$, $p<0.001$). When adjusting for age, gender and cardiovascular risk factors aPWV was independently associated with LV twist ($\beta=0.160$, $p=0.017$) and number of segments with DD ($\beta=0.221$, $p=0.011$). Stepwise, multiple regression models established that LV twist improved the prediction of arterial stiffness over and above age, gender and cardiovascular risk factors alone ($R2=0.17$, $p=0.01$)

Conclusions: Subclinical LV dysfunction, identified with 2DSTE is strongly associated with aPWV in CKD patients. This is the first study to provide a link between subclinical LV dysfunction and early peripheral arterial disease in CKD patients.
Acknowledgement/Funding: Fundacao para a Ciencia e Tecnologia - Portugal

P5421 | BEDSIDE
The effect of different treatment strategies on left ventricular myocardial deformation parameters in patients with chronic renal failure

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Background: Renal transplantation has lowered the risk of cardiovascular death compared with dialysis. However, there exists conflicting data about improvement in cardiac functions after transplantation.
Purpose: In our study, we aimed to compare the possible effects of different treatment strategies on left ventricular (LV) functions by speckle tracking echocardiography (STE) in patients with chronic kidney disease (CKD).
Methods: Three groups were formed with patients at predialysis stage (n=50), with those on three times a week hemodialysis program (n=50), or with those who underwent successful renal transplantation (n=50).
Results: Among mean LV strain values, circumferential systolic strain was lowest in the hemodialysis group. Among mean LV longitudinal strain rate (SR) values, longitudinal systolic SR was lowest in the hemodialysis group. Longitudinal early diastolic SR was highest in the transplantation group. Among mean LV circumferential SR values, circumferential systolic SR, early diastolic SR, and late diastolic SR were lowest in the hemodialysis group (Table 1).

Table 1. Left ventricular myocardial deformation parameters of the study groups

Mean values	Transplantation patients (n=50)	Hemodialysis patients (n=50)	Predialysis patients (n=50)	p
Longitudinal systolic strain (%)	−19.93±3.50	−17.47±3.28	−18.74±2.52	0.002
Circumferential systolic strain (%)	−25.87±4.20	−20.97±4.90	−24.74±4.55	<0.001
Radial Systolic Strain (%)	33.51±13.89	34.01±13.33	31.46±11.46	0.602
Longitudinal systolic SR (1/sec)	−1.31±0.24	−1.05±0.20	−1.19±0.21	<0.001
Longitudinal early diastolic SR (1/sec)	1.70±0.43	1.37±0.32	1.45±0.37	<0.001
Longitudinal late diastolic SR (1/sec)	1.06±0.26	1.04±0.28	1.19±0.25	0.024
Circumferential systolic SR (1/sec)	−1.98±0.48	−1.42±0.30	−1.75±0.46	<0.001
Circumferential early diastolic SR (1/sec)	2.41±0.47	1.77±0.48	2.15±0.51	<0.001
Circumferential late diastolic SR (1/sec)	1.18±0.36	0.92±0.31	1.20±0.40	<0.001
Radial systolic SR (1/sec)	1.84±0.52	1.55±0.52	1.65±0.58	0.025
Radial early diastolic SR (1/sec)	−1.86±0.61	−1.59±0.50	−1.71±0.46	0.040
Radial late diastolic SR (1/sec)	−1.09±0.47	−1.03±0.50	−1.17±0.48	0.415

SR, strain rate.

Conclusion: We have found by STE that LV functions of CKD patients who underwent successful renal transplantation tend to improve. However, CKD patients on hemodialysis treatment seem to have worse LV functions than CKD patients at predialysis stage.
Acknowledgement/Funding: This study was funded by the Ondokuz Mayis University, Samsun, Turkey (project number: PYO.TIP.1904.13.030)

P5422 | BEDSIDE
The impact of liver transplantation on myocardial function in patients with familial amyloid polyneuropathy

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Introduction: Familial amyloid polyneuropathy (FAP) is a genetic disorder characterized by amyloid depositon in multiple organs. Myocardial amyloid infiltration results in progressive diastolic dysfunction and subclinical changes in systolic function, better assessed by myocardial deformation parameters. Liver transplantation (LT) inhibits liver production of abnormal protein and prevent disease progression. However, its impact on myocardial deformation has never been investigated.
Objective: To evaluate the impact of LT on global myocardial deformation parameters as assessed by speckle-tracking echocardiography in patients with FAP.
Methods: Prospective study of patients with FAP undergoing LT. Global longitudinal strain (GLS) and global longitudinal systolic (GLSR-S), protodiastolic (GLSR-E) and end-diastolic (GLSR-A) strain rate were evaluated prior to surgery and repeated at least 1 year thereafter.
Results: Eighteen patients (66.7% female; 39±7 years) with FAP undergoing LT were included. At baseline neurophysiological median score was 5 [Interquartile range (IQR): 0–14]. All patients had mild neurological symptoms, but none exhibited cardiovascular symptoms. The severity of neurological involvement correlated with GLSR-S impairment (Pearson R: 0.49, P=0.042). Sixty seven percent of patients had significantly improvement of GLS 3.5 years (median) after LT (post-LT: −18.9±3.0% vs. pre-LT: −17.4±2.4%; p=0.05). There was consistency between GLS changes and the improvement of other deformation parameters (GLSR-S variation: Pearson r=0.66, P=0.003; GLSR-E variation: Pearson R=−0.55, P=0.019; GLSR-A variation: Pearson R=−0.55, P=0.017). Myocardial deformation indexes were not dependent on age, duration of symptoms and severity of neurological involvement.
Conclusion: FAP patients had subclinical changes in systolic function as assessed by myocardial deformation analysis, which correlates with the neurological involvement of the disease. After LT, changes in myocardial deformation tended to be reversed.

P5423 | BENCH
Causes and consequences of longitudinal left ventricular dysfunction assessed by 2D strain echocardiography in patients with cardiac amyloidosis

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Background: Cardiac amyloidosis (CA) is a condition of poor prognosis due chiefly to three forms of amyloidosis, light chain (AL), hereditary transthyretin (M-TTR), and wild-type transthyretin (WT-TTR). Two-dimensional (2D) echocardiography measurement of longitudinal strain (LS) has been reported to detect early left-ventricular systolic dysfunction. The pathophysiological underpinnings, regional distribution, and prognostic significance of LS in CA are unclear.
Objectives: To compare left ventricular LS evaluated by 2D echocardiography with cardiac magnetic resonance imaging (MRI) in CA, establish correlations between histological and imaging findings, and assess the prognostic usefulness of LS measurement and MRI.
Methods: All patients underwent echocardiography and 53 had MRI. The native hearts of the 3 patients who received heart transplants were subjected to histological examination. For each of the 17 left-ventricular segments in the American Heart Association model, we evaluated LS, late gadolinium enhancement (LGE) by MRI, and cardiac amyloid deposition. Univariate at 6 months and multivariate analyses were performed to identify variables associated with major adverse cardiac events (MACE).
Results: We studied 79 patients with CA; 26 had AL, 36 M-TTR, and 17 WT-TTR. Mean LS was −10±4%. Both LS and amyloid deposits showed a basal-to-apical gradient. Mean LS and number of segments with LGE were similar across the three CA types. LS correlated with LGE and amyloid burden (r=0.72). LGE was seen in the six basal segments in all WT-TTR patients.
During the median follow-up of 11 [4; 17] months, 36 (46%) patients experienced MACE. Independent predictors of MACE were apical LS (cutoff, −14.5%), N-terminal pro-natriuretic peptide (cutoff, 4000 ng/L), and New York Heart Association Class III-IV heart failure.
Conclusions: Basal-to-apical LS abnormalities are similar across CA types and reflect the amyloid burden. Apical LS independently predicts MACE.

P5424 | BEDSIDE
Relationship between inflammation and timing markers of LV rotation and untwist in psoriatic arthritis - a study of the mechanisms of early myocardial dysfunction in systemic diseases

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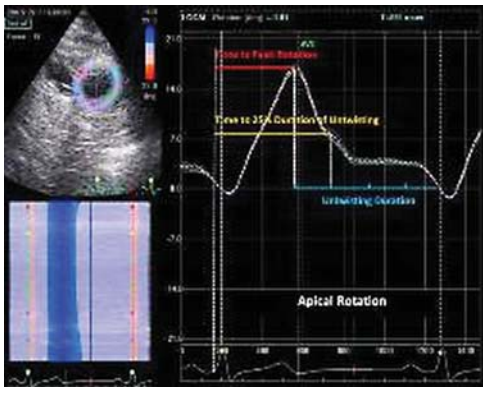
Purpose: To to evaluate the relationship between inflammation and left ventricular (LV) deformation in patients with Psoriatic arthritis (PsA).
Methods: Sixty-Three patients with PsA and 24 healthy control subjects received conventional echocardiography with speckle tracking imaging. Deformation measurements included global longitudinal (ϵ-long), apical circumferential (ϵ-circum) and radial strain (ϵ-radial), apical rotation and maximal untwisting rate (URmax). Timing markers were time to peak apical rotation and time to 25% duration of apical untwisting (Figure).
Results: All patients had normal LVEF but impaired LV deformation when compared to control subjects (ϵ-long: 19.5±3.0 vs. 21.7±2.5, ϵ-circum: 22.1±5.3 vs. 33.6±4.8, rotation: 10.6±4.3 vs. 19.4±4.9, URmax: 64.8±29.3 vs. 103.7±44.0; p<0.005). Furthermore, there were a significant correlation between timing markers, deformation and inflammation after adjusting for age and blood pressure (Table 1).

Table 1

	hsCRP	ESR
Time to peak apical rotation	r=0.417, p<0.001	r=0.347, p=0.008
Time to 25% duration of apical untwisting	r=0.389, p=0.003	r=0.282, p=0.033
Global LV apical rotation	r=−0.253, p=0.058	r=−0.293, p=0.027
Maximal untwisting rate	r=−0.359, p=0.006	r=−0.305, p=0.021

Conclusions: Patients with PSA have an evidence of subclinical myocardial dys-



function which was correlated with markers of chronic inflammation. Speckle tracking imaging could be used for detecting and monitoring subtle cardiac dysfunction in PSA.

P5425 | BEDSIDE
Diagnostic accuracy of global longitudinal strain by echocardiography for detecting cardiac involvement in patients with extra-cardiac sarcoidosis

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Background: Global longitudinal strain (GLS) quantified by echocardiography is a surrogate marker of left ventricular (LV) performance. Changes in GLS may signal the onset of structural alterations in the myocardium even before the development of overt LV dysfunction. Although it is expected that myocardial inflammation and scar associated with sarcoidosis may result in abnormal GLS, it has not been systematically evaluated. We examined the diagnostic characteristics of GLS in identifying patients with myocardial scar and/or inflammation in patients with extra-cardiac sarcoidosis.
Methods: We identified 40 consecutive patients with biopsy-proven extra-cardiac sarcoidosis who underwent a Rb82 and FDG cardiac PET for detection of inflammation and scar and a transthoracic echocardiogram within 60 days. GLS was quantified by speckle tracking (EchoPAC, GE Healthcare). Absence of Rb82 uptake and increased FDG uptake in the same myocardial segment represented inflammation; whereas, absence of Rb82 and FDG uptake in the same segment represented scar.
Results: Of 40 patients (47±10 y, 52% men), 25 had abnormal FDG uptake representing scar, inflammation or a combination of both. LV ejection fraction was lower (43±16% vs 54±7%, p=0.03) and GLS was increased (–13.6±4.5 vs –18.8±2.8, p=0.001) among patients with abnormal FDG-PET. The area under the receiver operating characteristic curve was 0.86, p=0.0001 with a sensitivity of 80% and specificity of 87% using a GLS cutoff of –16.9 for identifying patients with cardiac inflammation or scar detectable by FDG-PET.
Conclusion: GLS > –16.9 in patients with extracardiac sarcoidosis may point to myocardial involvement with scar and (or) inflammation. Validation of these findings in an independent group of patients is necessary in order to use alterations in GLS as a marker of cardiac sarcoidosis.
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P5426 | BEDSIDE
The usefulness of left atrial volume index and left ventricular mass index in determining subclinical cardiac involvement in patients with early-stage sarcoidosis

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Sarcoidosis is a multi-systemic granulomatous disease of unknown etiology. The present study has been designed to evaluate the importance of diastolic dysfunction with left atrial volume index (LAVi) and left ventricular mass index (LVMi) in determining subclinical cardiac involvement in subjects with stage I-II pulmonary sarcoidosis.A total of 54 patients under follow-up for sarcoidosis without cardiac involvement and 56 healthy subjects were included in the study. Among the 110 participants included in the study, 54 had stage I-II (49 stage I, 5 stage II) sarcoidosis and 56 were healthy subjects.There was no statistically significant difference between the two groups regarding age, gender, systolic and diastolic blood pressure, heart rate, body mass index and smoking. None of the patients with sarcoidosis was receiving oral or inhaled steroids. There was no clinical finding suggestive of cardiac involvement in any of the patients. The echocardiographic assessment of the patients revealed no significant difference between the two groups regarding left ventricular end-systolic and end-diastolic diameters, ejection fraction and annular velocity determined by tissue Doppler evaluation.The LVEF calculated with the modified Simpson's method was 61.8±7.8% in the sarcoidosis group versus 64.1±2.7% in the control group (p: 0.04).Left ventricular interventricular septum thickness, posterior wall thickness and relative wall thickness were significantly higher in the sarcoidosis group compared to the control group ($p<0.001$).The sarcoidosis group had higher LVM and LVMi values compared to the control group (sarcoidosis group 145±18.1 and 79±14 g/m^2, control group 135±27.7 and 74±14.2 g/m^2; respectively, p: 0.020 and p: 0.021).Left atrial end-systolic volume and left atrial volume index were higher in the sarcoidosis group (28.7±18.5, 15.6±10.2) compared to the control group (16.6±10.9, 8.9±5.5) with a statistically significant difference ($p<0.001$).The present study indicates diastolic dysfunction and increased LVMi despite normal systolic function in patients with early-stage sarcoidosis without cardiac involvement.Also, the diastolic parameters were normal without showing any significant difference compared to the control group while there was a statistically significant increase in LAVi.This finding suggests that LAVi may be the earliest marker of diastolic dysfunction in patients with early-stage sarcoidosis without cardiac involvement.

ASSESSMENT OF LEFT VENTRICULAR FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY

P5427 | BEDSIDE
2D speckle tracking-derived left ventricle global longitudinal strain: is it useful to discriminate left ventricular dysfunction stages?

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Background: 2D speckle tracking-derived left ventricle (LV) global longitudinal strain (GLS) is a validated method for LV systolic function assessment. We aimed to study LV GLS predictive power for impaired systolic function against 2D LV ejection fraction (LVEF).
Methods: We prospectively included 68 patients referred for echocardiography at a tertiary centre. Patients with significant valve disease, resting wall motion abnormalities or unsuitable images for GLS analysis were excluded. An independent operator confirmed the LVEF (biplane Simpson), followed by off-line GLS analysis by investigators blinded to the LVEF. Statistical analysis included LVEF and GLS correlation - linear regression, ROC curves construction for both GLS and GLS indexed for LV end-diastolic diameter (LVEDd) according to LVEF standard cut-offs, and optimal cut-off determination (Youden index).
Results: Mean age was 60±18 years; 62% were male, 22% had arterial hypertension, 38% heart failure and 20% ischemic heart disease. The mean LVEF and LV GLS were 48±16% and –14±6%, respectively, which were strongly correlated (r=–0.88, R2=0.78, $p<0.01$). We divided our sample in four pre-specified subgroups: normal LV function (LVEF≥55%, 48% of the sample) with mean LVEF 62±3% and GLS –20±3%; mild dysfunction (54≥LVEF≥45%, 19%) with LVEF 49±4% and GLS –14±5%; moderate dysfunction (44≥LVEF≥30%, 22%) with LVEF 37±5% and GLS –10±2%; severe dysfunction (LVEF<30%, 15%) with LVEF 22±15% and GLS –6±2%. The subgroups were similar in respect to age and sex ($p>0.05$). The performance of GLS and indexed GLS cut-offs for the stages of LV dysfunction are listed in the table. Indexed GLS was more specific in the discrimination, albeit less sensitive.

LV GLS cut-offs performance

Cut-offs	LVEF (%)	c-Statistic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
GLS -15.6%	<55	0.95	97.0	90.0	87.9	97.0
GLS -12.7%	<45	0.96	100	88.4	83.3	100
GLS -8.6%	<30	0.99	100	93.1	71.1	100
GLSindex -0.3%/mm	<55	0.97	95.0	93.3	94.7	93.3
GLSindex -0.2%/mm	<45	0.98	92.0	95.3	92.0	95.3
GLSindex -0.14%/mm	<30	0.98	90.0	91.3	64.3	98.1

PPV, positive predictive value; NPV, negative predictive value; GLSindex, GLS indexed for LVEDd.

Conclusion: LV GLS analysis was accurate in the discrimination of patients with normal LV function from those with progressive mild, moderate and severe levels of dysfunction.

P5428 | BEDSIDE
Relationship among left ventricular twist, torsion and contractility in hypertensive patients: one-beat real-time three-dimensional speckle tracking echocardiography study

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Purpose: Left ventricular (LV) twist and torsion caused by contraction of inner

and outer oblique muscle may reflect contractility and play an important role in squeezing the blood out of the heart and contribute a part of stroke volume. However, the difference between LV twist and torsion and the relation between torsion and LV function have not been fully examined. Recent advances in one-beat 3-dimensional speckle tracking echocardiography (3D-STE) with high volume rates enabled us to assess LV torsion and LV phasic strain rate (SR). Thus, we sought to examine the relation between LV twist and torsion and the relation between LV torsion and LV function using the 3D-STE.

Methods: A total of 81 subjects were enrolled {23 controls (age 62±12), 37 patients with hypertension (HTN) (age 69±12) and 21 patients with hypertensive heart failure (HHF) (age 75±18)}. LV twist and torsion were examined using the 3D-STE with 70–80vps. Twist was defined as the maximum difference in rotation angle between base and apex (unit is °). Torsion was defined as LV twist/LV long axis length (unit is °/cm). Torsion was derived from the time-twist curve and integrated by LV long axis length for every instance in time (each frame). We examined LV ejection fraction (EF) and LV strain and SR during systole as an index of contractility by the 3D-STE.

Results: LV twist, torsion, strain and SR during systole were measured with the novel 3D-STE within 3 minutes. There was significant correlation between twist and torsion in a total of 81 subjects (r=0.53). LV twist in HTN increased compared to control (control: 8.2±1.0, HTN: 9.4±1.4* and HHF: 9.0±1.6°, *p<0.05 vs control). LV torsion in HTN also increased but that in HHF decreased (1.35±0.18, 1.54*±0.29 and 1.17±0.19°/cm*, respectively). LVEF and LV strain and SR were reduced in HHF (LV radial strain; control: 35±6, HTN: 37±6 and HHF 24±14s-1*). LV torsion had a significant correlation with LVEF (r=0.43, p<0.01), whereas LV twist had no correlation with LVEF. LV torsion had a significant correlation with LV strain (longitudinal: r=–0.37, radial: r=0.43, circumferential: –0.38, p<0.05, respectively) and SR during systole in 2 directions (radial: r=0.50, p<0.01), whereas there was no correlation between LV twist and LV strain or SR.

Conclusion: This study demonstrated that LV torsion but not twist had a significant correlation with not only LVEF but also LV strain and SR during systole assessed by novel 3D-STE. This suggested that LV torsion may be an index which reflects LV contractility as well as an index of LV systolic function and more useful 3D-STE parameter than twist.

P5429 | BEDSIDE
Left ventricular mechanics: novel tools to evaluate function and dyssynchrony in controls and cardiac resynchronization therapy candidates

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Backgroud: Left ventricular (LV) pressure–strain loops (PSLs) have been recently validated as a non-invasive index of myocardial performance. Aim of the present study is to compare average cardiac work (avgCW), positive work (avgPW), negative work (avgNW) and work efficiency (WE) in normal subjects (NOR) and in cardiac resynchronization therapy candidates (CRT).

Methods: We included in this study 20 NOR and 61 CRT patients (mean LVEF, GLS and QRS duration: 64±5 vs 27±5%, –23±2 vs –8±3%, 71±21 vs 170±17 msec; respectively, all p<0.0001). Strain traces and valvular event times were used for the calculation of LV-PSLs.

Results: With respect to NOR, CRT patients showed an increase in avgNW (329±139 vs 174±67 mmHg%, p<0.0001), a significant decrease in avgCW (640±371 vs 2130±206 mmHg%, p<0.0001), avgPW (994±378 vs 2338±204 mmHg%, p<0.0001), and WE (74±10 vs 93±3, p<0.0001). The attached figure is displaying a typical example of a NOR and of a CRT patient. In CRT, the reduction in GLS (upper panel) is associated with a lengthening of time-to-peak GLS (TTP), particularly in the interventricular septum (IVS) (middle panel). The WE is globally reduced in CRT, but this reduction is greater in the IVS (lower panel).

Conclusions: Regional LV-PSLs allow the assessment of global and regional myocardial performance. Their relationship with LV dyssynchrony provides a window for a best understanding of LV mechanics and it will help in defining the most specific parameter for predicting the non-response to CRT.

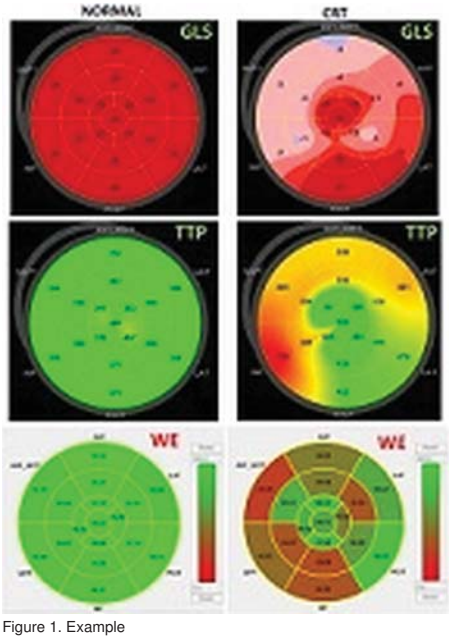

Figure 1. Example

P5430 | BEDSIDE
Less is more: three dimensional strain may not add much

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Background: Global longitudinal strain (GLS) is a robust and sensitive marker of subclinical cardiac dysfunction. Although 2-dimensional (2D) and 3D strains are different, it is unclear which is better.

Purpose: To compare the association of 2D and 3D GLS with cardiac anatomy, function, exercise capacity and the number of risk factors.

Methods: Using a commercially-available ultrasound system, both 2D and 3D echocardiography were performed in 345 (71±5yrs, 174 males) community-based patients with stage A heart failure. The 3D assessments were performed using a commercially available software. Exercise capacity was assessed by 6 minutes' walk distance (6MWD) and DASI score. Spearman's correlation coefficient was calculated and they were compared using z-transformation.

Results: Although 2D and 3D GLS were associated (rho=0.34, p<0.0001), there was a bias of 1.8%, large limits of agreement (7.3%). Both 2D and 3D GLSs were correlated with either of 2D or 3D ejection fraction (Table). Although 2D LV mass index was not associated with either GLSs (p=0.78, p=0.40), 3D LVMI was significantly correlated with 2D GLS only (p=0.03). 2D GLS was associated with exercise capacity (DASI Mets, p=0.012; 6MWD p=0.039) but 3D GLS did not (p=0.79; p=0.15, respectively).Similarly, the number of risk factors was only correlated with 2D GLS (p<0.001).

	2D GLS		3D GLS		P-value
	rho	P-value	rho	P-value	2D vs 3D
2D EF	–0.29	<0.001	–0.12	0.023	0.022
3D EF	–0.50	<0.001	–0.53	<0.001	0.64
2D LVMI	0.07	0.78	0.045	0.40	0.72
3D LVMI	0.12	0.032	0.059	0.27	0.46
LAVI	0.15	0.78	–0.047	0.38	0.01
E/e'	–0.005	0.92	0.003	0.96	0.92
DASI Mets	–0.13	0.012	–0.015	0.79	0.12
6MWD	–0.11	0.039	–0.078	0.15	0.72
No. of RFs	0.22	<0.001	–0.072	0.18	0.042

Conclusion: 2D and 3D GLSs are discordant. The stronger correlation of 2D GLS with LV mass index, exercise capacity and risk factors suggests that it may be a more accurate representation of LV function than 3D GLS.

P5431 | BEDSIDE
Early detection of myocardial injury by layer-specific strain imaging

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Background: The left ventricular wall of the heart comprises 3 myocardial layers, which differ obviously in cell structure, electrophysiological activity, blood perfusion and myocardial mechanics.

Purpose: This study aims to validate transmural strain gradient of myocardium measured by layer-specific strain imaging in different subjects.

Methods: Totally ninety-eight subjects were enrolled in this study, including 38 healthy people, 33 patients with cardiovascular risk factors but no coronary disease or heart failure (high-risk group) and 27 patients with heart failure. Using layer-specific strain imaging, peak longitudinal strain (PLS) and peak circumferential strain (PCS) of all three layers' myocardium were measured in the three groups.

Results: The PLS and PCS of endo-, mid-, and epi-myocardium (PLSendo, PLSmyo, PLSepi; PCSendo, PCSmyo, PCSepi) decreased gradually in all three groups (all P<0.001). The PLS and PCS of all the three layers were significantly lower in group with heart failure than in other two groups (all P<0.001). There

Differences of gradient in layer strain in three groups (healthy subjects > risk group > heart failure group)

Group	N	PLS			PCS		
		endo-mid	mid-epi	endo-epi	endo-mid	mid-epi	endo-epi
Healthy subjects	38	–4.66±1.40#	–4.57±1.86	–9.22±2.85	–10.12±3.09	–7.24±1.96	–17.37±4.89
High-risk patients	33	–2.99±0.71	–2.45±0.58	–5.44±1.29	–8.60±2.21	–5.23±3.77	–13.83±5.68
Heart failure	27	–1.54±0.79	–1.41±0.65	–2.96±1.36	–2.47±1.37	–1.80±0.86	–4.27±2.20
F		51.68	46.08	58.01	37.57	20.17	31.82
P		P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001

were no significantly differences in PLSendo, PLSmid, and PCSendo between healthy subjects and high-risk group. But the strain gradient among the three layers (PLSendo-myo, PLSmyo-epi, PLSendo-epi; PCSendo-myo, PCSmyo-epi PCSendo-epi) had statistically significant differences in three groups (healthy subjects> risk group> heart failure group) (all p<0.001).
Conclusions: There is a gradient of myocardial strain in PLS and PCS, both of which decrease gradually in the order of endo-, mid- and epi-myocardial strain in all groups. Compared with peak myocardial strain, differences of gradient in layer strain are more sensitive to detect early myocardial injury than peak myocardial strain.

P5432 | BEDSIDE
The Association between Early Stage Renal Insufficiency, Subclinical Left Ventricular Systolic Dysfunction and Torsion in Asymptomatic Subjects

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Background: Recent studies have highlighted a strong link between chronic kidney disease and adverse cardiovascular outcomes, including heart failure. However, left ventricular (LV) structural and mechanical adaptations in relation to earlier stage renal insufficiency remain unclear.
Methods: We consecutively studied an asymptomatic population underwent annual cardiovascular survey. Transthoracic echocardiography with tissue Doppler, myocardial deformations (longitudinal and circumferential) and torsion were analyzed by 2D speckle-tracking. We categorized subjects into 4 groups based on estimated Glomerular Filtration Rate (eGFR): >90,75–89, 60–75, and <60ml/min/1.73 m^2.
Results: Of all 3,898 asymptomatic subjects (mean age 49.86±10.83, female 34.6%), we observed a trend toward greater LV mass index, larger left atrial volume index and lower mitral annular relaxation velocity E' across 4 groups (Table 1, all trend p<0.001). There were also a trend toward longitudinal and circumferential functional decline (adjusted estimate: –0.5 & –0.09 in multivariate models, both p<0.05) though enhanced torsion (2.17, 2.20, 2.27, 2.45°/cm, respectively) among 4 eGFR groups (all trend p<0.001), with relatively preserved ejection fraction.

Table 1

Variables	Group 1 (n=1881)	Group 2 (n=1391)	Group 3 (n=553)	Group 4 (n=73)	Trend p
eGFR, ml/min /1.73 m^2	≥90	75–89	60–74	<60	
Age, years old	47.48±10.51	50.08±10.08	53.88±10.94	59.60±10.94	<0.001
NT-ProBNP, ng/ml	35.71±47.46	37.98±35.10	49.43±44.26	69.07±52.04	<0.001
Lateral E', cm/sec	10.96±2.94	10.21±2.72	9.47±2.68	8.06±2.26	<0.001
LVEF, %	62.60±5.14	62.31±5.09	62.35±5.16	61.27±6.37	0.081
Global longitudinal strain, %	–20.51±1.91	–20.14±1.91	–19.99±1.91	–19.54±1.94	<0.001
Global circumferential strain, %	–21.44±3.58	–21.31±3.62	–21.17±3.61	–20.95±3.22	0.320
Twist, °	13.52±5.30	13.86±5.35	14.30±5.39	15.53±5.45	0.001
Torsion, °/cm	2.17±0.90	2.20±0.89	2.27±0.92	2.45±0.87	0.016

Conclusion: Both renal and cardiac functions may deteriorate in parallel prior to clinical symptoms onset with augmented torsion mechanics, which may result in unchanged global ejection fraction. Our study demonstrated that depressed myocardial deformations in early renal insufficiency may be compensated by augmented torsion to maintain global pump performance.

P5433 | BEDSIDE
Do deformation patterns reveal the underlying pathophysiology in hearts with thick walls?

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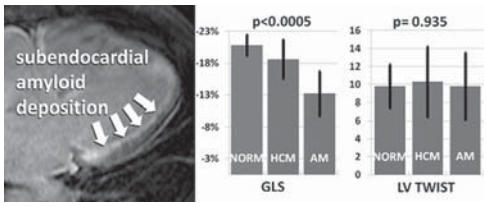
Purpose: To characterize subsets of "hypertrophied" hearts with preserved ejection fraction (EF) and to link deformation patterns with underlying pathophysiology.
Methods: We included 22 patients with biopsy-proven cardiac amyloidosis (AM) (68±11 years, 70% male, 60% AL type) with EF>50%, 20 hypertrophic cardiomyopathy (HCM) patients (51±17 years, 70% male) and 20 normal volunteers. All subjects had cardiac magnetic resonance (cMR) with late gadolinium enhancement (LGE) within 15 days pre/post echo. Regional and global longitudinal (GLS), circumferential (CGS) and radial (GRS) strain indices along with left ventricular (LV) twist were calculated based on the two-dimensional (2D) speckle tracking data.
Results: EF was not significantly different among groups (63.7±8.7% in AM, vs 66.2±8.8% in HCM vs 65.2±5.2% in controls, p=0.648). AM patients had significantly lower strain components compared to HCM and controls (GLS: –12.7±3.5% vs –18.1±3.1% vs –18±1.7%, GCS: –16.6±4.4% vs –21.5±5.3% vs –25.3±4.7%, GRS: 8.3±3.3% vs 14.6±4.4% vs 17.9±6.3%, p<0.0005 for all comparisons). In contrast, LV twist was preserved (9.8±3.7° vs 10.3±3.9° in HCM vs 9.8±2.4° in controls, p=0.935). After qualitative assessment of MRI LGE patterns



we hypothesize that this strain-rotation discordance in AM patients is attributed to a predominant subendocardial amyloid deposition, sparing the function of subepicardial fibers, which are mainly responsible for systolic twist (Figure).
Conclusions: The strain-rotation discordance observed in amyloidosis can be explained by the layer-specific deposition of amyloid. Deformation imaging offers useful insights in the pathophysiology of the disease and may facilitate a better diagnostic differentiation between various entities of hypertrophic LV pathology with preserved EF.
Acknowledgement/Funding: 2014 European Association of Cardiovascular Imaging Research Grant

P5434 | BEDSIDE
Automated quantification of global left ventricular performance in patients with cardiac contractility modulation by speckle tracking imaging

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Purpose: Cardiac contractility modulation (CCM) is a potential novel therapy for advanced systolic heart failure with normal QRS duration. Clinical favorable effect has been observed including functional status, symptoms and exercise capacity. However, it remains unknown whether left ventricular (LV) geometry, function, and reverse remodeling will be improved. Therefore, we aimed to assess the information with comprehensive echocardiography with speckle-tracking imaging.
Methods: CCM was implanted in 37 patients (age 62±11 years; 87% male) who had ejection fraction (EF) <35%, New York Heart Association (NYHA) Class III symptoms and QRS <120ms. Two-dimensional echocardiography was performed (GE Vingmed Ultrasound AS, Horten, Norway) before and 12 months after CCM therapy to measure LV volumes and LV mass. LV global longitudinal strain (GLS) was assessed with automated function imaging (AFI).
Results: At 12-month follow up, the LV end-systolic volume (ESV) (136±44 vs 114±58 ml, P=0.001) (Fig. 1A) and the LV mass (240±72 vs 221±64 g, P=0.003) (Fig. 1B) were decreased significantly, and was accompanied by a significant gain in LVEF (28.1±7.7% vs 36.7±9.7%, P<0.001) (Fig. 1C). Furthermore, GLS increased significantly at 12 months (7.0±2.4% vs 8.0±3.0%, P=0.042) (Fig. 1D).

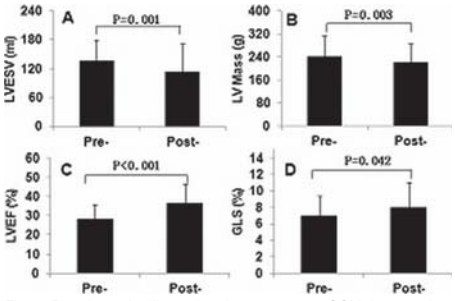

Fig. 1. Bar charts for illustrating the pre- & post-CCM therapy change of (A) left ventricular end-systolic volume (LVESV); (B) LV mass; and (C) ejection fraction (LVEF) and (D) global longitudinal strain (GLS), respectively.

Conclusions: Advanced HF patients with normal QRS duration could benefit from CCM therapy with improvement in LV remodeling as evident by the reduction in LV mass and LV volume. LV function was significantly improved with increase of both LV ejection fraction and LV GLS.

P5435 | BEDSIDE
Apical variant Tako-tsubo is associated with persistent myocardial strain dysfunction

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Purpose: Acute stress-induced Tako-tsubo cardiomyopathy (TTC) presents with sudden onset of chest pain that mimics a myocardial infarction and is precipitated by intense emotional/physical trauma. We have previously shown that myocardial energetics impairment and oedema persist for at least 4 months after presentation. This contrast with previous reports of echocardiographic normalisation of

LV twists mechanics at one month follow-up. In this work we comprehensively analysed myocardial deformation by 2D strain analysis at presentation and 4 months follow-up in a subgroup of apical TTC who presented predominantly with ST-elevation ECG.
Methods: Twenty patients (93% F, 66±12 years) with apical ballooning subtype of TTC fulfilling the Mayo criteria were studied within 3 days of presentation and after 4 months. Twenty-five age and gender matched controls (92% F, 65±11 years) underwent single echocardiographic assessment. Two-D strain, strain rate and twist mechanics were calculated.
Results: As shown in the Table, from acute presentation to follow up LVEF, global longitudinal peak systolic strain (GLPS), apical radial and apical circumferential strain improved significantly in TTC patients ($p<0.001$, $p<0.001$, $p=0.001$ and $p=0.012$ respectively). At follow up, LVEF normalized and was no longer different from controls ($p=0.658$). In contrast, GLPS and early diastolic relaxation (untwist rate) remained significantly impaired compared to controls at follow-up ($p=0.006$ and $p=0.022$, respectively).

	TTC acute (n=20)	TTC follow-up	p paired t-test$ between acute and follow-up	Controls (n=25)	P unpaired t-test$ between TTC follow-up and controls
EF, %	44.2±13.1	63.5±7.3	<0.001**	64.5±6.5	0.658
GLPS, %	−10.6±3.8	−16.03±2.5	<0.001**	−18.3±2.1	0.006*
Rad S - apex, %	15.0 (7.2–19.6)	34.0±19.0	<0.001**	28.4±14.1	0.283
Circ S - apex, %	−11.1±7.3	−18.1±5.6	0.012*	−20.3±4.1	0.145
Twist, °	10.6 7.9	13.5±7.1	0.444	15.2±5.5	0.408
Untwist rate, °/s	−71.3±38.9	−74.6±34.1	0.901	−99.7±30.8	0.022*

Mean ± SD or median (IQR) as appropriate. *p<0.05, **p<0.005, $or non-parametric equivalent.

Conclusion: In apical variant TTC presenting with predominantly ST-elevation on ECG global systolic deformation and early diastolic relaxation abnormalities persist following the acute event despite normalization of LVEF.

P5436 | BEDSIDE
Angiotensinogen gene M235T and T174M polymorphisms in systolic heart failure: changes of the left ventricular strain during six-month spironolactone therapy

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The aim of our study was to assess whether angiotensinogen (AGT) gene M235T and T174M polymorphisms affect response to the treatment with spironolactone. For this purpose we evaluated left ventricular longitudinal, circumferential and radial strain assessed by 2-dimensional speckle-tracking echocardiography (2DSTE) in patients (pts) with systolic heart failure.
Methods: We enrolled 39 pts (mean age 64 years) in stable state and NYHA class II or III. Mean left ventricular ejection fraction (LVEF) was 37,4%. All pts received an optimal HF therapy. Two-dimensional global longitudinal, circumferential, and radial strain were measured in each patient before starting spironolactone therapy and then after one- and six months. Circumferential and radial strain was measured at three levels: mitral valve, papillary muscles and apex.
Results: T235T allele of the AGT gene was found in 9 pts (23,1%). No carriers of the T174T allele of the AGT gene were found in the studied group. Serum aldosterone levels exceeded upper reference values (26 ng/ml) in 16 pts (41%) at baseline. LVEF increased insignificantly during the study (baseline – 37%, 1 month – 38,6%, 6 months – 39%; p=0,51). 2DSTE analysis showed significant improvement of the longitudinal, radial and circumferential strain parameters (average global longitudinal strain showed in the table). The analysis of a correlation between the presence of T235T allele and increased aldosterone plasma levels showed significant relationship for the radial strain in the middle level (papillary muscles) of the left ventricle only.

Global longitudinal strain

Global longitudinal strain	%	p value
Baseline	−11	p<0,01 for: baseline vs 1 month, 1 month vs 6 months, baseline vs 6 months
1 month	−14	
6 months	−15	

Conclusions: Left ventricular strain parameters are good indicators of improvement in left ventricular function during the treatment with spironolactone. Presence of T235T polymorphism in AGT gene does not seem to affect the response to treatment with spironolactone in patients with systolic heart failure.

P5437 | BEDSIDE
Early detection of chemotherapy induced biventricular cardiac dysfunction after bone marrow transplantation by speckle tracking echocardiography

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Purpose: The aim of this study was to detect chemotherapy induced cardiotoxicity on left ventricular (LV) and right ventricular (RV) performance, in patients early after bone marrow transplantation for hematologic malignancy, by means of both conventional and novel echo techniques.
Methods: We studied 28 patients (mean age 46±10 years, 14 men), admitted for bone marrow transplantation because of non-Hodgkin lymphoma, acute myelocytic or lymphocytic leukemia, multiple myeloma. Patients had preserved LV ejection fraction (LVEF) of >50%, without evidence of cardiac disease. We measured a) LV global (LVGLS-%) subendocardial and subepicardial strain and global strain rate (LVGLSR-l/s), RV longitudinal strain (RVGLS-%), LV circumferential strain-%, LV torsion-deg by speckle tracking b) three dimensional derived LV and RV ejection fraction (3DLVEF-%, 3DRVEF-%) c) tricuspid annulus plane systolic excursion (TAPSE-mm), and RV fractional area change (FAC-%) by two dimensional echocardiography and TDI derived lateral tricuspid annulus systolic velocity (S RV-cm/s). Studies were performed before (baseline) and 1 and 3 months after a single chemotherapy session followed by transplantation.
Results: Compared to baseline, LVEF and 3DLVEF did not change at 1 and 3 months post-chemotherapy (LVEF 58.9±6 vs 56.4±6 vs 56.8±5 respectively $P>0.05$, 3DLVEF 57.5±5 vs 57.2±5 vs 56.6±6 respectively $P>0.05$). However compared to baseline, impaired LVGLS and LVGLSR values were observed at 1 and 3 months (LVGLS 19.6±3 vs 18.2±3 vs 17.4±2.5 respectively, P=0.01 P=0.003 from baseline to 1 and 3 months respectively, LVGLSR 1.14±0.2 vs 1.03±0.15 vs 0.98±0.2 P=0.02 P=0.002 respectively). Myocardial layers deformation analysis, indicated that LVGLS changes were driven mostly by subendocardial longitudinal strain changes observed from month 1 post chemotherapy, whereas subepicardial GLS changes were observed at month 3 post-chemotherapy (subendocardial LVGLS 22±2.9 vs 20.1±2.8 vs 19.4±3.2 P=0.02 P=0.001 respectively, supepicardial LVGLS 17.5±2.8 vs 16.7±2.3 vs 15±2.3 P=0.07 P=0.02 respectively). No significant changes in LV circumferential strain and torsion were detected. RV TAPSE, FAC, S RV and 3DRVEF did not change post-chemotherapy. Compared to baseline, RVGLS was impaired post-chemotherapy (RVGLS 22.4±2.8 vs 20.1±2.8 vs 20.3±2.5 P=0.02 P=0.03 respectively).
Conclusion: Despite absence of alterations in cardiac performance assessed by conventional echo parameters and 3D echocardiography, speckle tracking imaging detects early subclinical dysfunction of both ventricles in bone marrow transplantation patients.

P5438 | BEDSIDE
Assessment of left ventricular dyssynchrony and prediction of response to cardiac resynchronization therapy: a new three-dimensionnal echocardiography integral-based indicator of longitudinal strain

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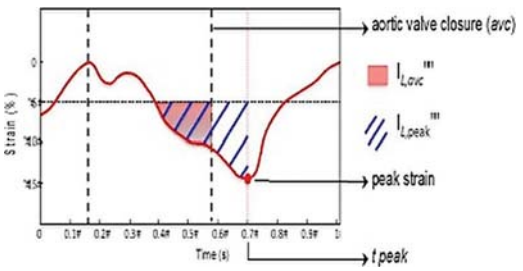
Background: So far, all attempts to improve patient selection for cardiac resynchronization therapy (CRT) by echo-derived mechanical dyssynchrony indices have failed. The aim of this study is to assess the performances of a new software for automatic quantification of integrals 3D regional longitudinal strain signals, combining temporal and functional information to explore left ventricular (LV) mechanics and to assess its potential value to predict CRT response.
Methods: 48 heart failure patients in sinus rhythm, referred for CRT device implantation (mean age: 65 years; LV ejection fraction: 26%; QRS duration: 160 milliseconds [160–170]) were prospectively assessed. 34,pts had positive response defined as LV end-systolic volume decrease >15% at 6-month. 3D longitudinal strain curves were exported for analysis by custom-made algorithms. The integrals of longitudinal strain signals were automatically measured and calculated for all 17 LV segments from the beginning of the cardiac cycle to the instant of the corresponding longitudinal strain peak (IL, peak).
Results: The standard deviation of IL, peak (SDIL, peak) for all 17 LV segments was larger in CRT responders than non-responders (1.18% s^{-1} [0.96; 1.35] versus 0.83% s^{-1} [0.55; 0.99], p=0.007). SDIL, peak (odds ratio [OR]: 12.1; 95% CI: 0.81–180, p=0.078) and septal flash (OR: 14.1; 95% CI: 3.08–64.9, p=0.001) were the only potential echocardiographic predictors of CRT response. The optimal cut-off value of SDIL, peak to predict response was 1.037% s^{-1}. In the 18 patients without septal flash, SDIL, peak was significantly higher in CRT responders.



Presentation of the method.

Conclusions: This new automatic analysis software of 3D longitudinal strain curves might be helpful to improve prediction of CRT response

MISCELLANEOUS

P5439 | BEDSIDE
Alterations of phasic left atrial strain in patients with pre-clinical diastolic dysfunction: 2D speckle tracking echocardiography-derived results from the BEFRI-echo study

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Background: Pre-clinical diastolic dysfunction (DD), defined by DD without signs of heart failure and normal left ventricular (LV) ejection fraction, has been associated with adverse outcome and identifies patients at high risk to develop heart failure with preserved ejection fraction (HFpEF). 2D speckle tracking analysis (STE)-derived data concerning changes of LA function in DD are scarce.
Purpose: We analysed echocardiographic data of a well-phenotyped cohort from the Berliner Frauen Risikoevaluation (BEFRI) study to assess changes of LA strain in preclinical DD.
Methods: Transthoracic echocardiography (Vivid E9, GE) was conducted in 449 female subjects of the BEFRI trial. Diastolic function was graded according to the recommendations of the EAE/ASE (DD0: healthy, DD1:impaired relaxation, DD2:pseudo-normalisation). Standard apical 4-chamber views were recorded, and LA strain was analysed using 2D STE (EchoPAC PC, GE Vingmed). Different phases of LA strain were identified: peak systolic strain (= LA reservoir function, LAR), strain during conduit phase (LAc), and strain during peak atrial contraction (LAa). LA conduit function was determined by (LAR – LAc), and LA pump function by (LAc – LAa). Differences of phasic LA strain were calculated using the Mann-Whitney-U test. To compare the diagnostic value for DD, linear regression and ROC analyses were conducted for LA strain and LA volume index (LAVI).
Results: 289 women were classified to DD0, 135 to DD1, and 25 to DD2. LAR and conduit function were significant predictors of DD ($p<0.001$), and were markedly attenuated in the presence of DD (reservoir/conduit function in DD0, DD1, and DD2, respectively: 43.1/27.2%, 33/16%, and 28.4/14.7%, $p<0.01$). This reduction was already significant in women with DD1, a mostly asymptomatic subgroup without LA enlargement, rises in filling pressures (E/E') or BNP. LA pump function was significantly higher in patients with DD1 (19%) compared to DD0 (17.6%); in women with DD2, LA pump function markedly decreased compared to DD0 and DD1 (14.6%, $p<0.05$). In ROC analysis, LA reservoir and conduit functions were superior to LAVI in diagnosing DD (sensitivity of LAR and conduit function: 73.7% and 87.2%, specificity: 80.4% and 75.8%), while the sensitivity of LAVI was markedly lower (51.5%;$p<0.001$).
Conclusion: All three LA phases show specific alterations with progressive stages of DD. Analysis of LA function is more sensitive in diagnosing early stages of DD compared to established parameters of LA enlargement. LA strain is easy to measure, and allows early diagnosis of DD, a recognised predisposing factor of HFpEF.

P5440 | BENCH
Subclinical IV systolic dysfunction in patients with chronic obstructive pulmonary disease

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Background: Patients with chronic obstructive pulmonary disease (COPD) can have left ventricule (LV) systolic dysfunction due to several reasons. We investigated subclinical LV systolic dysfunction in patients with COPD, and its correlation with the severity of airway obstruction, identified by GOLD classification
Methods: We studied 52 patients with COPD and 29 age and sex-matched controls, without any cardiac disease and with preserved LV EF. Conventional echocardiography and speckle tracking echocardiography (STE) based strain imaging were performed to analyze sub-clinical LV systolic function. All patients underwent spirometry.
Results: Conventional echocardiographic measurements (LV end diastolic diameter, LV end systolic diameter, LV EF) were similar between the groups. LV longitudinal peak systolic strain (14.76±2.69% to 20.27±1.41%, p=0.0001) and strain rate (0.75±0.25 1/s to 1.31±0.41 1/s, p=0.0001) were significantly impaired in patients, compared to controls, demonstrating sub-clinical ventricular systolic dysfunction. Significant positive correlation was obtained between LV strain/strain rate and spirometry parameters (FEV 1, FEV%, FEV 1/ FVC, PEF %) (r=0.78/0,68, p=0.0001; r=0,83/0.70, p=0.0001); r=0.74/0.55, p=0.0001; r=0.72/0.65, p=0.0001, respectively). Also there was significant negative correlation between LV strain/strain rate and GOLD classification (r=–0.80/–0.69, p=0.0001, respectively).
Conclusion: COPD can effect systolic functions in patients without known CAD. STE is a technique which provides additional information for detailed evaluation of subtle changes in LV myocardial contractility, significantly associated with the severity of the disease in COPD patients.

P5441 | BEDSIDE
Subclinic left ventricular dysfunction on echocardiography predicts long-term adverse events

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Background: Abnormal systolic or diastolic tissue Doppler parameters may occur despite normal left ventricular ejection fraction (LVEF). We investigate long term value of tissue Doppler imaging (TDI) in predicting cardiac events in patients with no history of heart disease and normal LVEF.
Methods: Subjects who underwent echocardiogram in our institution from 2002 to 2003 were included. They were aged 55 to 64 years, with no history of ischaemic heart disease, heart failure or structural heart disease and LVEF of ≥50%. TDI for this age group was divided into normal and abnormal according to published values. The composite primary endpoint (major adverse cardiovascular events, MACE) includes occurrence of myocardial infarction, coronary revascularization or congestive heart failure over a 10-year follow-up period.
Results: Of the 428 patients studied, 398 had normal TDI values while 30 patients had reduced mitral annular (septal or lateral) E' or S'. Although there was no significant difference in age between the 2 groups, patients with abnormal TDI had significantly lower LVEF and lower early diastolic trans-mitral flow velocities (Table). E/E' ratios were also higher in patients with abnormal TDI (Table). MACE was observed in 49 patients (12.3%) in patients with normal TDI while MACE occurred in 26.7% of patients with abnormal TDI ($p<0.001$, table). Reduced TDI E' or S' was associated with significant MACE (Kaplan Meier log rank = 5.77, P=0.016).

Table 1

	Normal TDI (n=398)	Abnormal TDI (n=30)	P value
Age (years)	59.0±2.9	58.9±2.7	0.92
LVEF (%)	65.2±4.0	63.1±5.4	0.002
Mitral E (cm/s)	71.8±16.1	62.0±16.6	0.002
DT (ms)	191.2±38.2	190.9±35.4	0.87
IVRT (ms)	80.6±17.3	85.7±15.3	0.13
Septal E' (m/s)	9.6±2.5	7.4±2.0	
Septal S' (m/s)	8.9±1.9	6.9±1.7	<0.001
Lateral E' (m/s)	12.1±2.9	9.1±3.0	
Lateral S' (m/s)	10.6±2.8	7.6±1.9	
Septal E/E'	7.8±2.2	8.6±2.2	0.05
Lateral E/E'	6.1±1.7	7.3±2.3	0.002
MACE (+)	49 (12.3%)	8 (26.7%)	<0.001
MACE (–)	349 (87.7%)	22 (73.3%)	

Conclusion: Subclinical left ventricular dysfunction predicts long term MACE.
Acknowledgement/Funding: No financial disclosures

P5442 | BEDSIDE
Left ventricular flow redirection towards the outflow tract: a marker for atrio-ventricular delay optimization

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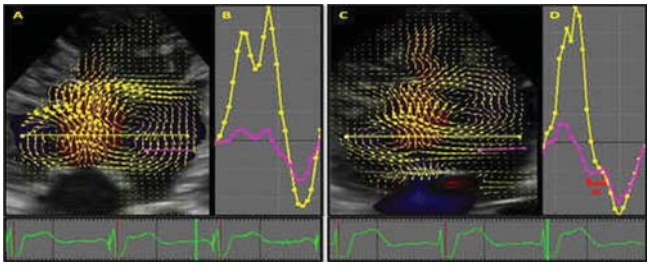
Introduction: Different echocardiographic algorithms have been defined to optimize of atrio-ventricular delay (AVD) in cardiac resynchronization therapy (CRT). Doppler-based techniques are commonly used, but slight changes in the position of the probe or the patients' breath can lead to error and inaccuracies.
Vector Flow Mapping (VFM) enables visualization of complex intracardiac flow patterns, allowing display and measurement of intracardiac vortices. Vortices are known to play a key role in left ventricular (LV) flow redirection towards the outflow tract, contributing to early ejection and minimising energy dissipation.
Methods: CRT patients in sinus rhythm underwent echocardiographic AVD optimization to compare concordance between trans-mitral flow optimization and vortex-flow guided optimization. VFM-based optimal AVD was considered the one in which the flow curve generated by the vortex was continued by the aortic ejection flow curve (Fig. 1, Panel B). Optimal AVD by trans-mitral flow was considered the shortest interval in which A-wave truncation was not observed. Results obtained with the two methods were compared using intraclass correlation coefficient (ICC).
Results: 12 patients (25% male, aged 68.7±10.5, LVEF 40.2±10.3) underwent



conventional trans-mitral and vortex-flow based optimization. ICC showed excellent concordance between the two techniques (0.94, CI [0.82–0.98], p<0.0005). Additionally, VFM-based optimal AVD calculation was faster then Doppler trans-mitral calculation (3.0±0.6 vs. 4.9±1.4 measurements, p<0.05).
Conclusions: AVD optimization guided by the optimization of the vortex-ejection flow curve is feasible and accurate. Additionally, it requires less repeated measurements than standard optimization guided by trans-mitral Doppler.

P5443 | BEDSIDE
Disturbed flow transit in heart failure with a history of decompensation

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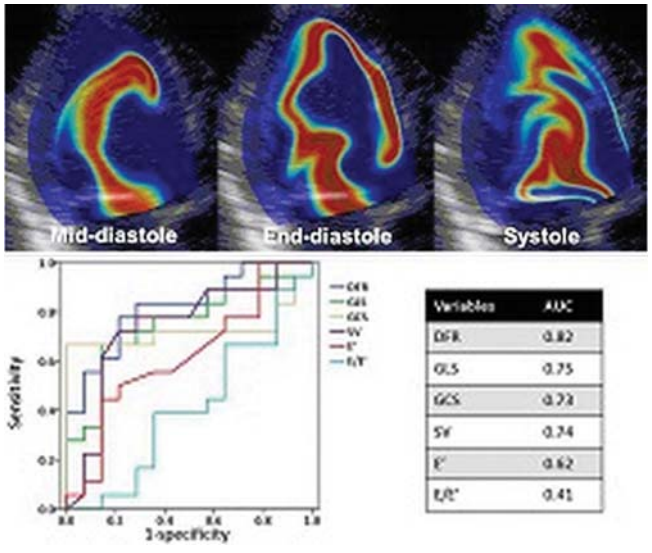
Background: The transition from diastole to systole is not a mere shift between the two distinct phases, but rather a continuous process in which intra-cardiac flows form vortices which help redirect flows toward the outflow. This smooth flow transition may contribute to the pump efficiency. We hypothesised that analysing flow transition can provide a new window for assessing left ventricular (LV) performance.
Methods: The present study examined 35 clinically stable patients with dilated cardiomyopathy (62±12 years old, LV ejection fraction = 33±12%, ischemic aetiology = 14 patients), including 15 patients with a history of decompensation and 20 patients without it. Blood transport inside the LV was visualised by tracking virtual ink tracers added over the diastole, using Vector Flow Mapping (Hitachi-Aloka, Tokyo). The amount of ink ejected in the following systole was quantified as direct flow ratio (DFR) = the amount of ink ejected in the following systole/the total amount of ink added over the diastole. LV global longitudinal and circumferential strains (GLS and GCS) were evaluated with speckle tracking. LV filling pressure was assessed by E/E'.
Results: DFR was correlated positively with stroke volume (r=0.49, p=0.003), GLS (r=0.73, p<0.001) and GCS (r=0.63, p<0.001), but not with E' (p=0.09) and E/E' (p=0.20). Patients with a history of decompensation had lower DFR than those without it (0.24±0.20 vs 0.48±0.18, p=0.001). ROC curve analysis revealed that DFR had a higher predictive value for the decompensation than GLS, GCS, stroke volume, E' and E/E'.



Conclusion: Flow transit is disturbed, although clinically stable, in heart failure patients with a history of decompensation.

CELL THERAPY AND BIOENGINEERING

P5444 | BENCH
Post-infarct administration of multilineage-differentiating stress-enduring (Muse) cells regenerates cardiomyocytes and microvessels and improves cardiac function and remodeling in rabbits

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Background: It has been reported that the mesenchymal stem cell (MSC) fraction in bone marrow aspirates contains pluripotent stem cells, Muse cells, which can self-renew and differentiate into cells with the characteristics of all three germ layers from a single cell. We investigated whether intravenously administered Muse cells could be mobilized to the ischemic myocardium, decrease the myocardial infarct size, and improve the cardiac function, comparing with the effects of MSCs.
Methods: Bone marrow (~2 mL) was harvested from the cavity of the femurs in male Japanese white rabbits. Bone marrow MSCs were cultured and expanded, and then Muse cells were isolated by FACS as SSEA-3(+) cells. In a 30-minute coronary occlusion and reperfusion rabbit model, 3x100000 of autologous Muse cells labeled with GFP (Muse group, n=10), saline (control group, n=10), 3x100000 of autologous MSC cells (MSC group, n=10), or 3x100000 of autologous non-Muse cells (non-Muse group, n=10) were intravenously infused at 24 hours after MI. The MI size, cardiac function, and general pathology of the heart were evaluated at 2 weeks post-MI. Confocal microscopy was performed to evaluate the regeneration of the myocardium.
Results: The MI size as a percentage of LV by Masson trichrome staining was significantly smaller in the Muse group (14.1±1.3%) than in the control group (31.7±1.3%), MSC group (21.7±1.3%), and non-Muse group (23.0±1.8). A smaller infarct size, smaller left ventricular (LV) dimensions, increased LV ejection fraction, and increased ±dP/dt were seen in the Muse group as compared with the other groups at 2 weeks post-MI. The number of CD31-positive microvessels was significantly greater in the Muse group than in the other groups. Transplanted Muse cells were preferentially attracted to the infarct border area in the ischemic area. Integrated GFP (+)-Muse cells were positive for ANP, a specific marker for neonatal cardiomyocytes, and troponin I, a specific marker for cardiomyocytes, and positive for CD31, suggesting the spontaneous differentiation of cardiomyocytes and microvessels from Muse cells.
Conclusions: The post-infarct administration of Muse cells reduces the myocardial infarct size and improves cardiac remodeling and functioning through the regeneration of cardiomyocytes and microvessels to a greater extent than MSCs. Muse cell transplantation may be a promising strategy for active acute MI-targeting treatment.

P5445 | BENCH
A novel cardiac bioprosthesis for myocardial repair

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Purpose: Cardiac tissue engineering, a novel therapeutical approach, combines the use of natural or synthetic supporting scaffolds with cardiomyogenic cells for myocardial damage restoration. In this context, we aimed to obtain a myocardial bioprosthesis based on decellularized myocardium refilled with adipose tissue-derived progenitor cells (ATDPCs).
Methods: Decellularized myocardial scaffolds were generated from porcine myocardium using two distinct decellularization protocols (DP): one protocol, named DP1, was detergent-based (SDS and Triton X-100), and the other, termed DP2, was trypsin based. Decellularization level was evaluated histologically and molecularly, the resulting scaffold structure was examined by scanning electron microscopy and matrix components were identified by immunohistochemistry.
Obtained decellularized scaffolds were refilled with RAD16-I peptide hydrogel and porcine ATDPCs. After one week of recellularization, cellular viability was assessed using a commercial kit, cell density was determined by nuclei counting and expression of cardiac (GATA4, connexin43 and cardiac troponin T) and endothelial (Isolectin B4) markers was analyzed through immunohistochemistry.
Results: After both protocols were finished, decellularized scaffolds were free of cellular debris and nuclear material, with a significant DNA content reduction of >90% compared to native myocardium (P<0.001). Decellularized myocardial scaffolds also preserved extracellular matrix main components, and its three-dimensional architecture and ultrastructure were retained once decellularization was completed.
One week following recellularization, ATDPCs were detected inside the decellularized scaffold and remained viable. However, in recellularized DP1 scaffolds the number of retained cells was significantly higher compared with recellularized DP2 scaffolds (236±106 and 98±56 cells/mm^2 for recellularized DP1 and DP2 scaffolds, respectively; P=0.04). Remarkably, in both recellularized scaffolds, ATDPCs expressed endothelial marker Isolectin B4, although only in recellularized DP1 scaffolds cells showed expression of cardiac markers GATA4, connexin43 and cardiac troponin T.
Conclusions: Acellular myocardial scaffolds, with preserved structure and matrix composition, were obtained with both decellularization protocols. However, in our hands, the detergent-based protocol (DP1) produced myocardial scaffolds with better cell recolonization and promoted ATDPCs expression of endothelial and cardiomyogenic markers, which suggests ATDPCs differentiation towards cardiac-like lineage in DP1 scaffolds.

P5446 | BENCH

Survival, migration and benefits of human cardiac progenitor cell seeded-collagen patches applied on failing right ventricle: preliminary results in a large animal model

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Background: Cell therapy using intramyocardial injections of cardiac progenitors issued from human embryonic stem cells showed benefits on overloaded right ventricular (RV) tissue remodelling and arrhythmic susceptibility but this delivery mode failed to improve RV function.
Purpose: Our aim was to evaluate in a porcine model of overloaded RV dysfunction a new cell delivery mode for such a therapy.
Methods: A combined overloaded RV dysfunction was obtained in piglets using a surgical procedure mimicking repaired tetralogy of Fallot. After 4 months, cell therapy was surgically administrated using 2 types of human NKX2.5+ cardiac progenitor cell-seeded collagen patches applied on the epicardium: QGel® and pressured-patches. Myocardial function was measured 1 month after transplantation by conductance catheter technique and echocardiography (standard and strain). The fate of progenitors was studied using antibodies directed against Nkx2.5, CD31, actinin and Islet1.
Results: All pigs survived without any complication. Pressured-patches allowed human progenitors to migrate towards the myocardium while QGel® patches restricted cell migration. In both cases, progenitors differentiated toward the cardiac lineage assessed by actinin expression and maintained their proliferation capacity. Concerning RV function, only pressured-patches (N=3) tended to improve the contractility (Emax slope). By contrast, this parameter decreased in QGel® patches animals (N=2). Moreover, in 2 pressured-patch animals, standard echocardiographic functional parameters (FAC, TAPSE, s'wave) were maintained while 2D strain and strain rate values increased.
Conclusion: Cell therapy using seeded-patches was more conservative for engrafted cells than intramyocardial injections but only pressured-patches seemed to give benefits on overloaded RV function and contractility. These promising results require further improvement in the design of the cell patch and to be confirmed on a long-term basis.
Acknowledgement/Funding: Leducq Fondation, Association Française contre les Myopathies,Centre Chirurgical Marie Lannelongue, INSERM, Université Paris Sud

P5447 | BENCH

Effects of cardiac stem cells in myocardial infarction; meta-analysis of preclinical studies

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Background: Cardiac stem cell therapy has emerged as a promising approach for cardiac repair after myocardial infarction (MI). Different populations of cardiac-derived stem or progenitor cells (CSCs) have been tested in animal models of MI; and although CSC clinical trials have already started it is unclear what the consistent effect is in experimental models.
Aim: Here we used meta-analysis to establish the overall effect size of CSCs in preclinical studies. We investigated whether small and large animal models have similar outcomes after CSC-injection. Next, we explored the influence of clinically relevant parameters to better predict and design future (pre)clinical studies using CSCs for MI.
Methods: We performed a systematic search of PubMed and Embase on Nov. 5th to identify all publications describing control-group based experiments of CSC therapy in animal models of MI. We determined the overall effect of CSC therapy on our primary endpoint; left ventricular ejection fraction (LVEF). We performed meta-regression analysis to investigate if clinically relevant parameters were of influence on LVEF; these parameters included animal type (large and small), cell type (cardiospheres/cardiosphere-derived cells (Cs/CDCs), c-kit+ cells and sca1+ cells), immunosuppression, cell structure in culture and administration (2D vs 3D) and donor specifics (comorbidity and allogeneity). We also assessed the quality of the included studies. Possible publication bias was assessed using Egger regression, Funnel plot and Trim and Fill analysis.
Results: We identified 64 relevant studies, reporting 1648 animals (993 treated, 655 controls). The overall effect of CSCs was an 11.1% (95% CI 9.6–12.6 $p<0.001$) improvement of LVEF compared to controls. Interestingly, CSC therapy had a greater effect in small animals compared to large animals 11.4% (95% CI 10.2–12.6) vs 7.0% (95% CI 3.0–11.0), respectively (p=0.039). Cell type was a significant predictor for LVEF improvement; Cs/CDCs (12.6%, 95% CI 11.0–14.2) performed better than c-kit+ cells (10.5%, 95% CI 8.0–12.9) and sca1+ cells (8.5%, 95% CI 5.6–11.3) (p=0.035). None of the other parameters were predictors of primary outcome. No publication bias was observed.
Conclusion: Treatment with CSCs resulted in a significant improvement of LVEF in all animal models of MI. There was a reduction in the magnitude of effect in large compared to small animal models, a trend that seems to continue in recent clinical trials. Although different CSC types have overlapping characteristics, we observe a significant difference in their effect in animal MI studies.
Acknowledgement/Funding: Alexandre Suerman program UMC Utrecht; Dutch Ministry of Economic Affairs, Agriculture and Innovation; Netherlands Cardiovasc Research Initiative (CVON)

P5448 | BEDSIDE

First-in-man experience with transendocardial injections of bone marrow-derived mesenchymal stem cells in idiopathic dilated cardiomyopathy. Results of the pilot phase of the MYOCYTE trial

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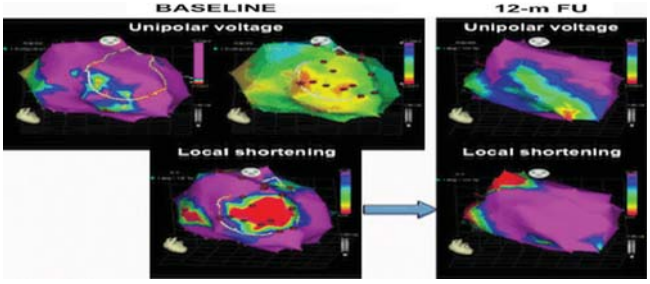
Background: In patients (p) with ventricular dysfunction, stem cell therapy has been studied mainly in the subset of ischemic heart disease.
Purpose: We present the first results of the first-in-man stem cell therapy trial in idiopathic dilated cardiomyopathy (IDC).
Methods: Randomized, double blind and placebo-controlled trial that will enroll 70 p with LVEF<45%, II-III NYHA and MVO2 12–21 ml/kg/min. In a first pilot phase, 10 p were all treated with bone marrow-derived mesenchymal stem cells (MSC) through 15 transendocardial injections (NOGA XP) in the anterior wall of the LV. In a second phase, 60 p will be randomized (3:1) to receive MSC or placebo. MSC are obtained after bone marrow harvesting and 3–4 weeks of culture in GMP facilities (dose: 30–40x10^6). Primary endpoints include MACE (all cause-death, admission due to heart failure, VT/VF, stroke), Holter, labs and incidence of complications with NOGA catheters (arrhythmias, perforation, myocardial ischemia). Secondary endopints include MVO2 and functional capacity, quality of life questionnaires, perfusion defects by SPECT and functional parameters by MRI. Follow-up with core-labs is scheduled for 2 years.
Results: Ten p have been included, 60,4±8,1 years and 6 p male (60%). Baseline LVEF was 32,3±8,4% by echo. Baseline MVO2 was 17,5±3,9 mL/kg/min, and 9 p were in II NYHA funcional class. One VF during injections was observed so far, with no more intra-procedural events. In the follow-up, we reported 1 sudden death (8.5 months after treatment). Echocardiographic follow-up at 3 months is available for all p, showing a LVEF of 39.0±11.6%.



NOGA XP electroanatomical maps, after FU

Conclusions: To the best of our knowledge this is the first randomized trial with transendocardial injection of MSC in this scenario. MSC injection seems to be safe, and could be potentially beneficial.
Acknowledgement/Funding: Funded by the Ministry of Health (General Direction of Pharmacy and Health Products) as a "Grant for Independent Research" 2010

P5449 | BENCH

Endothelial derivatives of human pluripotent stem cells show antiplatelet effects in 3D culture -steps towards vascular tissue engineering

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Background and purpose: Endothelial derivatives of human pluripotent stem cells may offer regenerative treatments in ischemic cardiovascular diseases. Here we studied differentiation conditions toward mature endothelial population as well as fate and function of these cells during 3D culturing.
Methods and results: To optimize endothelial development, human embryonic stem cells (hESC) were differentiated via embryoid body (EB) or monolayer method under normoxic and hypoxic conditions. CD31-positive endothelial cells (EC) were sorted by FACS and compared with human induced pluripotent stem cell-derived endothelial cells (hIPSC-EC) and human adult coronary arterial endothelial cells (HCAEC). Both hESC-EC and hIPSC-EC showed mature endothelial characteristics such as cobblestone pattern, ac-LDL uptake, and tube formation in vitro. Proteome profiling revealed high abundance of angiogenesis-related proteins in cell lysates and supernatant. As assessed by qPCR, angiopoi-

etin2 mRNA levels increased in hESC-EC when differentiated via EB method (EB in normoxia 353.17±86.29; EB in hypoxia 323.89±86.63, monolayer 27.20±9.92 vs. hESC, $p<0.001$). Expressions of arterial (EphrinB2, Notch1–2) and venous (EphB4) endothelial markers were increased, suggesting the presence of mixed endothelial population in culture. However, no significant differences were found in ratio of arterial and venous subpopulations in the different developmental protocols. For engineering 3D vascular constructs decellularised human aortic slices (300μm) were repopulated with hESC-EC and hIPSC-EC and cells remained viable on engineered matrices in vitro. Engineered bioscaffold were incubated with platelet rich plasma from healthy adults. 3D culture conditions activated antiplatelet effects of the cells (as shown by secreted levels of chemokine Rantes (pg/ml): hESC-EC 229.6±37.9, hESC-EC on bioscaffold 83.6±52.1; hIPSC-EC 234.9±22.8, hIPSC-EC on bioscaffold 127.9±63.6, $p<0.01$, n=6).
Conclusions: Differentiation conditions modulate endothelial development and angiogenic gene expression. 3D culturing increased antiplatelet effects. Functionally active endothelial derivatives of human pluripotent stem cells promises vascular tissue engineering for therapeutic purposes.
Acknowledgement/Funding: Hungarian Scientific Research Fund OTKA 10555

CARDIOVASCULAR PATHOLOGY AND STEM CELLS

P5450 | BENCH
Erythropoietin promotes cardiac autonomic dysfunction and does not modify end diastolic pressure in a myocardial infarction model in rats

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Background: The administration of erythropoietin (EPO) after myocardial infarction (MI) has been used to reduce myocardial infarct size and to improve cardiac function. Most of the evidence was obtained in short term after MI and the mechanisms involved in this improvement are not well known.
Purpose: To evaluate EPO effects on autonomic and hemodynamic parameters in an experimental model of chronic myocardial infarction.
Methods: Wistar rats were divided in three groups: control (C: n=9), infarcted (MI: n=9) and infarcted treated (EPO) rats (EMI: n=9). EPO was administered (1,000UI/kg/3 days on week) for 12 weeks. MI was induced by coronary occlusion. The animals were catheterized for direct blood pressure recording. Heart rate (HR), heart rate (HRV) and systolic blood pressure variability (SBPV) as well as end-diastolic pressure were evaluated.
Results: There were no differences in the HR values between the groups (C= 336.56±0.82, MI= 345.69±0.78, EMI= 353.30±1.26bmp). Mean Arterial Pressure was significantly higher in EMI group compared to MI and control groups (C= 104.31±0.69, MI= 94.79±0.54, EMI= 126.21±0.55 mmHg). Regarding HRV, pulse interval variance was lower in infarcted groups (MI and EMI) in comparison with control (C= 117.34±1.39, MI= 46.03±1.04, EMI= 61.46±1.15 ms^2). Moreover, low and high frequency components of HRV were lower in EMI group when compared to MI and C group (LF%: C= 23.79±0.48, MI= 17.53±0.57, EMI= 6.67±0.36; HF: C= 76.21±0.48, MI= 82.47±0.57, EMI= 48±0.81) suggesting a marked reduction of HRV in these animals. The SBPV was higher in the EMI group compared to IM and control groups (VARPAS: C= 24.45±0.54, MI= 25.45±0.65, EMI= 38.44±0.70 $mmHg^2$). In addition, the end-diastolic pressure (EDP) values of the left ventricle were higher in infarcted groups (MI and EMI) than in control group (C = 4,23±0,21, MI= 10,58±0,26, EMI= 9,60±0,20 mmHg).
Conclusions: The EPO administration in MI rats increased MAP and promoted autonomic dysfunction evidenced by decreased HRV and increased SBPV. Moreover no improvement was observed in EDP.
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P5451 | BENCH
Single-centre experience with 3D printing cardiac anatomy: feasibility and controversies

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Background: Patient-specific models of cardiac anatomy, and congenital heart disease (CHD) in particular, manufactured by means of rapid prototyping (3D printing) could facilitate communication between patients (and their families) and cardiologists, and improve patients' comprehension of their condition, with favorable repercussions on lifestyle adjustments. Albeit anecdotal evidence suggests that 3D models hold great promise for studying, interpreting and explaining cardiac anatomy, systematic testing is lacking.
Purpose: To evaluate patients', parents' and cardiologists' perspectives on the feasibility of using 3D models in clinical practice.
Methods: Questionnaires were administered to 97 parents of children with CHD and to their cardiologists during follow-up visits. Parents were divided into Group1 (n=52, normal consultations) and Group2 (n=45, with 3D models from magnetic resonance imaging printed with rapid prototyping technology additionally used). Participants and cardiologists completed ratings (0–10) to assess parental knowledge before and after the consultation. Both users (expert and non-expert) provided feedback on 3D models as communication tools. Moreover, 2 focus groups (n=13 teenagers with CHD, n=15 parents) explored features of 3D models, such as material options (rigid vs. compliant, white vs. colorful, transparent vs. opaque).
Results: Cardiologists rated models as "very useful" (8.8±1.1/10), stimulating parent interaction (9.1±1.4/10) without lengthening consultation time (93% cases), although consultations with models lasted 5 minutes longer (p=0.02). Parents also rated models as "very useful" (9.5±0.7/10) and more informative than medical images or diagrams. Generally parents self-reported improved understanding following their visits, however in 40% of cases two blinded cardiologists who re-analyzed the questionnaires were not able to gather even the primary diagnosis based on the information provided by parents, identifying a major knowledge gap. The focus groups highlighted that patients and parents found transparent models helpful in elucidating a specific defect and generally agreed that red-and-blue models are more familiar and descriptive.
Conclusion: Clinicians found 3D models useful in describing congenital defects. Models encouraged expert/non-expert users interaction. Employing this modality may stimulate patients' and parents' participation, as they appreciated the technology. Short-term parental knowledge, however, did not improve, highlighting the importance of further systematic testing alongside with regulatory work.

P5452 | BENCH
Insights into the anatomical sites of acute left atrial appendage reconnection after successful electrical isolation

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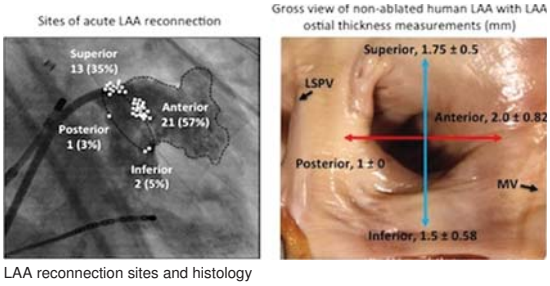
Introduction: The left atrial appendage (LAA) is reported to be a common trigger site in atrial fibrillation (AF). Due to the non-uniform ostial anatomy, LAA electrical isolation is challenging.
Purpose: We sought to evaluate the anatomical sites of acute LAA reconnection following successful isolation to define areas that may require more consideration during ablation.
Methods: 22 patients with longstanding persistent AF (mean duration 25±15 months) underwent LAA isolation with irrigated radiofrequency ablation following a standard AF ablation. LAA entrance and exit block were confirmed with intravenous adenosine after 60 min. Where reconnection was identified, ablation was performed to re-isolate the LAA.
A group of cadaveric human hearts were then examined macroscopically and histologically to assess regional variations in LAA ostial thickness in order to correlate with the observed sites of acute reconnection.
Results: 20/22 (91%) LAAs were electrically isolated. Acute LAA reconnection occurred in 17/20 (85%). In these cases, there were a total of 37 episodes of acute LAA reconnection, mean 2.2±1.2 episodes per case. All were successfully re-isolated.
We studied the LAAs of 4 human hearts without previous ablation for comparison. The thickest areas were at the anterior (2.0±0.8mm) and superior (1.8±0.5mm) LAA margins. This correlated with the recorded sites of acute reconnection.



LAA reconnection sites and histology

Conclusions: The addition of LAA electrical isolation to a persistent AF ablation has the potential to improve arrhythmia free survival. However, there is a substantial acute LAA reconnection rate, sites of which correlate with regions of thicker ostial tissue. This novel finding may improve our ability to deliver effective ablation to achieve durable LAA isolation.
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P5453 | BENCH
Central donepezil infusion prevents progression of cardiac remodeling and dysfunction in chronic heart failure rats with extensive myocardial infarction

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Introduction: Previous studies have proved that oral administration of donepezil

improves prognosis in chronic heart failure (CHF) rats, but its mechanisms remain unclear. As a centrally acting reversible acetylcholinesterase inhibitor, donepezil may exert the beneficial effects through a central mechanism. The present study aimed to test whether central infusion of donepezil would effectively prevent cardiac remodeling in CHF rats after extensive myocardial infarction (MI).
Methods: Rats survived for one week after MI were implanted with a blood pressure transmitter and a micro-infusion pump which connected with a cerebroventricular cannula. Animals were randomly assigned to central saline (CST, n=14) or central donepezil (CDT, n=13) infusion group. Donepezil was administered at a dosage of 0.1 mg/kg/day (one fiftieth of an oral dose used in the previous studies) for 6 weeks.
Results: Although there was no significant difference in the MI size between the two groups, CDT significantly decreased the heart rate (300±12 vs. 341±10 bpm, $P<0.05$) and prevented cardiac dysfunction [Left ventricular (LV) dp/dt max, +16%; Cardiac index, +25%; LV end-diastolic pressure (LVEDP), –5mmHg; Right atrial pressure (RAP), –3mmHg] compared with CST group. CDT also decreased biventricular weight and cardiac fibrosis (2.77±0.07 vs. 2.97±0.05g/kg, $P<0.05$; 4.9±0.8 vs. 9.0±0.9%, $P<0.01$). Plasma levels of BNP and norepinephrine were significantly lower in CDT than CST group (359±8 vs. 429±27pg/ml, $P<0.05$; 741±215 vs. 1566±217pg/ml, $P<0.05$).
Conclusion: The central mechanism plays an important role in the donepezil treatment which prevents the progression of cardiac remodeling and dysfunction in CHF rats.

P5454 | BENCH
Isolation, characterization and bio-grafting of perivascular progenitor cells from myocardial specimens of paediatric patients undergoing palliative surgical repair of congenital heart defects

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Background: Congenital heart disease (CHD) still represents the primary cause of death among infants in industrialized countries. Prostheses currently used to reconstruct complex cardiac defects are unable to grow and deteriorate over time. As a consequence, young patients undergo repeated and risky operations to replace failed grafts. Biological scaffolds integrated with progenitor cells able to grow and renew the prosthetic matrix may provide a definitive correction of CHD.
Purpose: To optimize a protocol for the isolation and expansion of Cardiac Pericytes (CPs) from infants affected by CHD, and to study the feasibility to integrate CPs within a clinically certified prosthetic graft (CorMatrix).
Methods: CD34+ CD31- CPs were immuno-sorted from small myocardial samples leftovers (n=10, weight <0.1g), expanded and characterized for surface antigens, secretome, cardiovascular plasticity, clonogenicity, pro-angiogenic potential and capacity to colonize a CorMatrix patch.
Results: We successfully expanded CPs in vitro for several passages to reach a high number of cells (>20 million at P5). At flow cytometry/fluorescent microscopy analysis, CPs at P4–5 express pericyte/mesenchymal antigens (NG2, PDGFRβ, CD105, CD44, Vimentin) but are negative for endothelial markers (CD31, CD146); they also express stemness markers (OCT-4, SOX-2, NANOG). Confocal microscopy showed that, in situ, CD34+CD31-NG2+ CPs are localised around capillaries and the external layer of arterioles. By single-cell sorting, we demonstrated the clonogenic capacity of CPs. When cultured with differentiation media, CPs failed to acquire mature endothelial or cardiomyocyte proteins, while they acquired markers of vascular smooth muscle cells (α-SMA, Calponin, non-muscle myosin B, RBP1, SM-MHC). When seeded on Matrigel, CPs form networks and support the angiogenic capacity of HUVECs. Moreover, they release pro-collagen type Iα, important for ECM remodelling, and chemo-attractant factors for c-kit+ cardiac stem cells. Finally, we succeed in growing CPs on a CorMatrix graft. After culture for 3 weeks in dynamic conditions in a bioreactor, we found CPs within the patch, indicating the ability to penetrate, colonize and form a cellularized scaffold.
Conclusions: We show for the first time that the heart of CHD neonates and infants harbours a population of pericytes endowed with high proliferative and reparative potential, and that expanded CPs can be successfully grown within a decellularized xenograft currently used in cardiac surgery. These data open new avenues for tissue engineering-based definitive correction of CHD.

P5455 | BENCH
Exosome secreted miR-27a-3p and miR543 are critical modulator of PDI activity in cardiac stem cells during hypoxia

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Background: The human heart is characterized by the presence of cardiac stem cell (CSC) stored in niches and widespread in myocardium. Stem cell niches are exposed to low oxygen tension and this metabolic adaptation offers a selective advantage to CSC compared to terminally differentiated cells, such as myocytes, during hypoxia. However, the molecular mechanisms are poorly understood. Protein disulfide isomerase (PDI), is a member of the unfolded protein response, which is activated to prevent the protein misfolding during stress, as occurs during ischemia. The objective of this work was to determine whether PDI is present and functional in CSC.
Methods: Specimens were collected from myocardium of 21 patients undergoing CABG. CSCs were isolated and characterized. The modulation of PDI in CSCs and its redox state were evaluated during hypoxia (1% O2) and analyzed at 12, 24, 48 and 96 hours. Exosomes from normoxic and hypoxic CSC conditioned medium were isolated and the RNA was extracted to evaluate the modulation of a panel of 174 microRNAs.
Results: The PDI was very low expressed in the myocytes. By qRT-PCR, a 2000-fold difference was found in PDI expression comparing CSCs and myocytes. Subsequently, the effects of hypoxia were studied in hCSCs in vitro and analyzed. With respect to differentiated cells, CSC showed consistently higher expression of PDI both at RNA and at protein level. Moreover, hypoxia led to upregulation of HIF1α transcripts in a time dependent manner both in myocytes and CSC. This results were coupled with an increase of the transcripts for the stemness associated genes Oct4, Nanog in CSCs. No differences were found in PDI expression comparing CSC cultured in normoxia vs hypoxia. However, hypoxia leads to an increase of the oxidative form (active) of PDI in CSCs, which induces an efficient folding of the substrate proteins, decreasing cellular apoptosis during hypoxia: when PDI was silenced with the use of specific siRNA a 4-fold increase in the rate of apoptosis was observed in CSCs ($p<0.005$).
We found that this effect is mediated by CSCs exosomal secreted miR-27a-3p and miR-543: the downregulation of these miRs during hypoxia led to an increased expression of the target protein ERO1L in CSCs that in turns oxidizes PDI, which directly catalyzes the formation of disulfide bonds, protecting the folding of proteins involved in CSCs survival such as IGF-1.
Conclusion: Our data indicate that PDI is a key regulator of CSC response to hypoxia and favours the conservation of their undifferentiated state. Exosomal secreted miR-27a-3p and miR-543 are critical modulator of PDI activity.

P5456 | BENCH
Creating new trans-species types of myocytes by forced fusion between cardiomyocytes and fibroblasts to counteract arrhythmias: breaking boundaries with muscular mixtures

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Purpose: The technology-driven, rapid lifestyle changes over the past century exceed the evolutionary and biological adaptability of the human heart, which renders it susceptible to degenerative diseases. Loss of ventricular cardiomyocytes (CMCs) is inadequately compensated by electromechanically incompetent fibroblasts. This maladaptive and pro-arrhythmic cellular response raised our interest in creating a new, cardiomyocyte-like cell type by forced fusion between fibroblasts and surrounding fibroblasts. We hypothesized such forced heterocellular fusion (FHF) transfers desirable electromechanical properties to fibroblasts and thereby ameliorates fibrosis-associated pro-arrhythmic effects on cardiac tissue.
Methods: Human ventricular scar cells (hVSCs) were isolated from myocardial scars of heart failure patients and co-cultured (1:4) with neonatal rat CMCs (nr-CMCs) into confluent monolayers. Prior to co-culture, hVSCs were transduced with lentiviral vectors encoding the enhanced green fluorescent protein (eGFP, control cultures) or eGFP and the fusogenic vesicular stomatitis virus G protein (fused cultures). The structural and functional effects of FHF were investigated by (human-specific) immunocytological staining, patch-clamp and optical mapping.
Results: hVSC-nrCMC heterokaryons were only observed in fused (VSV-G expressing) cultures. Such heterokaryons contained 6±3 nuclei (46±18% of human origin). These new, excitable and contractile cells expressed α-actinin and Cx43. Nuclear expression of NKX2.5 was absent in control hVSCs, while hVSC nuclei in heterokaryons stained positive. Expression levels of Cav1.2 and Cx43 did not relate to the percentage of human nuclei (R2=0.05), suggesting phenotypical dominance of CMCs. Additionally, FHF strongly reduced action potential duration (APD80, 313.1±6.3ms vs. 510.7±11.8ms, $p<0.05$ and dispersion of repolarization (75.1±4.3ms vs. 125.9±9.4ms, $p<0.05$). Importantly, early afterdepolarizations (EADs) rarely occurred in fused cultures (4.6% [n=65] vs. 43.4% [n=60], $p<0.0001$). Mechanistically, this enhanced repolarization force was due to an increased outward Kv current, as partial inhibition by tetraethylammonium chloride (TEA) reverted the anti-arrhythmic effects of fusion towards control values (7.9% to 34.2% EADs ($p<0.001$).
Conclusions: FHF between nrCMCs and hVSCs represents a novel approach to counteract pro-arrhythmogeneity of hVSCs by forcing a CMC-like phenotype that increases repolarization reserve. These results provide proof-of-concept for a previously unexplored therapeutic potential of heterocellular fusion.
Acknowledgement/Funding: Dutch Heart Foundation, grant number 2014T110

P5457 | BENCH
c-kit+ CSC-derived cardiomyocytes exhibit the typical transcriptional gene blueprint of adult cardiomyocytes

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Introduction: From embryonic to adult life, mammalian cardiomyocytes (CMs) generated from cardiac progenitors from mesodermal layers undergo a maturation process that is characterized by development of sarcomeric structure, binucleation, increased metabolic demand, and permanent exit from the cell cycle. This process is transcriptionally regulated by specific myogenic microRNAs (Myo-miRs). Adult cardiac stem/progenitor cells (CSCs) identified by the expression of c-kit are able to undergo cardiomyocyte commitment in vitro and in vivo. However, it is still unknown if adult CSC-cardiomyogenic specification recapitulates cardiac development and if CSC-derived cardiomyocytes closely overlap adult cardiomyocyte whole gene profile.
Purpose: To elucidate whether CMs generated from c-kit+CSC differentiation in vitro (c-kit-iCM) have a similar pattern of gene expression of adult CMs with a similar cell cycle exit through the activity of known Myo-miRs.
Methods: c-kit+ CSCs were clonally expanded from single cell deposition. Clonal-derived CSCs were primed in a stage-specific cardiopoietic growth factor cocktail to obtain spontaneously contracting cells in vitro. Freshly isolated CMs from adult mouse hearts were used as controls. RNA-Seq was employed to analyse and compare whole mRNA and microRNA profiles of cells collected at CSC, c-kit-iCM and adult cardiacmyocyte (aCM) stages.
Results: In the comparison of c-kitposCSCs vs. c-kit-iCMs, more than 4000 genes were up-regulated which mainly function in mitochondrial, sarcoplasm, sarcomere- specific and calcium regulating processes, among others. Several sarcomere-related genes highly expressed in adult CMs (i.e. Tnnt2, Tcap, Myl3, Tnni3, Tpm1, Myh7, Myh6) were indeed significantly up-regulated in c-kit-iCMs vs. CSCs in vitro. On the other hand, we found that most of cell cycle regulators/genes and a number of RNA processing genes were consistently down-regulated during differentiation from c-kitposCSCs to c-kit-iCMs in vitro. Interestingly, during differentiation from c-kitposCSCs to iCMs, known myo-miRs were upregulated while microRNAs positively regulating stem cell expansion and self-renewal were downregulated. Bioinformatics analysis built specific networks of miRNA-mRNAs that are precisely regulated during iCM generation from CSCs and that closely resemble miRNA-mRNA networks of adult CMs.
Conclusions: c-kitposCSCs robustly differentiate into functional beating cardiomyocytes in vitro. c-kitposCSC myogenic specification follow known developmental cardiomyocyte differentiation pathways and c-kit-iCMs transcriptome profile closely resemble adult CMs.

P5458 | BENCH
Circulating monocytes control myocardial regeneration in neonatal heart

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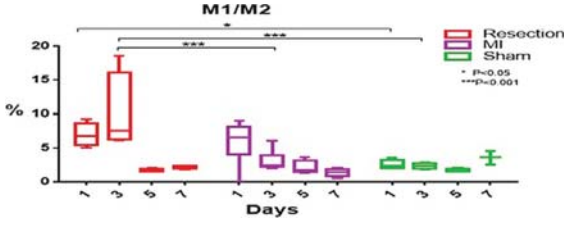
Purpose: Macrophages have been linked to myocardial regeneration in the neonatal heart. However, the relative contribution of circulating monocytes vs. resident embryonic-derived macrophages to myocardial regeneration remains unclear. We aimed to determine the relative role of circulating monocytes in myocardial regeneration.
Methods and results: We subjected 1-day-old newborn ICR mice to either apical resection, myocardial infarction (MI), or sham operation. Flow cytometry at 1, 3, 5 and 7 days post procedure revealed significant variability in the mode of regeneration and percent of cardiac macrophage subpopulations. Myocardial regeneration after apical resection was characterized by a sharp decrease in the proportion of M1 (CD86) to M2 (CD206), and increased cardiomyocyte proliferation on day 5 after surgery (Fig.). On the other hand, MI was associated with incomplete myocardial regeneration and a gradual decrease in the rate of M1/M2 macrophages, without an increase in cardiomyocyte proliferation (Fig). To determine the role of circulating monocytes in myocardial regeneration, we induced apical resection in 1-day-old ICR mice. To inhibit the recruitment of circulating monocytes to the resection site, we injected CCR2 abs IP at the time of resection, and again 3 and 5 days later. Notably, CCR2 treatment attenuated myocardial regeneration and produced a scar 21 days after apical resection.



Conclusions: The mode of cardiac injury affects the response of monocyte/macrophage subsets, and subsequent myocardial regeneration vs. repair. Our findings suggest that circulating monocytes, rather than resident embryonic macrophages, play an essential role in myocardial regeneration in the neonatal heart.

P5459 | BENCH
The Cre / Lox P fate mapping study on cardiac progenitor cells revealed its embryonic origin with its intrinsic methodological limitation validated by single cell qRT-PCR

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Background: Resident cardiac progenitor/stem cells in adult heart is a promising cell population that may contribute to tissue repair in a damaged heart such as myocardial infarction. Its embryonic origin, however, remains unclear.
Purpose: The aim of this study was to elucidate its embryonic origin by fate mapping study using embryonic stage-specific Cre-deleter lines.
Methods: Rosa26 reporter-tdTomato strains were crossed with Mesp1-Cre, Nkx2.5-Cre, aMHC-Cre, Wnt1-Cre, Islet1-Cre, Vav-Cre, Mef2c-AHF-Cre, Flk1-Cre, Tie2-Cre, cGata5-Cre and Wt1-CreERT2 strains. At 8 to 12 weeks old, hearts were excited, enzymatically digested and lineage MACS-depleted, followed by staining with Hoechst 33342 dye and antibodies for stem cell marker, Sca1, as well as the markers for its subpopulations, PDGFRα+ and CD31+. The fated cells driven by each Cre were determined as tdTomato positive whilst non-fated as tdTomato negative cells by flow cytometry. A part of sorted cells were seeded into a 96-well plate for a subsequent single cell qRT-PCR analysis to examine the difference in gene expression between subpopulations.
Results: Virtually all cardiac Sca1+ cells, whether SP or non-SP, PDGFRα+ or CD31+, were derived from Mesp1+ mesoderm. In contrast, neither SP nor Non-SP cells were derived from neural crest, hematopoietic cells, or pre-existing cardiomyocytes, defined using Wnt1-Cre, Vav-Cre, and aMHC-Cre, respectively. More than half the Lin-/Sca1+ cells were Nkx2.5-derived with an equal contribution from Isl1-fated cells. Less than 20% of SP and Non-SP cells were fated by second heart field Mef2c-AHF-Cre. A proepicardial origin was confirmed by cGata5-Cre and Wt1-CreERT2 in 50% and 35% of cardiac SP cells, respectively. By contrast to the proepicardial Cre line, Non-SP cells showed a greater contribution from Flk1- and Tie2-Cre. Finally, gene expression profiles were compared between SP and Non-SP cells from Nkx2.5-Cre strain in combination with PDGFRα- and CD31-expressing cells. Although there was a clear difference in gene expression profile between PDGFRα- and CD31- expressing SP cells, showing mesenchymal and endothelial property, respectively, no such clear difference was confirmed between Nkx2.5-fated and non-fated SP cells, suggesting identical population split into tdTomato positive or negative cells possibly due to incomplete Cre recombination.
Conclusion: We identified embryologic origin of PDGFRα+SP cells in mesenchyme of Nkx,-, Isl1-, cGata5- and Wt1- fated population. There was, however, a limitation of the interpretation of the results.
Acknowledgement/Funding: British Heart Foundation

P5460 | BENCH
Proteomic analysis of canine failing hearts induced by rapid pacing: evidence for the elevation of the protein levels related to either mitochondrial dysfunction or acute phase response signaling

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Background: The isobaric tags for relative and absolute quantification (iTRAQ) system, a newly developed proteomic analysis method, has enabled us to comprehensively compare the absolute protein levels among multiple samples. Although proteomic profiles of humans and dogs are highly conserved because of their physiological and anatomical similarities, proteomic analysis of canine heart failure model using iTRAQ has not been reported.
Purpose: We aimed to reveal the proteomic profile of canine failing myocardium using iTRAQ.
Methods: Dogs were subjected to sham (Sham, n=2) or right ventricular rapid pacing (220 beats/min) for 4 (4W, n=2) and 6 weeks (6W, n=4) to create the heart failure model. After echocardiographic examinations, dogs were sacrificed and isolated hearts were thoroughly perfused with phosphate buffered saline. Myocardial tissues from left ventricular (LV) free wall were subjected to iTRAQ system. The data were analyzed by Ingenuity Pathway Analysis (IPA).
Results: In echocardiogram, the larger LV diastolic diameter (LVDd) and the lower ejection fraction (EF) were observed in 4W and 6W compared with Sham (LVDd; 45.4 and 39.11 vs. 30.3mm, EF; 36.0 and 25.0 vs. 81.3%, 4W and 6W vs. Sham, respectively). First of all, of initially identified 2615 proteins, we excluded 1810 proteins which lacked expression in any of the samples. Among further analyzed 805 proteins, we focused on proteins with >1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these

proteins. Among the indicated canonical pathways, mitochondrial dysfunction and acute phase response signaling pathway were commonly identified in both 4W and 6W. Interestingly, while the proteins of acute phase response signaling pathway were comparable between 4W and 6W (11 and 12 proteins, respectively), the number of proteins included in mitochondrial dysfunction was larger in 6W (27 proteins) than 4W (11 proteins), that is mainly caused by increase in subunits of complex I, which may contribute to generate proton motive force and to create reactive oxygen species in mitochondria.
Conclusion: In canine failing heart induced by rapid pacing, proteins regarding either mitochondrial dysfunction or acute phase response signaling pathway were up-regulated; the proteins involved in mitochondrial dysfunction seemed to be more important for the progression of heart failure. These pathological pathway may play an important role by quantitative up-regulation of involving proteins.

CARDIOVASCULAR PATHOLOGY AND EMBRYOLOGY

P5461 | BENCH
Wilms tumor-1 expression in cardiac endothelial cells

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Background: Restoring the myocardial wall by cardiac progenitor cells is a promising therapy after myocardial infarction. Wilms' tumor-1 (Wt1) is expressed in the embryonic and reactivated adult epicardium and is therefore used as a marker for epicardial progenitor cells. Recently, it is suggested that also other cells within the heart express Wt1. Our goal is to determine the Wt1-expressing cell types during development and after cardiac injury in the murine and human heart, and to study the role of Wt1 in these cells.
Results: Immunohistochemical analysis revealed that Wt1 is expressed by cardiac endothelial cells (ECs) of the mouse heart from E12.5 onwards. In the adult heart, the expression of Wt1 is reduced, although a subset of coronary ECs remains positive for Wt1. Interestingly, after myocardial infarction a temporal upregulation of Wt1 in ECs is observed in the infarcted area and the border zone of the heart. In the human foetal heart, Wt1 expression is similar though broader then observed in the embryonic mouse heart. In addition to the ECs, Wt1 expression is also observed in the endocardial cells of the ventricles. The expression of Wt1 in the ECs suggests a role in angiogenesis. To test this hypothesis, we performed in vitro experiments and show that Wt1 can be induced in ECs by hypoxia, an angiogenic inducer, and that Wt1 enhances cell proliferation of ECs through increased mRNA expression of CyclinD1. In addition, ECs lacking Wt1 were not capable to establish a proper vascular network.
Conclusion: Together, these results suggest a role for Wt1 in cardiac vessel formation during development which is reactivated after cardiac injury.

P5462 | BENCH
Physiopathology of the ubiquitin ligase E3, PDZRN3, in the development of dilated cardiomyopathies

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Dilated cardiomyopathy (DCM) is a leading cause of sudden cardiac arrest. 20–48% of all cases are familial types, mainly due to mutations in cytoskeletal or sarcomeric proteins. But an important part of the DCM has still not known mechanism. During heart maturation, individual cardiomyocytes stretch out and connect some with the others via their extremities by junctional complexes. This planar and directional organization of the myocytes may allow a mechanical coupling and the distribution of the electric signal in the heart. Importantly, one of the hallmarks of DCM concerns alterations in the contact sites between cardiomyocytes. We propose here to analyze a novel role of the Wnt Planar Cell Polarity (PCP) signaling in the coordination and the polar organization of intercardiomocyte junctions, whereby it insures a correct cell alignment. Alteration of this polarization process could cause a default of growth and of functional organization of cardiomyocytes. We have previously identified a novel Wnt/PCP trigger, an Ubiquitine ligase E3, PDZRN3, which is expressed in cardiomyocytes. We have developed a transgenic model to overexpress PDZRN3 in cardiomyocyte around birth by crossing a pTRE-Pdzrn3-V5 mice with alphaMHC-tTA mice. Analyses by echocardiography and histology showed that mutant mice developed a dilated cardiomyopathy between 2–4 weeks of life, with an ejection fraction around 40% and a poor survival after 2 months. Western blot and immunohistochemistry analyses revealed a dramatic relocalization of zonula-occludens-1 (ZO-1) (nuclear when we overexpress PDZRN3) and a loss of Cx43 at the junctions as soon as 15 days after birth. This was associated with an alteration of myocyte survival, impairment in myocyte architecture and a progressive ventricle fibrosis starting after 3 weeks. We then deleted Pdzrn3 specifically in cardiomyocytes by crossing Pdzrn3f/f mice with aMHC-mer-Cre-mer mice after tamoxifen injection and reported an impairment of heart morphogenesis during embryonic development.
This study described a very important model to analyze mechanisms of cardiomyopathy. It reveals a novel role of the Wnt/PCP/PDZRN3 signaling in the coordination and the polarized organization of inter cardiomyocyte junctions.

P5463 | BENCH
Reduced number of active cardiac mitochondria in a rat model for long-term kidney disease

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Introduction - Cardiorenal syndrome (CRS) type 4 is characterized by primary chronic kidney disease (CKD) leading to an impairment of cardiac function. Two main known pathways may connect organs' dysfunctions: pro-inflammatory response and inappropriate upregulation of the Renin Angiotensin Aldosterone System (RAAS). We recently showed a reduced expression of several cardiac mitochondrial genes in short-term CKD rat model. We, thus, hypothesized that chronic inflammation and activation of RAAS in CKD may contribute to mitochondrial damage in the heart. We aimed to evaluate whether cardiac mitochondrial structure and function is modified in the setting of long-term CKD and if so, to characterize the potential associated mechanisms.
Methods: Lewis rats underwent 5/6 nephrectomy for induction of CKD. Renal and cardiac functions were confirmed by creatinine clearance, echocardiography and blood pressure. Upon necroscopy, eight months later, cardiac sections were fixed for histological and electron microscopy (EM) analyses. Total mitochondrial DNA content was determined by the mitochondrial gene, cytochrome B. Mitochondrial content was assessed by citrate synthase (CS) activity in tissue homogenate and respiratory chain function was determined by the activity of complexes I-IV in isolated mitochondria. The levels of PGC1a, a transcription factor for mitochondrial biogenesis, and cytosolic cytochrome C (CytC) were determined by western blot. Serum Angiotensin II (AngII) was measured by ELISA and cytokine serum profile was determined by microarray analysis.
Results: Long-term CKD model leads to significant cardiac hypertrophy and increased interstitial fibrosis. EM analysis revealed a massive spatial disarrangement accompanied by a considerably increased volume of swollen-damaged mitochondria in CKD hearts. A significant accumulation of cytosolic CytC confirmed the mitochondrial damage. While total mitochondrial function was extensively reduced in CKD hearts, the remaining mitochondria retained intact activity. Despite the marked decrease in cardiac mitochondrial content, no differences were observed in PGC1a expression. Interestingly, we documented negative correlation between increased levels of IL1a, INFg, IL2 and CS activity in CKD. Likewise, AngII plasma levels were slightly increased and negatively correlated to CS activity.
Conclusion: Altogether, the data suggest that CKD setting results in a marked reduction of active mitochondria in the heart. Pro-inflammatory cytokines and RAAS, which are induced in CKD, may set a deleterious environment to the cardiac mitochondria.

P5464 | BENCH
Inhibition of aortic valve calcification by local delivery of zoledronic acid. An experimental study

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Background: Aortic valve (AV) calcification is a common clinical problem with increased morbidity and mortality, that shares common molecular mechanisms with bone formation. Currently, treatment strategies for symptomatic AV calcification include careful monitoring and judicious timing of AV replacement. Bisphosphonates are components, which inhibit calcification.
Purpose: The aim of the present study was to evaluate the safety and effectiveness of local delivery of the bisphosphonate zoledronate on inhibition of calcium formation in an experimental animal model of aortic stenosis.
Methods: Sixteen New Zealand rabbits were placed on vitamin D enriched atherogenic diet for 3 weeks. At that time a cardiac ultrasound was performed to assess the aortic stenosis and aortic calcification of the aortic valve by measuring aortic valve area (AVA). Subsequently half of them were treated with local delivery of a mixture containing 500 μg/l zoledronate that was delivered on the cusps of the aortic valve, by a dedicated balloon catheter. A placebo mixture was administered on the rest eight animals, which were used as controls. At 28 days all animals were sacrificed. All aortic valves were fixed in 10% neutralized buffered formalin solution for 24 hours. The cusps (left, posterior and right) were separated in a radial direction and then embedded in paraffin waxes. Serial sections 4 μm thick were obtained and routinely stained with eosin –hematoxylin and von Kossa stain for calcium deposits. The stained slides were processed in a computer with the appropriate software (Image Pro Plus, version 5.1, MD, USA), and the calcified areas were expressed as the percentage to the total area. Statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS, Chicago, IL) release 13.0

Results: At baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (21.37±1.76 vs 21.98±3.12, p=0.53). In all animals the local delivery of zoledronate and placebo mixtures was successful and uncomplicated. A total of 24 cusps were histologically examined from each treated group. The cusps treated with zoledronate had significantly lower expression of calcium content compared to the controls (16.40±0.90 vs 26.92±1.60% of the area, p<0.0001)
Conclusion: Inhibition of aortic valve calcification by local catheter-based delivery of zolendronate is effective without evident short-term complications. The potential clinical implications should be confirmed in human studies.

P5465 | BENCH
Intraleaflet haemorrhages induce anti-inflammatory and osteoclastic cell phenotypes and are associated with osteogenic metaplasia in stenotic aortic valves

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Background: Calcific aortic valve degeneration is an active process similar to atherosclerosis. Involvement of intraleaflet (intraplaque) haemorrhages in progression of both pathologies has been recently postulated. Intraplaque haemorrhages induce expression of anti-inflammatory factors such as heme oxygenase-1 (HO-1) and IL-10. It is hypothesized that similar mechanisms are involved in aortic valve degeneration (AVD) but little is known about the impact of intraleaflet haemorrhages on the mode of calcific valve remodelling which is a hallmark of AVD.
Purpose: The aim of this study was to check whether the occurrence of intravalvular haemorrhages is associated with phenotypic modifications of monocyte derived cells and modification of calcific remodelling profile in human stenotic aortic valves.
Methods: Aortic valve specimens were obtained from 63 patients undergoing routine valve replacement surgery due to severe stenosis. Areas of intraleaflet haemorrhages were detected by immunohistochemical and histochemical methods (glycophorin C/fibrin/iron) and all cases have been divided into haemorrhagic group (HG, n=28) showing substantial, continuous intraleaflet haemorrhages and nonhaemorrhagic group (NHG, n=35) without or with very limited signs of previous haemorrhages. In the valves of both groups, the following parameters were assessed: overall macrophage infiltration, density of CD163+ macrophages and tartrate resistant acid phosphatase positive (TRAP+) cells, neovessel formation, heme oxygenase-1 (HO-1) protein expression and occurrence of chondro- and osteogenesis.
Results: Areas of haemorrhages were mostly located in the vicinity of focal calcifications. The HG group revealed more intense neovascularization (p<0.0001), higher density of CD68+ (all) macrophages (p=0.0001) and of CD163+ (M2, anti-inflammatory phenotype) macrophages (p=0.001), higher proportion of M2 macrophages to all macrophages (p=0.008) and higher density of HO-1 immunopositive cells (p<0.0001). Haemorrhages seemed to alter the mode of calcific remodelling, since more frequent cases with chondrogenic metaplasia and/or bone formation were found in HG group (p=0.004 and p<0.0001 for cartilage and bone respectively). Both, multinuclear osteoclasts and monouclear TRAP+ cells were more frequent in HG group (p=0.001).
Conclusion: The occurrence of intraleaflet haemorrhages seems to induce chondrogenic metaplasia, bone formation and osteoclastogenesis, expression of protective, antioxidative HO-1 as well as recruitment of anti-inflammatory macrophages in stenotic aortic valves.

P5466 | BENCH
Imaging mass spectrometry with focus microwave treatment reveals heterogeneity in directional glucose fluxes in and around ischemic myocardium

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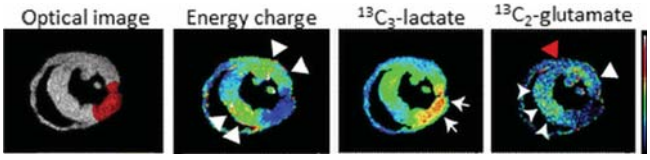
Introduction: Matrix-assisted laser desorption/ionization (MALDI)-imaging-mass spectrometry (IMS) combined with a focused microwave irradiation (FMW) for rapidly fixing tissue metabolism allowed us to quantify and visualize many metabolites within heart tissues in a region-specific manner.
Purpose: We demonstrated whether these techniques are applicable to visualization of regional changes in glucose metabolism of murine heart exposed to coronary ischemia.
Methods and results: FMW was found to be an optimal method to minimize postmortem changes in metabolites as compared with traditional ways of sacrifice. After 10 min of myocardial ischemia by LAD ligation, quantitative imaging of various metabolites showed the highest levels of lactate, succinate, NADH in the ischemic core. Distribution of these metabolites was demarcated to that of ATP. Imaging of distinct metabolic fluxes from 13C6-glucose revealed that the anaerobic glycolytic pathway defined as production of 13C3-lactate is predominant in ischemic regions (white head arrows), while the concomitant conversion of 13C2-glutamate resulting from incorporation through Krebs cycle was predominant in non-ischemic regions (white arrows). Notably, non-ischemic regions adjacent to the ischemic core (white arrows) exhibited greater TCA cycling than those distal from the ischemic core (red arrows). In good agreement with these results, non-ischemic regions adjacent to the ischemic core displayed greater energy charges than those distal from the core (white arrows).



Imaging-MS combined with a FMW

Conclusions: In conclusion, this study is the first to demonstrate usefulness of IMS combined with FMW to visualize regional metabolic flux of glucose oxidation, revealing compensatory responses of energy management in the marginal regions between the ischemic core and intact regions.

P5467 | BENCH
Heterogeneity of patterns and distribution of myocardial fibrosis in end-stage hypertrophic cardiomyopathy (ES-HCM) undergoing heart transplant: a morphometric analysis of 24 explanted hearts

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Background: Myocardial fibrosis is frequently found by cardiac MRI in HCM, particularly in cases with left ventricular (LV) dysfunction, and has been shown to carry an ominous prognosis. Nonetheless, extension and distribution of fibrosis have never been extensively pathologically characterized.
Purpose: To assess overall extension, apex-to-base, radial and epicardial/endocardial distribution (histomorphometric analysis), and type of myocardial fibrosis in a group of transplanted ES-HCM.
Methods: For each heart the following sections have been considered: midventricular short axis ventricular section with analysis of radial and transmural distribution, as well as 3 samples from basal and 3 from apical level. Histomorphometric analysis was carried out with a dedicated software and graphics workstation.
Results: Twenty-four hearts were examined between 2005 and 2014. One patient with previous alcohol ablation was excluded.
LV base-to-apex distribution (% of assessed myocardium; mean values). Basal level: 33; medium level: 41; apical level: 43.
Midventricular short axis section: radial distribution (% of the overall fibrosis within the section, mean values): anterior LV:11.6; anterolateral LV:16.1; inferolateral LV:6.3; inferior LV:24.4; anterior septum:11.5; medium septum:10.0, posterior septum:11.6; anterior RV:3.6; inferior RV:4.9.
Midventricular short axis section: epicardial-endocardial distribution (% of the overall fibrosis within the section, mean values): trabecular 24.3; subendocardial 21.3; midwall 33.1; subepicardial 21.3. Four main patterns were identified: midwall and subendocardial 21.7% (5/23), midwall and subepicardial 17.4% (4/23), transmural 43.5% (10/23), midwall 17.4% (4/23).
Type of fibrosis: In all patients both types of fibrosis were detectable, whereas fibrosis was mainly of replacement type in 17 patients, and mainly perimyocytic type in 7 patients.
Conclusions: In hearts of ES-HCM undergoing heart transplantation the amount of myocardial fibrosis is very marked. Moreover both replacement and perimyocytic fibrosis extensively affects the LV myocardium with some differences between base, mid and apex. Fibrosis involves more frequently midventricular and subepicardial layers with a relative sparing of subendocardium (never exclusively involved). While the entire septum and the inferior and anterior portions of LV are maximally involved, the inferolateral wall tends to be spared. These observations have potential implications on the comprehension of the pathophysiology of HCM and on interpretation of imaging techniques

P5468 | BENCH
Proliferating myofibroblasts contribute to extracellular matrix remodeling in a porcine model of ischemic cardiomyopathy

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Background: Fibroblast (Fb) differentiation is involved in the development of fibrosis and contributes to collagen maturation and cross-linking. This leads to stiffening of myocardial tissue and ultimately deterioration of heart function.
Purpose: In this study we sought to determine the Fb phenotypes responsible for extracellular matrix remodeling in ischemic cardiomyopathy.
Methods: A copper-coated stent was implanted in the left anterior descending coronary artery (LAD) of porcine hearts leading to a reduction in perfusion and development of a myocardial infarction (MI, 10% of left ventricular mass). Biopsies

were collected from the myocardium adjacent to the MI (not from scar tissue) and remote to the MI and from corresponding regions in SHAM operated animals (N=6 SHAM, N=6 MI). Sirius red staining was used to assess fibrosis and polarization microscopy to quantify collagen subtypes in the interstitial and perivascular area. Fb were isolated via enzymatic digestion and cultured in DMEM culture medium with 10% fetal bovine serum for 4 days to determine Fb phenotypes and for 8 days to evaluate proliferation capacity. F-actin was assessed using immuno-fluorescent staining. Immunostaining and Western blotting were used to assess lysyl oxidase (LOX) as marker for collagen cross-linking activity.
Results: Overall interstitial fibrosis was not increased in the adjacent or remote myocardium. However, there was a 3 fold increase of cross-linked collagen type I within the interstitial area of the adjacent myocardium; presence of cross-linked collagen bundles was confirmed by electron microscopy. Concomitantly, arteriole perivascular fibrosis was increased (2-fold increase of perivascular collagen type I and III). Fb from MI hearts from both regions compared to SHAM were larger (27% increase in the adjacent and 20% in the remote myocardium) and the number of Fb with f-actin stress fibers was increased 2-fold. Immunostaining showed nuclear LOX accumulation. These myofibroblasts maintained proliferation capacity after 8 days in culture.
Conclusion: Proliferating myofibroblasts underlie increased collagen cross-linking in the MI-adjacent myocardium and may contribute to myocardial stiffening. Fb differentiation in the remote myocardium could be triggered through increased hemodynamic load.
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P5469 | BENCH
Toll-like receptor 7 is involved in adverse ventricle remodeling after myocardial infarction

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Introduction: Toll-like receptor 7 (TLR7) detects viral nucleic acids to fight against viral infection. TLR7 also recognizes endogenous single-strand RNA (ssRNA) shed from dying cells that induces an inflammatory response in autoimmune diseases. A role for TLR7 in Myocardial Infarction (MI) is unknown. We showed that Toll-like receptor 4 activation deficiency results in a decreased inflammatory response and improved heart function after MI. We hypothesize that TLR7 detects ssRNA released from the dying heart cells, increasing the inflammatory response and deterioration of left ventricle function after MI.
Methods: C57BL/6J wild type (WT) and TLR7 null mice, 10–12 weeks old, were subjected to myocardial infarction via permanent ligation of the left anterior descending artery (LAD). Cardiac function was assessed by Vevo2100 echocardiography at baseline, 7 and 28 days after MI. Mixed ANOVA for repeated measures was used to compare Ejection Fraction (EF) between WT (N=15) and TLR7 null mice (N=26) that had echocardiography at all 3 timepoints. Log rank test was used to assess differences in survival between WT and TLR7 null mice.
Results: Despite similar infarct size, survival of TLR7 null mice after MI was better than WT (p=0.010). After MI, 3 out of 31 TLR7 null mice (10%) died while 12 out of 34 WT mice (35%) died of cardiac rupture. TLR7 deficiency reduced left ventricular remodeling and preserved cardiac function (EF±SEM: 32.5±1.8 for TLR7 KO and 21.4±3.2 for WT mice, p=0.002).
Conclusion: TLR7 is involved in cardiac remodeling after MI, independent from infarct size. Lack of TLR7 preserves cardiac function and survival after MI and identifies TLR7 as a potential therapeutic target for adverse ventricle remodeling.

P5470 | SPOTLIGHT
PEAR1: a novel link between IgE-mediated allergy and cardiovascular disease

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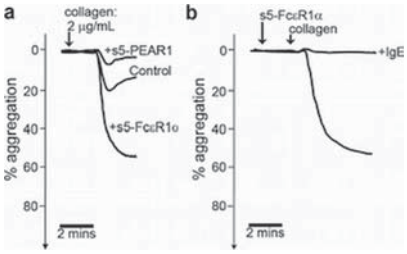
GWAS for platelet function and cardiovascular disease repeatedly identified polymorphisms linked to Platelet endothelium aggregation receptor 1 (PEAR1), a cell surface receptor involved in stabilizing platelet aggregates. We sought to identify the extracellular ligand(s) of PEAR1.
We created a protein microarray representing the secretome and receptor repertoire of the human platelet. 173 Recombinant proteins were expressed. Using an avid soluble recombinant PEAR1 protein and a systematic screening assay designed to detect extracellular interactions, we identified the high-affinity IgE-binding subunit FcεR1α, as a PEAR1 ligand. FcεR1α and PEAR1 interacted with a strong affinity (KD ~30nM). Pre-complexing FcεR1α with IgE potently inhibited the FcεR1α-PEAR1 interaction. Oligomerised FcεR1α potentiated platelet aggregation and led to PEAR1-phosphorylation, an effect that was inhibited by IgE (Figure 1). This provides a mechanistic basis for the initiation of PEAR1 signaling in aggregation. The identification of FcεR1α as an activating ligand for PEAR1 and the finding that IgE can inhibit this interaction suggests a link between IgE and platelet function. The in vivo prevention of IgE binding to FcεR1α by a clinical anti-IgE monoclonal antibody omalizumab, showed that omalizumab can relieve IgE-mediated inhibition of the FcεR1α-PEAR1 interaction and may provide an explanation for the increased risk of cardiovascular disease associated with omalizumab use.



IgE inhibits s5-FcεR1α platelet aggreg.

Conclusion: We developed a platelet protein microarray resource to gain new insights into the function of platelet receptors. We identified, the FcεR1α-PEAR1 interaction and its regulation by endogenous IgE, which provides a mechanism to explain previously under-appreciated interactions between allergy and cardiovascular disease.

P5471 | BENCH
Aging impairs cardiac Akt activity leading to myocardial sarcopenia

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Background: Aging causes skeletal muscle atrophy (i.e. sarcopenia). In heart, aging is also known to cause cardiac dysfunction such as diastolic dysfunction; however, the impact of aging on myocardial cell growth remains uncertain.
Purpose: Because of the pivotal role of protein kinase Akt in cellular aging and growth of cardiomyocytes, the purpose of this study was to elucudate whether #1 aging may impairs cardiac Akt activation leading to myocardial remodeling (including atrophy) in aged heart and #2 regular exercise may restore the aging-induced cardiac remodeling via activation of Akt signaling.
Methods: *Cohort-1:* Male aged (40 week-old) C57BL6 mice, age-matched Akt knockout mice (C57BL6-background, heterozygotes; AktKO), and young counterparts (14 w/o) were evaluated changes in each cardiac function by echocardiography, remodeling by pathology, and molecular signaling by biochemical procedure. Mice were randomly allocated to the regular exercise (EX, 60-min running by treadmill/day for 6 months).
Cohort-2: Male genetically senescence-accelerated [(SAM; senescence-accelerated prone (P10)) and senescence-resistant counterpart (R1) were allocated to EX [45-min running by treadmill/every 2 day for 6 months and EX-free control.
Results: We first observed the impact of aging on cardiac Akt. In naturally aging mice, the cardiac Akt activity was reduced compared to those young counterpart, which was restored by EX. Aged C57BL6 exhibited systolic and diastolic dysfunction and reduced heart weight, all which were restored by EX. Independently of EX, the aged AktKO exhibited reduced HW snd systolic dysfunction. Interestingly, ERK activity was modestly increased by aging, however, it was unaffected by EX. In R1, EX promoted LV hypertrophy and enhanced cardiac Akt-mTOR-S6K activity. Of note, the baseline Akt activity was elevated in P10 heart, which was unaffected by EX. Because insulin-mediated autophagic regulation plays a pivotal role in skeletal muscle hypertrophy, we hypothesized the EX-induced increase in cardiac Akt/mTOR axis may modulate cardiac autophagy that restores aging-induced cardiac remodeling. Circulating insulin level remained unchanged by EX, however, the EX ameliorated cardiac insulin resistance (assessed by Ser307 phosphorylation of IRS-1) and subsequent autophagy (LC3 turnover and p62 level) observed in the aged mice.
Conclusion(s): Aging causes cardiac sarcopenia and systolic dysfunction via affecting cardiac Akt activity and subsequent insulin resistance. Exercise restored the cardiac insulin resistance induced by aging through the Akt/mTOR-dependent autophagy.

P5472 | BENCH
Genetic cardiomyopathy overlaps can modify phenotypic features in dilated cardiomyopathy patients - a comprehensive next-generation sequencing (NGS) study

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Introduction: Patients with dilated cardiomyopathy (DCM) show heterogeneous phenotypic features and outcomes, some of which are typical for other major CM types. We hypothesize that this may be a result of overlapping mutations.
Purpose: In this study we aimed to investigate CM types on a genomic level and to evaluate if phenotypic features of DCM patients are associated with mutations known to cause CMs other than DCM.
Methods: We performed a meta-analysis of the INHERITANCE sequencing project of a cohort of 639 patients with DCM. Individuals were classified according to their known and annotated disease mutations from Human Gene Mutation Database (HGMD). As a control cohort we used a number of 448 individuals from the 1000 genomes project. Benign variants, those reported in Exome Sequencing Project (ESP) database and those with a frequency of $\geq$1% in the control cohort, were removed. Patients were categorized into subgroups with variants associated with CM types other than DCM and their phenotypic variables were compared with each other.
Results: After applying our filtering protocol, 139 unique variants were found in the DCM cohort that matched one of the HGMD CM entity mutations. Eighty-three (13%) DCM patients of the cohort presented variants which are already reported to cause DCM. Variants annotated to Brugada syndrome (BrS), hypertrophic cardiomyopathy (HCM) or long QT syndrome (LQTS) were present in 2.3–10% of DCM patients of the cohort, whereas 68 (10.6%) DCM patients of the cohort presented variants annotated to ARVC. Comparing the phenotypes in these subgroups showed noticeable findings: DCM patients with BrS-associated variants showed a significantly higher rate of heart transplantation. DCM patients who carried HCM-associated variants showed milder clinical manifestations and disease progression (lower NYHA functional class, higher left ventricular ejection fraction and lower cardiac transplantation rate). DCM patients with LQTS-associated variants presented more often with advanced NYHA functional classes, whereas patients with ARVC-associated variants did not show any significant phenotypic deviations in comparison to patients without these variants.
Conclusions: We showed in this large-scale genotype-phenotype association study that coexistence of variants which are normally known to cause CMs other than DCM could influence phenotypic features and the clinical course of DCM patients. Performing NGS in these patients helps to identify all relevant variants and enables physicians to better risk stratify DCM patients.

AORTIC VALVE DISEASE

P5473 | BENCH
Valvular heart disease and pulmonary hypertension in fawn-hooded rats: the role of 5HT2B receptors

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Background: Patients with elevated serotonin levels are prone to develop valvular heart disease and also pulmonary hypertension (PH) via induction of pulmonary vasoconstriction and proliferation of pulmonary artery smooth muscle cells. In order to explore the role of 5HT2B receptors, we treated Fawn Hooded rats by terguride, a 5-HT2B inhibitor.
Methods: Fawn Hooded rats (FH of age 1, 3, 6 and 9 months, n=6 rats/group) which genetically exhibit a platelet storage pool disease, hence are unable to store serotonin in platelets were compared with Brown Norway rats (BN of age 1, 3, 6 and 9 months, n=6 rats/group). Pulmonary artery systolic pressure (PAPs) was assessed by in vivo hemodynamic measurements (Millar catheter) and echocardiography. Cardiac fibrosis was evaluated by Masson's trichrome staining and aortic valve calcification by Von Kossa staining. Serotonin receptor expression was measured by qRT-PCR. Proliferation and serotonin receptor expression in response to various stimulations were evaluated in cultured cardiac fibroblasts.
Results: FH rats presented with elevated PAPs starting at 3 months of age compared to age-matched BN rats (level of PAPs in 2 groups, $p<0.05$). Once developed, PAPs remain elevated. PAPs was reduced by treatment with the 5-HT2B inhibitor terguride (values), as evidenced by decreased right ventricle-body weight ratio (a marker of right ventricular hypertrophy), and increased pulmonary acceleration time.
Aortic and mitral valvular abnormalities progressively developed in FH but not BN rats as demonstrated by increased transaortic gradient (values) and inappropriate presence of chondrocytes and fibrosis in the valves. Von Kossa staining also revealed calcification in aortic valves of Fawn Hooded rats, which was completely rescued by terguride treatment.
Progressive fibrosis did not limit to the valves, but pervaded left ventricular (LV) myocardial interstitium. These findings were associated with a progressive LV remodeling, at echocardiography.
In response to serotonin and fetal calf serum Brown Norway-derived cardiac fibroblasts showed increased proliferation and upregulation of 5-HT2B receptor (RT-PCR), which was reversible with terguride.
Conclusions: Fawn Hooded rats developed both PH and valvular heart disease. Both PH and cardiac valvulopathy were attenuated by treatment with the 5-HT2B antagonist terguride.

P5474 | BEDSIDE
Scaling systolic volume to body surface area and its influence in the diagnosis of low-flow/low-gradient aortic stenosis

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The definition of low-flow/low-gradient aortic stenosis (LFLGAS) is based on the scaling of systolic volume (SV) to body surface area (BSA). Assuming an isometric relationship, the allometric coefficient (AC) should be 3/2 instead of 1 as generally applied. The aim of this study was to evaluate the correlations between measurements of body size and SV in order to calculate the precise AC (b) for a correct scaling.
Methods: Sixty-four individuals without evidence of heart disease were included. Mean age was 45±13 years, 35.9% males. The ranges of weight and height were 48–124 kg and 147–190 cm. SV was measured as the difference between end-diastolic and end-systolic left ventricular volumes. The b-value was calculated after a logarithmic transformation of the formula used to scale biological variables: $Y=X/Z^b$, where X is the variable to be scaled, Z is the body size and b the AC.
Results: SV was linearly correlated with all the variables that measure body size except body mass index: height r=0.63; $p<0.0001$, weight r=0,52; $p<0.0001$, BSA r=0.60; $p<0.0001$ and body mass index r=0.19; p=0.161. After the logarithmic transformation we found an allometric coefficient b=1.3 for appropriate scaling to BSA (r=0.59; $p<0.0001$). The normal values obtained after scaling SV to BSA were 16.7 to 40.7 mL/m^2. However, scaling to the 1.3 exponent provided values ranging from 14.0 to 34.0 mL/(m^2)$^{1.3}$. When the difference between scaled SV were plotted against different values of BSA (Figure 1), we noted that an AC of 1 overestimates SV at low BSA and underestimates SV at high BSA values.

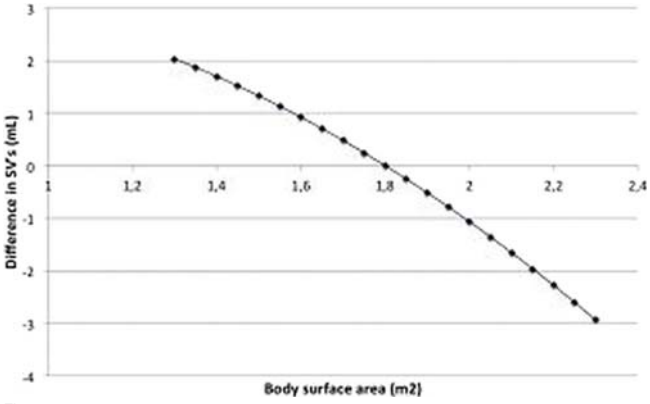

Figure 1

Conclusions: Scaling SV to BSA with an allometric coefficient of 1 incorrectly classifies patients low SV when BSA is either low or high. This finding has important clinical implications when the diagnosis of LFLGAS is considered.

P5475 | BEDSIDE
Transcatheter aortic valve implant vs surgical aortic valve replacement in low- to intermediate risk patients: a Meta-analysis

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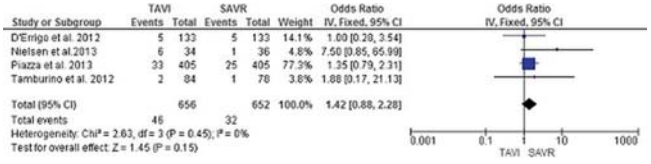
Objectives: To test the hypothesis that Transcatheter aortic valve implant (TAVI), when compared with surgical aortic valve replacement (SAVR), have favourable clinical outcomes in patients with low or intermediate risk.
Methods and results: A PubMed, EMBASE and Medline search yielded 6 studies, of which 2 were abstracts. Over 2100 patients were randomised to TAVI vs SAVR. 30-day mortality was not different (Risk ratio was 1.4 (95% CI 0.88, 2.3). There was also no statistically significant difference in 1-year mortality, stroke, life-threatening bleeds, and major vascular complications. However, TAVI was associated with significantly shorter hospital stay.

Table 1. A summary of the clinical outcomes in low to intermediate risk patients – TAVI vs. SAVR

Outcomes	Risk ratio	95% CI
30-day mortality (primary outcome)	1.4	0.88, 2.28
1-year mortality	1.0	0.79, 1.27
Major stroke	2.0	0.56, 7.42
Life-threatening bleeds	1.8	1.00, 3.09
Major vascular complications	8.6	0.57, 130

Conclusion: In low to intermediate risk patients, 30-day or 1-year mortality, risk of stroke, major vascular complications and life-threatening bleeds were not significantly different between patients treated by TAVI when compared with SAVR.



30-day mortality: TAVI vs SAVR

However, TAVI was associated with significantly shorter hospital stay which may be an important consideration in patient-centred decision making.
Acknowledgement/Funding: None

P5476 | BEDSIDE
High implantation is a new parameter that affects the outcome of patients that undergo transcatheter aortic valve implantation with self-expandable bioprosthesis

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Background: Transcatheter aortic valve implantation (TAVI) is an emerging treatment option for inoperable or high risk patients. Very low as well as supra annulus valve implantation is associated with poor valve performance. Currently an implantation depth around 4 mm is recommended for the self-expandable Medtronic Core Valve. However despite satisfactory valve functions, the final valve depth may be significantly different from the goal of 4 mm. Whether a higher implantation versus a lower implantation has any impact on outcome of the procedure, has not been evaluated. The purpose of this study is to assess whether in a satisfactory positioned valve the final position affects the short- and long-term outcome of the procedure.
Methods: Consecutive patients (81±5 years, 91 males) who underwent TAVI were evaluated. Echocardiographic parameters were recorded before the procedure, at discharge of the patient and during one month- and one year- follow-up. One month- as well as one year- mortality was recorded according to VARC criteria. ID was defined as the distance both from the native non coronary cusp (NCC) and the left coronary cusp (LCC) to the deepest edge of the deployed bioprosthesis in the left ventricle, using an offline program. The patients were separated into two groups according to the ID. Group I included all patients with implantation depth from 4 to 12 mm and Group II included those with implantation depth under 4mm (distance from either LCC or NCC <0 mm) but without significant regurgitation requiring repositioning techniques.
Results: One hundred sixty four patients were evaluated. When Group I (81±4.5 years, 75 males (56%)) was compared with Group II (81±6.5 years,16 males (53%)), peak gradient at discharge (17±7.5 vs. 14±7 mmHg, p=0.01) proved to be significantly higher in Group I. This remained significant after adjusting for the AR index, the post procedural systolic blood pressure and LVEFat discharge using the linear regression model (p=0.03, B=–0.18). Mean gradient at discharge (9±4 vs. 8±4, p=0.04) also differed significantly among two groups. In-hospital and one month mortality did not differ among two groups. However, one year, all-cause mortality was significantly different among two groups (13.4% vs. 0%, p=0.04).
Conclusions: In conclusion, implantation depth under 4mm seems to have a positive effect on both short- and long-term outcome of the procedure. Furthermore, it proved to be an independent predictor of peak gradient.
Acknowledgement/Funding: State Scholarships Foundation

P5477 | BEDSIDE
External validation and decision curve analysis of EuroSCORE 2, STS and German AV score in the selection of high-risk patients with aortic stenosis to TAVI

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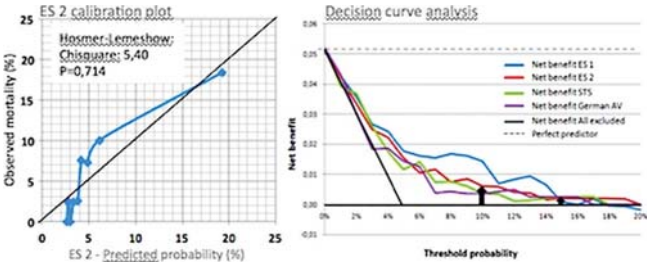
Introduction: Risk prediction in aortic stenosis (AS) interventions is increasingly important, potentially improving selection of pts for aortic replacement (AVR) or TAVI.
Purpose: To evaluate the predictive value of EuroSCORE 2 (ES2), STS, and German AV (GAV) scores in hospital mortality for patients with AS undergoing AVR and define which score has the greatest accuracy to predict death in high-risk pts.
Methods: Prospective cohort, all patients with severe AS consecutively operated on Jan2010-Dec2014. Predictive ability of scores was evaluated for O/E mortality ratio, calibration (calibration plot, Hosmer-Lemeshow - HL), discrimination (ROC Curve) and NRI. Decision curve analysis evaluated clinical impact (Net Benefit) of the scores.
Results: 403 pts, 66±13 years, 62.5% male. Procedures: AVR 61%, AVR+CABG 39%; ES2 2.55±2.46, STS 2.75±2.27, GAV 2.39±1.51. In hospital mortality was 5.2%. All scores were independent predictors of death and MACCE and are highly correlated with each other ($r>0.8$), but they have a trend to underestimation (O/E >1.5 for all). ES 2 and STS were well calibrated (HL: p=0,71/p=0,32), and GAV were miscalibrated (p=0,03). Discrimination was better for ES2 (AUC ROC 0.77) and STS (AUC ROC 0.75) than GAV (AUC ROC 0.73). Comparing the 3 scores, NRI of ES2 was better than STS and GAV (ES2 x STS, NRI=+4,8%; ES2 x GAV, NRI=+4,8%, $p<0,05$ for both). Decision curve analysis (Fig) showed that ES2 correctly predicted 1 extra death in 163 pts (10% threshold), without missing any death. It does that better than STS and GAV (1 extra death in 278 pts - 10% threshold).



Calibration/Decision curve analysis

Conclusion: ES2 and STS are accurate and well calibrated. ES2 showed the largest NRI and Net Benefit. ES2 should be the risk model of choice for selection of AS pts for TAVI.

P5478 | BEDSIDE
Aortic prosthesis-patient mismatch halters regression of secondary mitral regurgitation after isolated aortic valve replacement: 6-year follow-up analysis

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Background: Secondary mitral regurgitation (SMR) is generally reduced after isolated aortic valve replacement (AVR). Prosthesis-patient mismatch (PPM) may hinder normalization of left ventricular geometry and pressure overload following AVR.
Purpose: We aimed to investigate the relationship between PPM and regression of SMR following AVR for aortic valve stenosis (AS).
Methods: A total of 578 patients with AS who underwent isolated AVR at two institutions and presenting moderate SMR (mitral regurgitant volume (MRV) 30–45ml/beat) not considered for surgical correction were included in this study. Clinical and echocardiographic follow-up were completed at a median follow-up time of 72 months. PPM was defined as an indexed effective orifice area (EOAi)$\leq 0.85 cm^2/m^2$.
Results: Aortic PPM and was found in 219/578 patients (37.9%). There were no significant differences in baseline and operative characteristics between patients with or without PPM. Patients with PPM had less regression of SMR following AVR compared to those with no PPM (change in MRV: –12±5 vs. –19±4 mL, respectively; $p<0.0001$). Variables significantly associated with postoperative change in MRV on univariable analysis were entered in a multivariable linear regression model which showed EOAi ($p<0.0001$) and LA diameter (p=0.006) to be independently associated with MRV improvement. Patients with PPM also had less postoperative improvement in 6-minute walking test distance (82±74 vs. 43±39m, $p<0.0001$).
Conclusions: PPM is associated with lesser regression of SMR following AVR. This unfavourable effect was associated with worse functional capacity. These findings emphasize the importance of operative strategies aiming to prevent PPM in patients with AS and concomitant SMR.

P5479 | BEDSIDE
Study of mitral valve prolapse and chronic anxiety in patients with breast cancer

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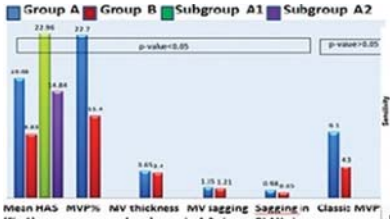
Background: Mitral valve prolapse (MVP)is more prevalent in females and is associated with chronic anxiety.We aimed to assess its prevalence in females with breast cancer before initiation of cancer specific therapy and to examine if anxiety as a part of MVP syndrome is a link between both conditions.
Methods: We included 110 females (GpA) with recently diagnosed breast cancer, and 70 healthy females as control (GpB). Group A was subdivided into sub A1 which included 25 patients with both breast cancer and MVP and subA2 which included 85 patients with breast cancer but no MVP.MVP was considered non classic if there is only leaflet sagging $\geq$2mm & classic if there is also an increase in leaflet thickness $\geq$5mm. All patients underwent echocardiography & Hamilton anxiety scale (HAS) interrogation to detect anxiety and its degree.
Results: The prevalence of non classic & classic MVP in GpA & GpB was 27.7%,

11.4%, 9.1 & 4.3% respectively. The means of HAS, thickness and sagging of mitral valve (MV) leaflets were significantly (p-value <0.05), higher in GpA than GpB and in subgroup A1 than A2 (Fig. 1). There was a statistically highly significant (p≤0.000) correlation between mean HAS and both MV leaflet thickness (r=0.60) and sagging, as recorded in the parasternal (r=0.384) and apical long axis (r=0.387) views. Using ROC curve analysis (Fig. 2), the cutoff value of MV leaflet thickness in to predict severe anxiety in GpA is 3.9350 mm.



HAS=Hamilton anxiety scale, MVP=mitral valve prolapse, 4-C&PLAX=4-chamber anc parasternal long axis views

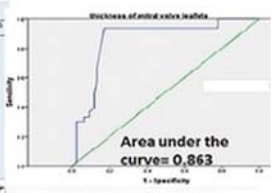


Figure (2)ROC curve for mitral valve leaflet thickness to predict severe anxiety.

Conclusion: MVP, especially when mitral leaflet thickness ≥3.9 mm, correlates significantly with severe anxiety. The prevalence of both conditions is significantly increased in patients with breast cancer. Larger studies are recommended to further elucidate this relationship.

P5480 | BEDSIDE
Prediciton of systemic vascular resistance non-invasively in patients with moderate-severe mitral regurgitation with a formula taking inspiration from pulmonary hypertension guideline

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Purpose: Mitral regurgitation (MR) is a frequent valvular disorder primarily and secondarily accompanying various heart diseases. Significant MR initially decreases afterload. Increase in systemic vascular resistance (SVR) accelerates progression of MR severity and myocardial dysfunction. Determining SVR is helpful in management of significant MR, as well as various cardiac disorders.
Pulmonary vascular resistance can be predicted non-invasively via a formula based on ratio of tricuspid valvular regurgitant flow maximal velocity (Vmax) to velocity time integral (VTI) obtained at right ventricular outflow tract. In this study, we aim to investigate whether this rationale would fit to the left side of the heart for determining SVR.
Methods: Patients undergoing cardiac catheterization for various reasons except for congenital heart diseases, who had moderate-severe MR were included in our study. Fick's method was used for SVR calculation. Echocardiography was performed to patients just after cardiac catheterization. Mitral regurgitation Vmax and left ventricular outflow tract (LVOT) VTI were measured. Pearson correlation test was performed to determine the relationship between SVR and MR Vmax/LVOT VTI ratio.
Results: A total of 21 patients (12 female; 56.7±14.3 years) were included in our study. There was a very strong correlation between SVR values and MR Vmax/LVOT VTI ratios (r=0.833; p<0.001) (Figure 1). We generated a regression equation to predict SVR non-invasively as follows: SVR = 0.625 * [MR Vmax (cm/sec)/LVOT VTI] + 1.252. Our model calculated SVR values with a mean variability of 9%.

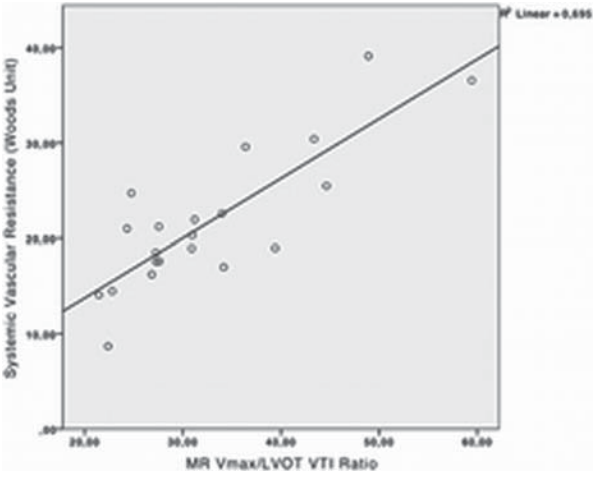

Figure 1

Conclusion: Systemic vascular resistance may be predicted via a formula based on MR Vmax/LVOT VTI ratio, in an easy and reliable way. However, our sample size is limited to make definite concerns.

P5481 | BEDSIDE
Papillary muscle free strain in patients with degenerative and functional mitral regurgitation

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Objective: Papillary muscle dyssynchrony is an important mechanism leading to mitral regurgitation (MR) in patients with ischemic and nonischemic cardiomyopathies. There is not much knowledge about papillary muscle function in patients with degenerative and functional severe mitral regurgitation. The aim of this study is to find a potential relationship between the papillary muscle strain and severe mitral regurgitation in patients with degenerative and functional severe mitral regurgitation.
Design: 38 degenerative severe mitral regurgitation patients with normal left ventricular ejection fraction (group I) and 23 functional severe mitral regurgitation patients (group II) and 12 control patients with normal mitral and left ventricular function (group III) were studied. The clinical and echocardiographic findings were recorded. Papillary muscle function was evaluated by free strain in diastole for anterolateral papillary muscle on apical four chamber images (PAFSTR4) and for posterolateral papillary muscle on apical three chamber images (PAFSTR3)and left ventricular global strain (GLSTR) were evaluated by applying 2D speckle-tracking imaging.
Results: There is no significant differences among three groups in terms of basic characteristics (age, sex p>0,05). Among groups; PAFSTR4 (group I: –32±16.5, group II: –18,9±7,8, group III: –32.0±19; p: 0.001, in post hoc analysis group I vs II p: 0.01, group I vs III p: 0.99, group II vs III p: 0,02); PAFSTR3 (group I: –33.4±13.4, group II: –21.0±10.6, group III: –34.0±9.9; p<0.001, in post hoc analysis group I vs II p<0,001, group I vs III p: 0.95, group II vs III p: 0.005), GLSTR (group I: –16,8±5.4, group II: –9.5±3.7, group III: –19.9±1.9; p<0.001, in post hoc analysis group I vs II p<0.001, group I vs III p: 0.10, group II vs III p<0.001). In addition a modarate negative correlation was detected between PAFSTR3 and mitral regurgitation PISA r:- 0.37 and MY EROA r: –0.40.
Conclusion: In functional severe mitral regurgitation papillary muscle strain is decreased and this decrease is modarately correlated with the degree of mitral regurgitation.

P5482 | BEDSIDE
The impact of arterial load on left ventricular performance in severe mitral stenosis

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Background: Left ventricular (LV) function in rheumatic mitral stenosis (MS) remains an issue of controversy, due to load-dependency of previously employed assessment methods.
Purpose: The aim of this prospective study was to investigate LV performance in MS employing relatively load-independent indices robust to the altered loading state.
Methods: We studied 106 subjects (32±8 years, 72% female) with severe MS (0.8±0.2 cm^2) and 40 age-matched controls. MS subjects underwent simultaneous bi-ventricular catheterization and transthoracic echocardiography (TTE) before and immediately after percutaneous transvenous mitral commisurotomy (PTMC). Sphygmomanometric brachial artery pressures and TTE recordings were simultaneously acquired in controls. Single-beat LV elastance (Ees) was employed for LV contractility measurements. Effective arterial elastance (Ea) and LV diastolic stiffness were measured.
Results: MS patients demonstrated significantly elevated afterload (Ea: 3.0±1.3 vs. 1.5±0.3 mmHg/mL; p<0.001) and LV contractility (Ees: 4.1±1.6 vs. 2.4±0.5 mmHg/mL; p<0.001) as compared to controls, with higher Ea in subjects with smaller mitral valve area (MVA) ≤0.8cm^2 and pronounced subvalvular fusion. Stroke volume (49±16 to 57±17 mL; p<0.001) and indexed LV end-diastolic volume (LVEDVindex: 57±16 to 64±16 mL/m^2; p<0.001) increased following PTMC while Ees and Ea returned to more normal levels. Elevated LV stiffness was demonstrated at baseline and increased further following PTMC.
Conclusion: Our findings provide evidence of elevated LV contractility, increased arterial load and increased diastolic stiffness in severe MS. Following PTMC, both LV contractility and afterload tend to normalize.

AORTIC VALVE INTERVENTIONS

P5483 | BEDSIDE
The type of surgical indication determines patients' prognosis in infective endocarditis

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Purpose: Current guidelines recommend surgery during the active phase of infective endocarditis (IE) in 3 situations, heart failure (HF), uncontrolled infection (UI), and prevention of embolic events (EE). Our aim was to assess patients' prognosis according to the type of surgical indication.
Methods: From 1996 to 2014, 1053 patients with left-sided IE were prospectively and consecutively recruited at 3 referral hospitals, 614 of them underwent surgery. They were classified in 4 groups according to the type of surgical indication: HF-Group (n=232), patients with HF or severe valvular regurgitation; EE-Group (n=19), patients with embolisms or large vegetations; UI-Group (n=84), patients with perivalvular complications or persistent signs of infection; M-Group (n=279), patients with two or more indications.
Results: There were no differences in age, gender distribution and comorbidities between the 4 groups. S.aureus was more frequently isolated in UI-Group ($p<0.001$). Blood cultures were positive in a higher proportion of patients in EE and UI groups ($p<0.001$), and these remained positive after 48 hours more frequently in patients from UI-Group ($p<0.001$). Acute onset was more common in UI-Group ($p<0.001$). Post-surgical evolution revealed some differences according to the surgical indication. Patients from UI-Group developed more frequently septic shock despite surgery, and mortality was higher in this group (Table).

In-hospital events after surgery

Variables	HF-Group	EE-Group	UI-Group	M-Group	p
Fever	35.8% (83)	42.1% (8)	41.7% (35)	37.7% (106)	0.781
Heart failure	32.3% (75)[a]	5.3% (1)	32.1% (27)[c]	25.3% (71)	0.033
Renal failure	32.3% (75)	31.6% (6)	32.1% (27)	25.3% (71)	0.307
Septic shock	10.8% (25)[b]	0% (0)	19% (16)[c]	7.1% (20)	0.006
Stroke	5.3% (12)	21% (4)	8.3% (7)	8.1% (21)	0.067
AV-block	8.6% (20)	0% (0)	14.3% (12)	10.7% (30)	0.219
Mortality	24.6% (57)[b]	21.1% (4)	45.1% (37)[c]	30.8% (86)	0.005

[a]Statistically significant differences between HF-Group and EE-Group. [b]Statistically significant differences between HF-Group and UI-Group. [c]Statistically significant differences between EE-Group and UI-Group.

Conclusions: Post-surgical evolution and prognosis are determined by surgical indication. The probability of success decreases in those patients with UI. Although more studies are necessary, patients with S.aureus infection and those with persistent positive blood cultures after 48h have the worst prognosis.

P5484 | BEDSIDE
Why do we need dedicated tools to quantitate the tricuspid annulus by 3D transthoracic echocardiography?

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Background: Despite an accurate measurement of tricuspid valve (TV) annulus (TA) size is important for indicating surgical TV repair, there is limited knowledge regarding the normal TA size and function, mainly due to the lack of dedicated software able to to perform a dynamic quantitative analysis of TA 3D geometry. Our goal was to quantify the normal TA dynamics by transthoracic 3D echocardiography (3DTTE) and custom software (CS), as a basis for better understanding of TA physiology and of its implications for TA sizing by 2DTTE.
Methods: 74 normal subjects (44±14 yrs, range 20–83, BSA 1.8±0.2m^2, 36 men) underwent 3DTTE of the TV from the apical approach (Philips iE33 and GE Vivid E9). Using CS, TA hinge points were initialized in mid-systole in 8 rotated planes and tracked throughout the cardiac cycle. TA non-planar area, antero-posterior (AP) and septal-lateral (SL) diameters corresponding to 2DTTE 2- and 4-chamber views, maximal (Max) and minimal (Min) diameters and their ratio (TA circularity) were measured.
Results: Normal TA is highly dynamic during the cardiac cycle, with a mean area change of 3.5 cm^2. TA area and linear dimensions were smallest at end-systole and largest in late diastole (Table, fig. B). TA shape was elliptical and became slightly rounder at end-systole (circularity=0.85±0.09 vs 0.82±0.09; p=0.01) as the AP dimension decreased more than the SL dimension. Of note, both AP and SL underestimated TA Max throughout the cardiac cycle by 4–6 mm (Table). TA fractional changes in AP and SL dimensions and area were 15%, 16% and 32%, respectively. TA non-planarity also varied from 3.4 to 6.6 mm during the cardiac cycle.
Conclusions: TA is a complex non-planar, elliptical and highly dynamic structure. Linear measurements in 4- and 2-chamber views significantly underestimate true maximal TA size, irrespective of their timing, and are inappropriate for tracking changes in TA geometry. Dynamic TA analysis by dedicated software is pivotal for quantifying TA geometry and dynamics by 3DTTE.

TA changes during cardiac cycle

	Onset of systole	End-systole	Late diastole
Area (cm^2)	8.5±2.1	7.3±1.9	10.8±2.5
Septal-lateral diameter (cm)	30±4	29±5	35±5
Antero-posterior diameter (cm)	32±6	30±4	35±6
Maximal diameter (cm)	36.5±4	33±5	40±5

P5485 | BEDSIDE
First-in-human of a transcatheter tricuspid valve repair in a severely regurgitant tricuspid valve patient

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Background: Severe tricuspid regurgitation (TR) is associated with poor prognosis however there are limited class 1 indications for intervention and high surgical risk patients may go untreated. We report the first-in-human successful transcatheter tricuspid valve repair (TTVR) for severe TR.
Methods: Compassionate use approval for the procedure was obtained from regulatory organization in Germany. To perform the transcatheter bicuspidization of the tricuspid valve, the Mitralign system was used to place pledgeted sutures via a trans-jugular venous approach. Insulated radiofrequency wires were positioned 2–5 mm from the base of the posterior leaflet, 2.6 cm apart. The sutures were drawn together and locked, plicating the posterior annulus.
Results: Reconstruction of the 3D TEE dataset at baseline revealed a tricuspid valve annular area = 14.1 cm^2, and effective regurgitant orifice area (EROA) = 1.35 cm^2. (Figure 3) There was a significant reduction in annular area (57%) and EROA (53%) measured, with 3D TEE respectively at 6.05 cm^2, 0.63 cm^2. Hemodynamic parameters also improved with a reduction in right atrial pressure from 22 mmHg at baseline, to 9 mmHg and an increase in LV stroke volume from 42 cc at baseline to 72 cc.
Conclusion: TTVR could become an effective treatment for high surgical risk patients that are non-responsive to optimal medical therapy.

P5486 | BENCH
In vivo tissue-engineered, autologous, valved conduit "Biovalve" with robust wall tissues

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Objective: Pediatric patients with congenital heart disease would benefit from replacement heart valves, particularly pulmonic valves. We developed an autologous valved conduit (Biovalve), formed by in-body tissue architecture technology (IBTA) using subcutaneously embedded plastic molds. Excellent hemodynamic performance and beneficial leaflet movement after implantation were observed in both goat and beagle experimental models. Moreover, Biovalves might potentially serve as pediatric replacement valves because they are composed of mainly autologous fibroblasts and collagen fibers. However, in the small-diameter molds required for pediatric patients, connective tissue formed based on active cell migration around the mold generally tends to be thin. Therefore, Biovalves with thin conduits have required careful surgical handling. Accordingly, we aimed to develop a mold with a paling structure to enhance IBTA for producing Biovalves with robust conduits.
Methods and results: The paling mold consisted of a two-layer structure. The inner part (outer diameter, 14 mm), which mainly formed the leaflets, was surrounded by the paling (width, 2 mm) that lined the conduit at equal intervals of 1.0 mm (total length, 20 mm). A 1-mm space was designed between the inner and outer parts as the conduit wall. After the embedding period, the space for the conduit wall was completely filled with connective tissue from outside the mold via the palings. After trimming the excess peripheral tissues and removing the mold, completely formed Biovalves with approximately 1-mm conduit walls (inner diameter, 14 mm) were obtained. There was a smooth and clear boundary between the conduit and leaflets, which consisted of mainly fibroblasts and collagen fibers. The paling mold allowed maintenance of the structure, including the lumen, and greatly improved handling of the Biovalves.
Conclusion: The paling structure facilitated the formation of approximately 1-mm thick conduit wall and leaflets through a small aperture inside the inner portion. The paling mold with a two-layer structure enabled better handling of the Biovalves, and may eventually lead to clinical applications. We are planning an implantation study of Biovalves to investigate their in-vivo durability. We hope that this type of Biovalve will be clinically used in heart valve replacement even in pediatric patients.

P5487 | BEDSIDE

Atrioventricular conduction disturbance after transcatheter aortic valve implantation: incidence and predictive factors

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Purpose: Atrioventricular (AV) conduction disturbance leading to pacemaker (PM) implantation is frequent after transcatheter aortic valve implantation (TAVI). The aim of this study was to assess the incidence and the predictors of PM implantation after TAVI.
Methods: Between 2010 and 2014, 198 consecutive patients underwent TAVI in our center. 42 patients were excluded from the study because of a pre-existing PM before TAVI. 156 patients (62 Corevalve (CV), 94 Edwards Sapiens valve (ES) were included and prospectively followed during 1 year.
Results: Complete AV block occurred after TAVI in 29 patients (19%), second degree AV block in 3 (0.05%), new left bundle branch block (LBBB) in 53 (34%). A PM was implanted in 40 patients (26%). CV patients were more frequently implanted than ES (35% vs 19%; p=0.03). Post-procedure PR, QRS duration were longer in the PM group (227 vs 196 ms; 159 vs 129 ms, respectively, p<0.001). LBBB was also more frequent (79% vs 53%; p=0.01). At hospital discharge, 83% of the PM group was stimulated. At 1 month, 10% were PM dependent and 4% at 6 months. At 1 month, 29% were stimulated less than 5% of the time and 25% at 6 months. Multivariate analysis showed that the predictors of PM implantation were a pre-existing RBBB (OR 4.7, IC 1.43–15.52, p=0.01), a pre-existing LBBB (OR 7.28, IC 2.34–22.6, p<0.001), a per-TAVI complete AV block (OR 4.21, IC 1.52–11.63, p=0.006), a high prosthesis/annulus diameter ratio (OR 1.1, IC 1.04–1.18, p=0.003) and post-procedure PR and QRS long duration (OR 1.03, IC 1.01–1.06, p=0.009; OR 1.04, IC 1.01–1.07, p=0.009 respectively). PM implantation had no impact on survival after TAVI (Logrank=0.92). The increase in LVEF post-TAVI was lower in PM group: 0.2 vs 8%, p=0.05 at 6 months and –5 vs 9.6%, p=0.004 at 1 year. The NYHA class was similar in both groups at follow up.
Conclusion: TAVI is associated in a great proportion of patients with AV disturbances which are mostly regressive over time. Patients with pre-existing RBBB, LBBB and high prosthesis/annulus diameter ratio are at increased risk of complete AV block. LVEF increase was lower in PM group even with a low percentage of stimulation time.

P5488 | BEDSIDE

Changes of implanted prosthetic valve stent morphology during transcatheter aortic valve implantation with a ballon-expandable valve

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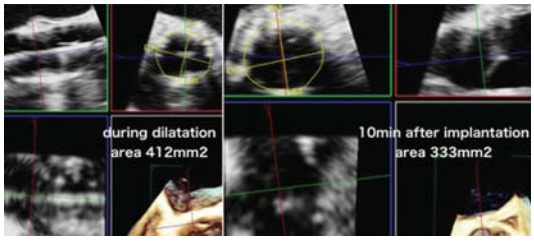
Background: It has been reported that transcatheter aortic valve implantation (TAVI) with a ballon-expandable valve was associated with valve stent recoil after balloon deflation.
Methods: 3D transesophageal echocardiography (TEE) analysis of implanted prosthetic valve stent morphology in 57 consecutive patients who underwent TAVI with a balloon-expandable valve (SAPIEN XT) was performed. We measured cross-sectional area, minimum diameter and maximum diameter of implanted stent at the basal ring of aortic valve annulus 10 minutes after prosthetic valve implantation. We also measured those parameters at the time of valve implantation in 16 patients. Annulus ratio is defined as implanted valve stent area, divided by aortic valve annulus area which were evaluated before implantation.
Results: Implanted prosthetic valve stents were expanded as intended size at the time of valve implantation (412±6.1 mm^2, SAPIEN XT 23mm valve n=10, 522 mm^2, SAPIEN XT 26mm valve n=1, not nominal volume inflation were excluded). 10 minutes after implantation, stent areas got back to almost the same size of aortic valve annulus areas before implantation (annulus ratio 0.97±0.07). Annulus ratio was between 0.9 and 1.1 in 44 (77%) cases, between 0.8 and 0.9 in 9 (16%) cases and less than 0.8 in 2 (4%) cases. These 2 cases had commissure fusions. Implanted stents were more circular than aortic valve annulus before implantation (Sphericity index; 1.10±0.05 vs 1.29±0.09, p<0.0001).



Conclusions: Implanted prosthetic valve cross-sectional area got back to almost the same size of intrinsic annulus areas soon after implantation.

P5489 | BEDSIDE

Comparison of feasibility and efficacy of transcatheter aortic valve implantation in patients aged 75 years and older versus patients less than 75 years of age

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Background: Transcatheter aortic valve implantation (TAVI) is a treatment option for younger patients with symptomatic severe aortic stenosis (AS) who seem to be high risk for surgical aortic valve replacement due to significant co-morbidities. However, very few studies have investigated the feasibility and efficacy of TAVI for younger patients. Thus, the aim of this study was to evaluate the feasibility and efficacy of TAVI in younger patients.
Methods and results: Between October 2006 and October 2013, 790 consecutive patients undergoing TAVI were included in the current analysis. The cohort was divided into 2 groups: patients aged ≤75 years (n=79) and >75 years (n=711). There were significant differences with regard to major co-morbidities which were more frequent in patients aged ≤75 years compared to patients >75 years: history of cancer (22% vs 12%, p<0.001), previous coronary artery bypass grafting (30% vs 11%, p<0.001), and renal insufficiency requiring hemodialysis (11% vs 1%, p=0.007). With regard to echocardiography findings, ejection fraction was significantly lower in patients aged ≤75 years compared to patients >75 years (50.2% vs 54.4%, p=0.016). With regard to outcomes, there were no significant differences in the procedural success rate (92% vs 92%, p=0.908), 30-day mortality (10% vs 11%, p=0.747) and 30-day combined safety endpoint (21% vs 22%, p=0.802) between the 2 groups. However, regarding mid-term outcome, the survival rate of patients aged ≤75 years was significantly higher in comparison with patients aged >75 years (log-rank p=0.037). The COX regression model showed IDDM, life-threatening bleeding and creatinine clearance (<60 ml/min) as the independent predictors of mid-term cumulative mortality among younger patients.
Conclusions: Although patients aged ≤75 years have more co-morbidities compared to patients aged >75 years, TAVI can be feasible and safely performed. Furthermore, the mid-term outcome seems to be better among patients ≤75 years compared to patients aged >75 years.

P5490 | BEDSIDE

Feasibility and safety of early discharge after transfemoral transcatheter valve implantation with balloon-expandable prosthesis: a prospective study

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Introduction: There is currently no consensus on the duration of hospitalization required after transfemoral transcatheter valve implantation (TF-TAVI). We recently reported, retrospectively, that early discharge (within 3 days) was feasible in 31% and safe without any death and a low rate of re-hospitalization at 30 days. We therefore aimed to confirm the feasibility and safety of early discharge after TF-TAVI in a prospective study.
Methods: After implementation of an early discharge pathway in our center in January 2014, we included prospectively, between January 2014 and January 2015, 130 consecutive patients scheduled for TF-TAVI with Edwards prosthesis using exclusively local anesthesia. The primary end-point combined death and re-hospitalization from discharge to 30-day follow-up. The proportion of early discharge (within 3 days) and the cause of "non-early" discharge were also assessed.
Results: During the studied period, the mean length of stay was 4.0±2.7 days and 76 (58.6%) patients were discharged early within 3 days including 55 (42.3%) patients discharged within 2 days after the procedure. The main causes of non-early discharge were conduction abnormalities in 33 (25%) patients, major vascular complications in 18 (13.8%) patients, social issues in 11 (8.5%) patients, heart failure in 3 (2.3%) patients, and acute kidney injury in 2 (1.5%) patients. Finally, between discharge and 30-day follow-up, there was no death and only 5 (6.5%) patients required re-hospitalization.
Conclusions: Early discharge is feasible in slightly over 50% of cases in selected patients scheduled for TF-TAVI using a balloon-expandable and local anesthesia, and is associated with no death and a very low rate of readmission at 30 days. The two main causes of non-early discharge are occurrence of new conduction disturbances and major vascular complications.

P5491 | BEDSIDE

Prevalence and classification of mitral regurgitation in TAVI population

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Background: Mitral regurgitation (MR) is a frequent finding in patients with aortic stenosis (AS) with important clinical and prognostic implications. Aim of the study is to evaluate the prevalence and classify MR, and assess background differences between functional and organic MR in TAVI population.
Methods: Between 2007 and 2014, 642 patients underwent TAVI for native se-

vere AS. We classified MR etiology according to valve morphology: organic or functional (normal valve leaflets), unknown, mixed (functional plus organic). Among organic MR (OMR), pts were divided in to fibro-calcific changes group, prolapse, rheumatic and post-radiation group. Functional MR (FMR) was subclassified in tethering, annular dysfunction/dilation and mixed (tethering + annular dysfunction) groups. MR severity was graded according to multiparametric approach.

Results: MR≥2+ was present in 43.4≥%. In this group, MR was organic in 72.7%, functional in 13.9%, mixed in 5.4%. OMR was found to be due to fibro-calcific degeneration, prolapse, rheumatic and post-radiation in 95%, 3.4%, 1.5% and 0.5% respectively. FMR was caused by tethering in 84.6%, annular disfunction/dilation 12.8% and mixed functional mechanism in 2.6%. There were significant background differences between OMR and FMR groups in EF (51.6±12.4 vs 38.3±15.0%; p=0.0001), Log. Euroscore (22.2±15.4 vs 34.9±24.2; p=0.0001), left ventricle volumes (EDV 102.2±35.2 vs 150±61.3; ESV 49.9±28.3 vs 100.6±55.3 ml; p=0.001) and mean trans-aortic gradient (53.9±16.9 vs 43±14.49 mmHg; p=0.004). Moreover, OMR was more frequent in females (60.8%) and FMR in males (63.2%) (p=0.04). In OMR group a significant negative correlation between MR severity and aortic valve area (p=0. 03) was found, whereas no significant correlation was found in FMR group (p=0.07).

Conclusion: Our study shows that in TAVI population the most frequent cause of MR is fibro-calcific disease, especially in women. In these group of patients MR severity was negatively correlated to aortic valve area.

P5492 | BEDSIDE
Prediction of mortality after transcatheter aortic valve replacement: developement of a novel risk score

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Objective: Based on data from the German Aortic Valve Registry (GARY) a novel scoring system to predict perinterventional- and 1 year-mortality in patients undergoing transcatheter aortic valve replacement was developed.

Methods and results: 3875 pt undergoing TAVI were included in this ongoing non-randomized national multicenter registry. In-hospital mortality was chosen as a binary outcome measure. First, potential risk factors were tested in an univariate manner by Fisher's exact test for significant influence on mortality and multiple logistic regression with backward and forward selection. Calibration was ascertained by the Hosmer-Lemeshow method. In order to define the quality of discrimination, the area under the receiver operating characteristic (ROC) curve was calculated. In 3772 of 3875 (97.3%) pts. survival status was known and in 3221 (85.4%) pts a complete data set was available. One-year mortality was 22.7% (n=730) for all patients. Based on multiple logistic regression, 22 risk factors impacting mortality were identified, including age, body mass index and left ventricular function categorized in two (left ventricular function) or three subgroups (age). The area under the ROC curve with a value of 0.712 affirmed the quality of discrimination of the established scoring model.

Conclusions: Based on GARY data the above model allows the prediction of 1-year mortality after TAVI in low-, moderate- and high-risk groups, thus supporting continuous improvement of patient selction interventional aortic valve procedures.

CARDIOMYOPATHIES

P5493 | BEDSIDE
Sex-correlatad differences in a population affected by hypertrophic cardiomyopathy referred to a single italian regional center

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Background: Hypertrophic Cardiomyopathy (HCM) is a disease with an autosomal dominant pattern of inheritance. Gender-related differences have been described in a large multicenter population of patients with HCM.

Purpose: To examine which, if any, clinical or instrumental features in our outpatients HCM-clinic appeared to be sex-related.

Methods: We studied 526 consecutive patients followed-up in our centre from 1983 to 2013. Mean follow-up duration was 15±11 years (yrs), no difference in length between male and female was found.

Results: Main characteristics in male (M) and female (F) patients, at first evaluation, are listed in table 1.

Twenty-three (11%) female and 24 (7%) male (p=0.2) were lost at follow-up. After a mean f.u. of 15±11 yrs:

1) Mean age is still higher in women [62±18 and 56±16 yrs in F and M respectively (p=0.0003)].

2) Women remain more symptomatic [mean NYHA FC: 1.5 M and 1.8 F (p<0.0001)].

3) Differences in medical treatment tend to disappear.[F=168 (90%) M=251 (86%) (p=0.15)].

4) Women are underinvestigated with treadmill test [F 100 (53%) M 213 (72%) (p<0.0001)] and cardiac magnetic resonance [F=85 (45%) M=177 (60%) (p<0.001)]. Thirty-two (17%) women and and thirty-two (10%) men (p=0.05) died during f.u. Sudden death occured in 14 (5%) men and in 4 (2%) women (p=0.04) while heart failure related death occurred more frequently in women than in men [F=10 (3%) M=19 (10%) (p=0.001)]

Table 1

First evaluation	Overall	Female patients	Male patients	p value*
Number	526	209 (40%)	317 (60%)	
Age (yrs)	52±18	56±19	50±17	0.001
NYHA F.C.	1.5	1.6	1.3	<0.0001
LVOT obstruction	209	94 (44%)	115 (35%)	0.04

LVOT, left ventricular outflow tract. *n.s. For p value >0.05.

Conclusion: As previously reported, also in our population women, either at first evaluation and at f.u., are under-represented, older and more symptomatic. This could be, at least in part, explained with an underdiagnosis and a higher prevalence of the obstructive form of the disease. We observed a trend toward higher mortality rates in women, in particularly for heart failure related-death; if, to avoid delay in diagnosis in women translates in a better quality of life or even in a mortality reduction, remains unresolved.

P5494 | BEDSIDE
Clinical usefulness of next generation sequencing techniques analysis in hypertrophic cardiomyopathy

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Background: Next generation sequencing (NGS) techniques are substituting old conventional ones (Sanger) due to a faster and broader analysis. In patients (P) with hypertrophic cardiomyopathy (HC) the incremental diagnostic value has not been completely defined.

Methods: A cohort of 104 non-genetically related P with HC included in an Inherited Cardiovascular Disease Program were genotyped from September 2011 to May 2014. In 45 P, 5 sarcomeric genes (MYBPC3, MYH7, TPM1, TNNT2, ACTNC1) were analyzed by Sanger and in 59 P, 25 structural genes were studied by NGS.

Aim: To compare the clinical information provided by different genetic test techniques.

Results: P studied by Sanger and NGS techniques had comparable data (Table1). A total of 135 variants were reported. Causal mutations (truncated proteins or described mutations) were observed in 34%, uncertain significance variants (USV) in 19%, variants without clinical relevance (polymorphism or missense variants in HC minor related genes) in 19% and negative results in 27%. NGS found a higher number of variants (2.14 vs 1.12, p<0. 001), due to non-clinical significant variants (2% vs 32%, p<0.001). Causal mutations detected were not different (Sanger 38% vs NGS 31%, p=0.285). In the NGS group 9 P (15%) had clinical-significant variants in genes that wouldn't had been analyzed by Sanger: 4 mutations (ACTC1 p.A297S; TNNC1 p.A8V; ACTN2 p.E849*; VCL p.L277M) and 5 USV but likely to be familial disease-causing.

Table 1

Variable	Sanger (n=45)	NGS (n=59)	p
Age (years)	55 [41–65]	58 [41–70]	0.442
IVS (mm)	21±5.4	20±5,8	0.992
LVEF (%)	62±8,1	60±7,8	0.417
FSCD (n)	10 (22%)	16 (27%)	0.368
FHC (n)	25 (55%)	25 (42%)	0.138
LVEF <50% (n)	4 (9%)	7 (12%)	0.415

HC, hypertrophic cardiomyopathy; IVS, Interventricular septum; LVEF, Left ventricular eJection fraction; FSCD, familial sudden cardiac death; FHC, familial HC.

Conclusion: NGS can detect a broader spectrum of genetic variants that increase the detection of clinically significant variants including new mutations. Nevertheless, interpretation of genetic results might be complicate and it should be performed in referral centers.

P5495 | BEDSIDE
Prevalence and clinical significance of life threatening arrhythmias in takotsubo cardiomyopathy

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Background: Although prognosis of Takotsubo cardiomyopathy (TTC) is generally thought to be favorable, the initial presentation can be accompanied by various complications including life threatening arrhythmias. In view of lacking data, the present study sought to determine the prevalence and prognostic relevance of arrhythmias in patients with TTC.

Methods and results: Continuous electrocardiographic monitoring and serial 12-lead ECG recording was performed in 178 consecutive patients presenting with TTC. The primary endpoint was the occurrence of life threatening arrhythmias consisting of ventricular tachycardia, ventricular fibrillation, asystole, and

complete atrioventricular block. Secondary endpoints were the frequency of complete sinoatrial block, syncope, atrial fibrillation, and cardiopulmonary resuscitation. Short-term mortality was determined 6 months after initial presentation.
The primary endpoint was reached by 24 TTC patients (13.5%). The prevalence of ventricular tachycardia, ventricular fibrillation, asystole, and complete atrioventricular block was 7.3%, 2.3%, 2.8% and 2.2% respectively. 6-month mortality was significantly higher in patients experiencing life threatening arrhythmias compared to patients without arrhythmias (35% versus 8%; odds ratio = 5.96; 95% confidence interval 2.10 to 16.88; $p<0.01$). Cardiopulmonary resuscitation was performed in 8.5% of patients and 27% had a history of atrial fibrillation. The need for cardiopulmonary resuscitation and a history of atrial fibrillation were also associated with increased 6-month mortality.
Conclusion: Life threatening arrhythmias are a common finding in the acute and subacute phase of TTC and associated with increased short-term mortality.

P5496 | BEDSIDE
Multiple gene sequencing reveals striking genetic diversity in patients with dilated cardiomyopathy

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Introduction - Dilated cardiomyopathy (DCM) is characterized by enlarged ventricles and contractile dysfunction, and is a common cause of heart transplantation. Familial DCM accounts for 30–50% of the cases, and the inheritance pattern is primarily autosomal dominant. This suggests single-gene germline mutations as an important cause of the disease. Mutations in more than 40 genes have been associated with DCM. However, most previous studies focus on one or a few genes only, leading to a gap in the knowledge regarding the prevalence of, and relation between, mutations in the different genes.
Purpose: The purpose of this study was to determine the prevalence of mutations in DCM-associated genes in patients with DCM, to investigate the co-occurrence of more than one mutation in the same patient, and to determine the ratio of novel versus previously reported mutations in each gene.
Methods: DNA was extracted from blood samples of 176 patients, collected in 10 different centres in Sweden. Sixty (34%) patients had familial or suspected familial DCM. The exons of 41 genes previously associated with DCM were sequenced using the Illumina platform. After filtering out variants that occur in healthy control populations (1000 Genomes and ESP6500), the results were compared to an integrated catalogue of 1173 known and candidate DCM variants from the NCBI ClinVar database and recent large-scale sequencing studies.
Results: In total, 71 rare protein-altering variants were found in 24 different genes. Twenty subjects carried rare loss-of-function mutations, defined as nonsense, frameshift and splice site variants undetected in the control populations. For 43 additional patients, we observed rare variants of uncertain significance (missense and in frame insertion/deletion variants). Seven patients had more than one rare protein-altering variant. Of the variants found in the study, 63 were novel and 8 (3 stopgain and 5 missense variants) were previously reported in patients with DCM. The genes with the highest prevalence of variants were TTN, DSP, LMNA, and SCN5A.
Conclusion: This study provides a framework of the genetic alterations found in patients with DCM. We found few recurrent variants and, in several cases, variants in different genes co-occurring in the same patients. The vast majority of variants found were not reported before, highlighting the genetic heterogeneity of DCM. The complex pattern of mutations makes it difficult to determine a single disease-causing mutation in a patient, suggesting caution in the interpretation of single-gene sequencing in patients with DCM.

P5497 | BEDSIDE
Prevalence of fabry disease in patients with hypertrophic cardiomyopathy: preliminary results of a multicenter nationwide screening study

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Introduction: The prevalence of Fabry disease (FD) in patients with hypertrophic cardiomyopathy (HCM) remains unclear. Previous studies have reported different results due to different inclusion criteria, study designs and screening methods, but also because genetic variants of unknown significance are commonly found on screenings of FD.
Aim: To determine the prevalence of FD in patients with HCM through a multicenter nationwide screening study.
Methods: Multicenter nationwide study involving 12 hospital centers and including all patients diagnosed with HCM (LV wall thickness $\geq$15mm). We evaluated demographic, clinical, electrocardiographic and cardiac imaging data. The screening of FD was performed by dried blood spot test with measurement of the enzymatic activity of alpha-galactosidase A in males and also molecular analysis of the GLA gene in females.
Results: This screening included so far 483 patients with HCM, predominantly males (61%), with mean age 62±15 years.
The pattern of HCM was asymmetric (70%), symmetric (15%), apical (13%) or other (2%). Thickness of IVS was 18±5 mm and posterior wall 11±3 mm. LV mass was 182±80g/m^2. LV ejection fraction was 66±10%. Obstruction was present at rest in 36% and diastolic dysfunction in 75%. MRI detected delayed gadolinium enhancement in 52%. Family history of HCM was present in 30% and 31% had sarcomeric gene mutations.
The screening of 483 patients with HCM identified 19 patients with GLA gene mutations (3.9%): 1 female with mutation p.M290I, 1 female with mutation p.E203X, 1 male and 1 female with mutation p.R118C, 1 male with mutation p.A143T, 1 female with mutation p.D175E and 9 males and 4 females with mutation p.F113L. Most of the patients presented the pathogenic mutation p.F113L, a mutation associated with later onset phenotype characterized mainly by cardiac manifestations. These patients belong to the same geographic region, where a founder effect of FD was documented. The mutations p.M290I and p.E203X were found to be pathogenic. There is some controversy about the pathogenic role of mutations p.R118C and p.A143T. The study of the mutation p.D175E is ongoing, so it remains a genetic variant of unknown significance.
Conclusion: In this multicenter nationwide screening study, the preliminary prevalence of GLA gene mutations in patients with HCM is 3.9%. This high prevalence is mainly explained by a founder effect of FD in one of the geographic regions of this screening. All screening studies of FD face the problem of finding genetic variants of unknown significance and further studies are needed to clarify their clinical meaning.
Acknowledgement/Funding: Shire Human Genetic Therapies

P5498 | BEDSIDE
Long term results in a geographical cohort of hypertrophic obstructive cardiomyopathy: Pacemaker-therapy has comparative survival and a lower need for re-operations than surgical myectomy

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Background: Prospective randomized treatment studies using short AV-delay right ventricular pacing to reduce left ventricular outflow tract obstruction (LVOTO) in hypertrophic obstructive cardiomyopathy (HOCM) have reached conflicting results regarding gradient reduction and symptomatic improvement, and pacing is no longer recommended in international guidelines. Surgical myectomy is still considered the gold standard for treatment of LVOTO resistant to medical therapy. However there are no reported long term survival figures for pacing treatment.
Purpose: A comparison between myectomy and pacing regarding total and event-free survival in a complete geographical cohort.
Methods: A systematic diagnostic code search in all ten hospitals in West Götaland region for patients attending between 2002 and 2013 identified 44 patients treated with myectomy (surgery at a tertiary center), and 89 patients with pacing as first procedure, with respective mean follow up of 13 versus 12 yrs. Total and event-free survival were compared with Kaplan-Meier survival curves and significant factors influencing outcome with Cox regression. No patient was lost to follow up.
Results: In the total patient cohorts 5 yr and 10 yr survival were 90.7% v. 90.7% and 71.6% v. 86.9% in the pacing and myectomy groups respectively, but survival curves were not significantly different with Log Rank testing (P=0.146). The groups were well matched in terms of LVOTO before procedure (mean gradients 71mmHg versus 78mmHg) and maximum septum thickness (20mm versus 19mm). However there was a significant difference in age at procedure between the treatments groups (mean 61yrs versus 39yrs), and Cox analysis showed this to be a significant survival factor. Accordingly we also compared survival after the two treatments with case controls matched for age and gender. The matched cohorts had overlapping survival curves with no trend to difference (Log Rank P=0.94), and 5 and 10 yr survival of 93.8% v. 90.5% and 77.5% v. 85.2% respectively. Annual mortality postop was 2.1% in pacing and 1.9% in myectomy group. There was no significant difference in event-free survival either (p=0.95). In the matched groups 3.1% of paced patients required a second procedure for LVOTO whereas 28.1% in myectomy group did (p=0.0127 Fishers's exact test). Heart transplants were needed for 3.1% versus 9.4% respectively.
Conclusion: It seems premature to discard short AV-delay pacing as a treatment option for patients with HOCM. The long-term survival and event-free survival is comparable to results after myectomy, and need for further procedures is lower.

P5499 | BEDSIDE

Diagnostic utility of whole exome sequencing for the elucidation of genetic architecture in familial dilated cardiomyopathy (DCM): examination of a representative Czech cohort with recent-onset DCM

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Introduction: Clinical heterogeneity of dilated cardiomyopathy (DCM) and its complex genetic architecture complicate disease risk stratification and genetic counseling. Genetic testing might be particularly useful in recent-onset DCM (RO-DCM) with highly variable outcomes.
Methods: Three generation family history was ascertained in 109 consecutive, unrelated patients with RO-DCM (i.e. history of symptoms ≤6 months, 72% males, mean age 44±10 years, median duration of symptoms 2 months, LVEF 23±7%). Familial DCM was defined as confirmed diagnosis of this disease in ≥2 family members. Cases with familial DCM underwent non-invasive cardiologic clinical workup followed by whole exome sequencing (WES; TruSight Exome; Illumina, USA). Detected variants were confirmed by Sanger DNA sequencing and their segregation in the families under study.
Results: A total of 18/109 individuals (16%) with RO-DCM had familial disease. In 10 of 14 families (72%) indicated for WES we identified a pathogenic variant in the following genes: TTN in 3 cases (21%), followed by MYO1C, TNNI3, MYH7, FLNC, RBM20, BAG3 and DOLK each in one family (7%, for each mutation), while WES was inconclusive in 4 families (28%).
Conclusion: Application of WES represents a promising strategy for the evaluation of genetic architecture of familial forms of DCM since we were able to identify a pathogenic variant in 72% of these families.
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P5500 | BEDSIDE

Assessment of systolic and diastolic function in systemic light chain amyloidosis: an echocardiographic and cardiac magnetic resonance study

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Background: Cardiac involvement in systemic light-chain amyloidosis (AL) is characterized by normal or slightly decreased left ventricular (LV) ejection fraction, using 2D-echocardiography (TTE) and typically a diastolic dysfunction with left atrial (LA) enlargement. To assess cardiac involvement, the Mayo Clinic staging (MC) using NTproBNP and troponin, allows risk stratification of patients into 3 groups with different outcomes. Cardiac magnetic resonance (CMR) assesses accurately chambers size and function. We aimed to compare features of LV systolic and diastolic function, obtained by TTE, and morphological functional parameters derived from CMR, namely LV myocardial late gadolinium enhancement (LGE) and indexed max LA volume (LAVi) and emptying fraction (LAEF).
Methods and results: Forty-two consecutive patients (66±10 years, 57% males) in sinus rhythm with confirmed AL, underwent simultaneously TTE and CMR within 24 hours. LAEF was calculated after assessing the maximal and minimal LAVi (by area/length formula) using 4 and 2 chambers views. Diastolic parameters and 2D-LV global longitudinal strain (GLS) obtained by TTE were stratified according to LAEF, to LAVi and to the presence or not of LGE. Patients in MC stage III had the worse TTE and CMR parameters. LV GLS (–10.1±3.1 vs. –17.3±3.7, $p<0.001$), mitral deceleration time, E/A ratio and lateral E/e' ratio, were significantly altered in patients with low LAEF <17.5% (cutoff) vs. those with higher LAEF, whereas, they were not significantly different according to maximal LAVi. GLS was decreased in patients with LGE when compared to those without LGE: –10.8±2.8% vs. –16.5±5.2%, $p<0.0008$.
Conclusion: In systemic AL, reduced LV GLS is associated with presence of LGE while impaired LV filling pressures are rather related to decreased LA emptying fraction. Multimodality imaging in patients with AL may allow complementary and better assessment of LV hemodynamics.

P5501 | BENCH

FOXO3a deficiency protects from pathogen-induced myocarditis in mice and men

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Background: Coxsackievirus B3 is known to induce myocarditis leading to DCM. Cardiac injury is mediated by viral damage and the hosts immune response. FoxO3a is a transcription factor involved in cell metabolism, stress resistance, and differential outcomes in inflammatory disease. Moreover, FOXOs play key roles in immunoregulation. Therefore, the role of FOXO3a in murine CVB3 myocarditis and human virus(+) DCMi was investigated.
Methods: CVB3 myocarditis was induced in WT and FOXO3a–/– mice. mRNA/miRNA expression, SNP analysis and viral load was assessed by QRT-PCR. Hearts were stained with H/E and evaluated by inflammatory score. NK cells were analyzed for cytotoxicity, IFN-γ production and activation markers by FACS. Human endomyocardial biopsies were analyzed for viral genomes and inflammation, functional parameters were determined at entry and 6 months follow-up.
Results: FOXO3a–/– mice showed significantly lower cardiac viral titers compared to wild-type mice accompanied by a reduced inflammatory score and diminished expression of CD3+ T cells, CD14+ monocytes. as well as Nkp46+ cells. Moreover, expression of proinflammatory cytokines was diminished in FOXO3a–/– mice at 7d p.i. Importantly, there was no difference in myocardial mRNA expression of Coxsackievirus B3 receptor. Interestingly, FOXO3a gene transfer in vitro had no effect on viral adhesion and entry but significantly inhibited CVB3 replication in cardiac myocytes. On day 3 p.i. FOXO3a–/– mice showed cardiac accumulation of activated NK cells as well as enhanced cardiac IFNy expression. Ex vivo, NKp46+ NK cells of FOXO3a–/– mice exhibited a higher activation status and enhanced cytotoxic activity with higher frequencies of activated CD69+ and CD27+CD11b+ effector NK cells as well as enhanced expression of IFN-γ accompanied by an upregulation of miR-155. Moreover, healthy humans heterozygous or homozygous for the longevity-associated FoxO3a SNP rs12212067 exhibited significantly reduced IFNg expression and cytotoxic degranulation of NK cells. Carriers with this SNP suffering from virus(+) DCMi showed a poorer outcome characterized by enhanced myocardial inflammation and attenuated viral clearance while susceptibility to viral infection was not regulated by FOXO activation.
Conclusion: Our results implicate FoxO3a in regulation of NK cell function and suggest that FoxO3a plays an important role in the innate immune response to viral infection. Thus, enhanced FoxO3a activity may be protective for diseases associated with chronic inflammation such as cancer and cardiovascular disease but disadvantageous to control acute viral infection.

P5502 | BEDSIDE

The impact of atrial fibrillation on a large population with hypertrophic cardiomyopathy

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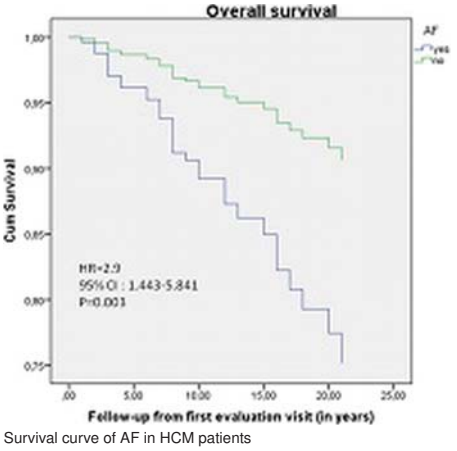
Purpose: Conflicting evidence exists about the prognostic implication of atrial fibrillation (AF) in patients with Hypertrophic Cardiomyopathy (HCM). The aim of our study was to evaluate the prevalence and prognostic significance of AF in a large northern Greek population with HCM.
Methods: The echocardiographic and clinical correlates of AF were assessed in 509 patients with an established diagnosis of HCM (age first evaluation 52.4±15.8



Survival curve of AF in HCM patients

Abstract P5500 – Table 1

	LA emptying fraction		CMR	Maximal LAVi		CMR	LGE		
	<17.5%	≥17.5%	p	<44 mL/m²	≥44 mL/m²	p	–	+	p
Mitral E/A ratio	2.98±1.82	0.89±0.28	<0.001	1.51±1.4	2.22±1.8	0.2	1.35±1.3	2.43±1.9	0,05
DT TTE (ms)	158±45	217±56	<0.001	190±65	183±53	0.7	219±51	145±39	<0.001
Lateral E/e'	16.9±6.8	12.1±6.4	<0.04	14±7	14.8±7	0.8	13.6±7.4	15.7±6.4	0.4
GLS	–10.1±3.1	–17.3±3.7	<0.001	–14.2±5.3	–12.7±4.6	0.4	–16.5±5.2	–10.8±2.8	<0.0008

years; 67% male). Overall and HCM-related mortality were evaluated during a follow-up of 11±7 years.
Results: A total of 119 (23.37%) of 509 patients were diagnosed with AF at index evaluation visit. Paroxysmal AF was present in 79 (15.52%) and non paroxysmal in 40 (7.85%) HCM patients. Functional impairment was more significant in patients with AF at first evaluation (NYHA class III-IV 29.4% vs 9.7%, $p<0.001$). Echocardiographically, left atrial (LA) size, E/E' of the intraventricular septum (IVS) and of the lateral (LAT) wall were significantly higher in patients with AF (LA size 4.6±0.6 vs 4.1±0.1 cm, E/E' IVS 16±8 vs 13±6 and E/E' LAT 11±7 vs 9.5±5, all $p<0.01$). The occurence of stroke was highly associated with the arrhythmia (13.4% vs 6.7%, p=0.019). AF conferred an increased risk for overall mortality in our cohort (HR=2.9, 95% CI 1.443–5.841) (figure). Also, AF displayed high predictive value for HCM-related death (HR=3.238, 95% CI 1.462–7.172). Even in a multivariable model adjusted for established risk factors AF remained an independent predictor for overall (HR 2.32, 95% CI 1.079–5.008) and HCM-related mortality (HR 2.49, 95% CI 1.047–5.945).
Conclusion: The prevalence of AF in northern Greek patients with HCM is 23.37%. AF was a strong predictor for overall and HCM-related mortality in this HCM population.

PULMONARY CIRCULATION, IMAGING, OTHER I

P5503 | BENCH
Under-developed bronchial arteries in patients with chronic thromboembolic pulmonary hypertension: a risk factor for hemoptysis associated with balloon pulmonary angioplasty

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Background: In recent years, balloon pulmonary angioplasty (BPA) has been proposed as a new therapy for chronic thromboembolic pulmonary hypertension (CTEPH). However, concerns regarding complications such as hemoptysis and reperfusion pulmonary edema require careful application to this new therapy. Although there have been a few reports assessing the risk factors for complication associated with BPA, definite risk factors for hemoptysis have yet to be elucidated. Bronchial arteries (BAs) in patients with CTEPH are often markedly developed as source of collateral perfusion to lung. Since BAs supply up to 30% of cardiac output into lung in patients with CTEPH, and supply not only lung field, but also vasa vasorum of pulmonary artery, their dilatation may have some role in hemoptysis associated with BPA.
Purpose: The purpose of this study was to investigate whether the development of BAs is protective or aggravating for hemoptysis associated with BPA.
Methods: We analyzed the subjects who received BPA during Jan 2013 to Dec 2014. To assess the development of BAs, we analyzed enhanced computed tomography (CT) images of chest, obtained with 64-row multi detector CT scanner within 3 months prior to first BPA session. BAs were identified as round enhanced vessels running together with right and left bronchus. Cross sectional areas of bronchial arteries were measured at 1cm distant from their origin from aorta. 4 patients were excluded due to poor image quality, which left 50 patients underwent total of 231 BPA sessions.
Patients were divided into two groups, developed BA group and under-developed BA group, with median cross-sectional areas of BAs. Hemoptysis associated with BPA was defined as hemoptysis observed during and within two days after each BPA session. Mann-Whitney's U test, Student's t test and Pearson's chi square test were used as appropriate to compare patient's characteristics between these two groups.
Results: Background patient's characteristics such as age, sex, nor hemodynamic indices, such as mean pulmonary artery pressure, cardiac index, 6 minutes walk distance, and WHO functional class, were not significantly different between two groups.
Of total of 231 BPA sessions, 18 hemoptysis events were observed. The percentage of hemoptysis events in the developed and under-developed BA group were 3.8% (4 hemoptysis in 105 sessions) and 11.1% (14 hemoptysis in 126 sessions), respectively (P=0.039, Pearson's chi square test).
Conclusion: Under-developed BAs was associated with increased risk for hemoptysis associated with BPA in patients with CTEPH.

P5504 | BENCH
Components of elastic lamina from endothelial cells and smooth muscle cells of pulmonary arteries

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Background: Pulmonary arterial hypertension (PAH) is characterized by the abnormal outgrowth of pulmonary artery smooth muscle cells (PASMCs), although the precise cause remains unclear. Internal elastic lamina (IEL), constituted of elastin sheet, has been reported to inhibit the proliferation and migration of PASMCs. In contrast to its degeneration, little is reported on the source of components of IEL in pulmonary arteries.
Aims: The aims of this study were to elucidate the source of structural components of IEL, and to seek the mechanism of inadequate formation of IEL in PAH.
Methods: We quantified mRNA expressions of genes related to IEL formation such as elastin, lysyloxidase (LOx), fibulin-4 and/or -5, fibrillins and integrins in PASMCs derived from control and PAH, and pulmonary artery endothelial cells (PAEC) in vitro by real-time quantitative PCR.
Results: Elastin, fibulin5, fibrillin2 and LOx were expressed in PASMCs, while they were barely expressed in PAECs. PAECs expressed Integrin alpha-v and integrin beta-3 more strongly compared to PASMCs. LOx expression was similar level in PASMCs from PAH and those from control without stimulation. It was decreased by PKA stimulant trapidil in PASMCs from PAH, while it was unchanged in PASMCs from control.
Conclusions: Structural components of IEL were derived mainly from PASMCs, presumably, anchoring to the integrins on the membrane of PAECs, resulting in the appropriate positioning of IEL between endothelia and vascular media. LOx is an extracellular matrix enzyme that catalyzes the cross-linking of elastin in IEL. The distinct pattern of LOx expression in PASMCs of PAH might disturb conformation of elastin and facilitate the fragmented elastic lamina as well as ectopic deposition of elastin precursor.

P5505 | BENCH
Non-invasive assessment of effect of exercise on Pulmonary artery systolic pressure in healthy subjects

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Aims: Exercise is increasingly being used to diagnose pulmonary hypertension in its early stages but there are no normal values for Pulmonary Artery Systolic Pressure (PASP) with peak exercise known for different age groups. The aim of current study was to explore the range of PASP with peak exercise in healthy individuals of various ages and look at the factors affecting them.
Methods and results: Our study involved patients free of pulmonary hypertension investigated in our centre with treadmill stress echo for atypical chest pain. 201 individuals with a good tricuspid regurgitation signal at rest and exercise were included in the study. Individuals with poor echocardiographic images, inadequate tricuspid regurgitation signal, abnormal echocardiogram or any cardiorespiratory disease were excluded. PASP was estimated using four times tricuspid valve regurgitation velocity squared adding a right atrial pressure of 5mmHg. During exercise, PASP increased from rest (27.6±4.1) to peak (39.7±7.7). PASP at peak exercise was higher in individuals >50 years old compared with those ≤ 50 years (35.4±7 vs. 42.5±6.8, p=0.0001). PASP at peak exercise ≥ 50 mmHg was found in 14.8% of individuals >50 Years old compared with 3.7% of individuals ≤ 50 years old. Age and PASP at rest were independent predictors of PASP at peak exercise. There was no effect of gender.
Conclusion: PASP at peak exercise can reach values ≥ 50mmHg in healthy individuals older than 50 with good exercise capacity. However, high levels of PASP for low level of exercise should be considered abnormal.

P5506 | BENCH
Inhibitory effects of TIR/BB-loop mimetic AS-1 on proliferation of pulmonary artery smooth muscle cells from patients with pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is characterized by pulmonary vascular remodeling with inappropriate increase of vascular cells and perivascular inflammation. Advanced glycation end-products receptor (RAGE) is implicated in PAH etiology. We have recently reported that Toll/IL-1 receptor (TIR) adaptor protein transduces RAGE signaling. In this study, we tested the hypothesis TIR/BB-loop mimetic AS-1, an inhibitor of TIR domain-mediated signaling, has antiproliferative effects on pulmonary artery smooth muscle cells (PASMCs) from patients with PAH.
Methods and results: PASMCs were obtained from 12 patients with PAH (including 2 patients with BMPR2 mutation and one patient with SMAD9 mutation) who underwent lung transplantation. PDGF-BB (10 ng/mL) stimulated proliferation of PASMCs as assessed by 3H-thymidine incorporation ($P<0.001$). Western blot analysis revealed that PDGF-BB increased the expression of RAGE in PAH-PASMCs. PDGF-BB also activates inflammatory signaling in PAH-PASMCs including translocation of NFkB from the cytoplasm to nucleus as assessed by immunofluorescence staining. AS-1 significantly inhibited PDGF-stimulated proliferation of PASMCs ($P<0.0001$).
Conclusions: TIR/BB-loop mimetic AS-1 had an antiproliferative effect on PAH-PASMCs. Inhibition of RAGE signaling may be therapeutically useful in patients with PAH.

P5507 | BEDSIDE

Accuracy of echocardiography to evaluate pulmonary vascular and right ventricular function during exercise

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Background: Exercise echocardiography may enable early diagnosis of pulmonary vascular disease, but its accuracy is untested.
Objectives: We compared the accuracy of echocardiography and cardiac magnetic resonance imaging with simultaneous invasive pressure registration (ExCMRip) for the assessment of pulmonary vascular and right ventricular (RV) function during exercise.
Methods: Exercise imaging was performed in 61 subjects (19 athletes, 9 healthy non-athletes, 8 asymptomatic subjects with familial pulmonary hypertension (CTEPH), 5 with dyspnea post pulmonary embolus and 20 patients with chronic thromboembolic pulmonary hypertension before (n=14) or after (n=6) pulmonary endarterectomy). Echocardiographic measurements included mean and systolic pulmonary artery pressure (mPAP and sPAP), cardiac output (CO), RV fractional area change (RVFAC), tricuspid annular systolic excursion (TAPSE) and RV end-systolic pressure-area ratio (RVESPAR). ExCMRip provided measurements of CO, RV ejection fraction (EF), mPAP and sPAP and RV end-systolic pressure-volume ratio (RV SP/ESV) at rest and during bicycle exercise. Abnormal pulmonary vascular reserve was defined as mPAP/CO slope >3 mmHg/L/min by ExCMRip.
Results: Determination of mPAP/CO was possible in 53 of 61 subjects (87%). One (4%) healthy subject, 1 (13%) BMPR2 carrier, 3 (60%) post-pulmonary embolus, 12 (86%) CTEPH and 6 (100%) post-pulmonary endarterectomy patients had abnormal pulmonary vascular reserve. mPAP/CO by echocardiography was higher than obtained by ExCMRip (+0.9 mmHg/L/min, 95% limits of agreement –3.6 to 5.4), but enabled accurate identification of patients with abnormal pulmonary vascular reserve [area under the receiver-operating-characteristic curve 0.88 (0.77 to 1.00; $p<0.0001$)]. Simplified relationships between sPAP and exercise intensity had similar accuracy to identify subjects with pulmonary vascular disease [AUC 0.95 (0.88–1.01), $p<0.0001$]. RVFAC by echocardiography correlated strongly with RVEF by ExCMRip, whereas a moderate correlation was found between TAPSE and RVEF. As a surrogate measure of RV contractility, RVESPAR correlated strongly with RV SP/ESV ($r=0.70$; $P<0.0001$) relative to exercise intensity.
Conclusion: Echocardiography is a feasible and accurate tool for the evaluation of pulmonary vascular and RV functional reserve during exercise in clinical practice. Simplified relationships between sPAP and exercise intensity in Watts can be used to identify pathology and may represent a simpler clinical tool by avoiding the need for CO quantification.

P5508 | BEDSIDE

Serum amyloid A is elevated in chronic thromboembolic pulmonary hypertension

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Background: Pulmonary hypertension (PH) is a progressive disease characterised by remodelling of small pulmonary arteries, caused by immunological and inflammatory mechanisms, leading to an increase in pulmonary vascular resistance, right ventricular dysfunction and death.
Serum amyloid A (SAA) is known for its role during the acute phase response to an inflammatory stimulus. The association of SAA with increased cardiovascular risk and venous thromboembolism has been reported. The involvement of SAA in the pathogenesis of PH is unknown.
Aim: To investigate baseline plasma levels of SAA in PH.
Methods: Blood samples of 176 patients with chronic thromboembolic pulmonary hypertension (CTEPH) and 78 patients with pulmonary arterial hypertension (PAH) were collected at time of diagnosis, and SAA concentrations were determined by a latex-enhanced nephelometric immunoassay.
Results: Baseline plasma levels of SAA were significantly increased in PH (mean 26.12 mg/L; range 3.10–985) compared with controls (mean 2.5 mg/L; range 0–6.4).
We found a significant correlation of plasma baseline levels of SAA (rho=0,545, $P<0,001$) with high sensitive C reactive protein (mean 0.89 mg/dL; range 0.01–7.30).
CTEPH patients had significantly higher plasma levels of SAA (mean 30.66 mg/L; range 3.53–985; P=0,019) than PAH patients (mean 16.37 mg/L, range 3.1–134). No significant difference was found between operable and non-operable CTEPH patients.
Conclusion: Baseline plasma levels of SAA are increased in pulmonary hypertension. CTEPH patients have higher levels of SAA than patients with PAH. Data are in agreement with the concept of inflammatory thrombosis in CTEPH.

P5509 | BENCH

The effect of prostacyclin analogues on right heart function is abolished by right heart failure

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Background: Prostacyclin analogues are vasodilatory and antiproliferative agents used in the treatment of pulmonary arterial hypertension. The direct effects of prostacyclin analogues on right ventricular (RV) function are still poorly understood. The aim of this study was to investigate the direct effects of prostacyclin analogues on right heart function in hearts with and without RV failure.
Methods: Rats (n=31) were subjected to pulmonary trunk banding to induce right ventricular failure. Rats without banding served as healthy controls (n=30). Seven weeks after the operation RV failure was confirmed by echocardiography, showing hypertrophy and dilatation of the RV and reduced tricuspid annular plane systolic excursion (TAPSE). The rat hearts were excised and connected to a pressure controlled Langendorff system and perfused with iloprost, treprostinil, epoprostenol or the selective IP receptor agonist, MRE-269 in increasing concentrations. The effect on RV function was evaluated using a balloon tipped catheter, inserted into the RV, measuring the hemodynamics.
The expression of prostanoid receptors IP, FP, DP1, TP, EP1, EP2, EP3 and EP4 in the RV was examined using quantitative polymerase chain reaction.
Results: All four drugs increased coronary flow rate in healthy hearts as well as in hearts with RV failure.
In healthy control hearts, iloprost, treprostinil and MRE-269 increased RV rate pressure product ($p=0.015$, $p=0.0003$ and $p=0.035$, respectively). Only treprostinil was effective in clinically relevant concentrations (0.5ng/mL and 1.5ng/mL).
In the failing RV, MRE-269 decreased RV rate pressure product ($p<0.0001$), while iloprost and treprostinil showed no significant effect.
Epoprostenol had no significant effect on RV function neither in the healthy nor the failing RV.
Healthy hearts expressed all prostanoid receptors, but in RV failure EP2, EP3 and IP receptor mRNA were increased, while EP4 and DP1 were decreased.
Conclusion: Iloprost, treprostinil and MRE-269, but not epoprostenol, improved RV function in the isolated healthy rat heart. RV failure abolished the positive effect of the prostacyclins and MRE-269 even reduced function of the failing RV. The greater potency of treprostinil in the normal heart may be explained by its reported high affinity to EP2 receptors. The abolished effect in the failing RV may be related to the changes in prostanoid receptor subtype expression.

P5510 | SPOTLIGHT

Effects of Trimetazidine on patients with chronic obstructive pulmonary disease and pulmonary hypertension

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Background: Pulmonary hypertension (PH) often complicates the course of patients with chronic obstructive pulmonary disease (COPD), and portents a worse prognosis. This study was aimed at evaluating the utility of oral trimetazidine in COPD patients with pulmonary hypertension.
Methods: In a double-blind, and parallel design, 57 COPD patients with PH were randomly assigned to receive either placebo or trimetazidine (60 mg per day) over a period of 6 months. Baseline characteristics were similar in both groups. A thorough clinical, comprehensive echo Doppler evaluation and 6-min walk test was performed before enrollment in the trial to establish the diagnosis and obtain baseline data. At the end of therapy period, the patients were evaluated for systolic pulmonary artery pressure using echo Doppler and repeated 6-min walk test. The differences in the above variables at the end of trimetazidine and placebo therapies were compared.
Results: Fifty-four patients completed the study protocol. Baseline characteristics including 6-min walk test were similar between groups. Initial and follow up echo showed normal left ventricular systolic function (65.9 vs. 62.5%, p=0.12). Trimetazidine, compared to placebo, was associated with decrease in Doppler-estimated pulmonary artery systolic pressures (60.00±20.64 mmHg v. 48.22±12.59 mmHg; p=0.044).Trimetazidine group showed improved exercise tolerance in 6-min walk test at follow-up compared with control group (411±112 vs. 382±123m, p=0.03). There was significant improvement in the Borg dyspnea score after administering trimetazidine.Trimetazidine was well tolerated with no untoward effects.
Conclusions: Trimetazidine decreases pulmonary artery pressures and improved exercise tolerance in COPD patients with pulmonary hypertension.

P5511 | BEDSIDE

Right ventricular function assessed by 2D speckle-tracking echocardiography in pulmonary hypertension. Relation with cardio-pulmonary exercise testing

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Background: Right Ventricular (RV) function is an important prognostic marker in Pulmonary Hypertension (PH) that can be quantitatively assessed by 2D echocardiography speckle-tracking.
Objectives: To assess whether RV longitudinal strain (RVLS) acquired by 2D speckle-tracking predicts exercise performance measured by Cardio-Pulmonary Exercise Testing (CPET) in PH patients. We also related CPET and RVLS to prognostic markers recommended by the American Society of Echocardiography: Fractional Area Change (FAC), RV myocardial performance index (RVMPI), indexed Right Atrial (RA) area, Systolic and Diastolic left ventricular eccentricity index (EIs, EId) and Tricuspid Annular Plane Systolic Excursion (TAPSE).
Methods: We prospectively recruited 93 consecutive patients with precapillary PH who were referred for CPET and transthoracic echocardiography within a month of each other. Global RVLS and free wall RVLS were analyzed from an apical four chamber view. CPET parameters included Peak oxygen consumption (PeakVO2), percentage of predicted VO2max, maximum workload, ventilatory equivalent of carbon dioxide (VE/VCO2) and O2pulse. Linear then multiple regression analysis was performed with RVLS and prognostic markers as predictors and the CPET parameters as dependent variables.
Results: RVLS predicted VE/VCO2. Global RVLS (R2=14%, $p<0.001$) was a stronger predictor than free wall RVLS (R2=11%, p=0.001). With multivariate regression (R2=39.1%), global RVLS (p=0.03) was an independent predictor of VE/VCO2.
Global RVLS was a stronger predictor of VE/VCO2 than FAC (R2=12%, $p<0.001$). Global and free wall RVLS were stronger predictors than RVMPI (R2=8%, p=0.003), EId (R2=7%, p=0.006) and TAPSE.
Global RVLS also predicted percentage of predicted VO2max (R2=5.2%, p=0.016), but was not an independent predictor with multivariate regression.
There was no relation between RVLS and peakVO2, maximum workload or O2pulse.
Conclusions: Global RVLS is closely related to function and is an independent predictor of VE/VCO2, a prognostic measure derived from exercise performance. It is a stronger predictor than TAPSE, RVMPI, EId and FAC.

P5512 | BENCH

The cardioprotective effect of soluble guanosine monophosphate stimulation is abolished in the hypertrophic and failing right ventricle

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Background and aim: Phosphodiesterase 5 inhibition protects the healthy right ventricle against ischemia and reperfusion injury. We aimed to investigate whether the cardioprotective effects of phosphodiesterase 5 inhibition and soluble gyanulate stimulation is preserved in the hypertrophic and failing right ventricle.
Methods: De-compensated right ventricular failure was induced in male Wistar rats (n=47) by pulmonary trunk banding. The hearts were isolated and perfused in a pressure controlled modified Langendorff setup and randomised to control (CON) or ischemic preconditioning (IPC, 2 x 5 min of global ischemia) to investigate if cardioprotection by IPC was preserved. The cardioprotective effects of cGMP up-regulation were studied by adding the phospodiesterase 5 inhibitor vardenafil (VAR, 66nM), the soluble guanylate cyclase stimulator BAY 41–2272 (3 uM, BAY) or their combination (VAR+BAY) to the buffer. To evaluate whether intrinsic cGMP up-regulation inherently induced cardioprotection, we added the cGMP-dependent protein kinase (PKG) blocker KT 5823 (1uM, KT) to the buffer in one group. Subsequently, we used 40 min of global ischemia and 120 min of reperfusion in all groups. The effects of IPC on the right ventricle were evaluated by measurement of the infarct size/area-at-risk ratio (IS/AAR).
Results: Pulmonary trunk banding induced right ventricular hypertrophy and de-compensated heart failure. IPC did not induce protection against ischemia and reperfusion injury. Inhibiting cGMP breakdown, stimulating cGMP formation or a combination of both did not protect against ischemia and reperfusion injury. Blocking PKG did not increase infarct size (Fig. 1).

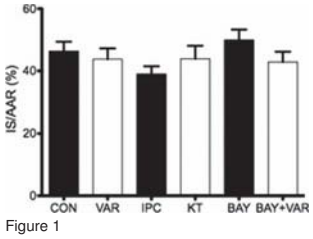

Figure 1

Conclusion: The cardioprotective effect of cGMP stimulation is abolished in the hypertrophic and failing right ventricle,

CHRONIC PULMONARY HYPERTENSION

P5513 | BEDSIDE

Non-invasive multi-modality imaging evaluation of pulmonary arterial elastance in patients with pulmonary hypertension

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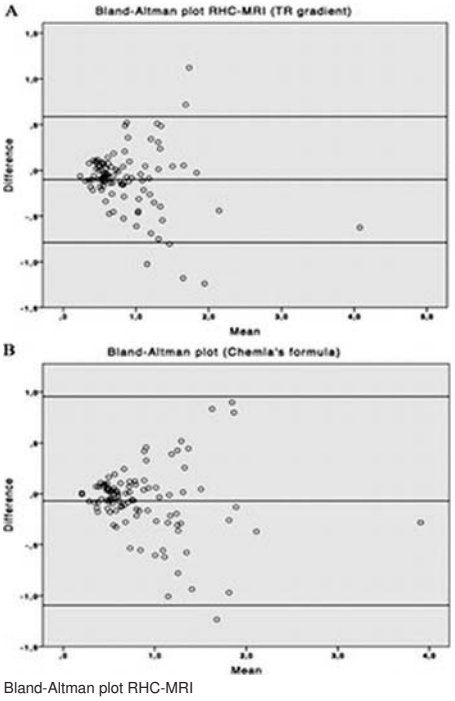
Introduction: Effective pulmonary arterial elastance [(Ea: end-systolic pressure (ESP)/stroke volume (SV)] reflects a global measure of total afterload. In pulmonary hypertension (PH), ESP is best approximated by pulmonary artery mean pressure (mPAP). Along with SV, both are ideally assessed during right heart catheterization (RHC). Novel imaging modalities, mainly phase contrast (PC) MRI, may offer new insights in Ea estimation through non-invasive surrogates.
Purpose: To test if pulmonary artery elastance can be assessed non-invasively as the ratio of mean pulmonary artery pressure issued from trans-thoracic echocardiography (TTE) to stroke volume estimated either by PC-MRI or TTE.
Methods: 121 patients were evaluated for group 1 and 4 PH with multimodal imaging and RHC within 48 hours. mPAP was estimated using 2 validated methods: the Chemla's formula (mPAP = 0.61 x sPAP + 2 mmHg), mean tricuspid regurgitation (TR) gradient added with estimated right atrial pressure based on inferior vena cava. Right ventricle (RV) SV was either measured by PC MRI or extrapolated from Doppler left ventricle (LV) output track SV.
Results: There were good correlations and concordances between RHC and non-invasive derived Ea using TTE mPAP/MRI RV SV (TR: n=96, r2=0.805, Figure 1A; Chemla's formula, n=100, r2=0.807, Figure 1B). Correlations were significant but weaker when using TTE derived LV SV (TR: n=98, r2=0.630; Chemla's formula: n=102, r2=0.673).



Bland-Altman plot RHC-MRI

Conclusion: Ea defined as the ratio of echocardiographic mPAP (mean TR gradient or Chemla's formula) and PC-MRI SV correlated well with gold-standard RHC invasive values. Added to other parameters of RV morphology and performance, non-invasive Ea may help further estimation of right ventriculo-arterial coupling in PH.

P5514 | BEDSIDE

Prevalence and prognostic significance of CT criteria for pulmonary veno-occlusive disease in systemic sclerosis-associated pulmonary hypertension

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Background: Radiological appearances of pulmonary veno-occlusive disease (PVOD) have been reported in more than sixty per cent of patients with systemic

sclerosis-associated pulmonary arterial hypertension (SSc-PAH). Half of these patients developed pulmonary oedema in response to vasodilator therapy.
Purpose: Our experience is that PVOD is rare in SSc patients with pulmonary hypertension. We sought to determine this by performing an evaluation of the CT scans of such patients.
Methods: 100 SSc patients with pulmonary hypertension confirmed by right heart catheter were included in the analysis. CT scans were blindly scored by consensus by two chest radiologists for the presence of lung disease and CT criteria of PVOD (interlobular septal thickening, centrilobular ground glass opacities, lymphadenopathy). Kaplan-Meier curves compared up to five year survival according to number of features of PVOD in all 100 patients and in those with SSc-PAH. Case note review determined the presence of overt PVOD, i.e. increased centrilobular ground glass opacification, worsening oxygen saturations and pulmonary oedema in response to vasodilator therapy.
Results: 73 patients had pulmonary hypertension secondary to SSc-PAH and 27 patients had pulmonary hypertension secondary to lung disease (PH-LD). In those with SSc-PAH, 62 (84.9%) had 0–1 features of PVOD and 11 (15.1%) had 2–3 features of PVOD. Of the PH-LD group, 20 patients (74.1%) had 0–1 features of PVOD and 7 (25.9%) had 2–3 features of PVOD. Therefore, a total of 18 out of 100 patients (18.0%) with SSc-associated pulmonary hypertension had 2–3 features of PVOD. Interestingly, only four of these 18 patients (22.2%) developed overt PVOD. In terms of survival, two or three radiological features of PVOD conferred worse survival than did 0–1 features of PVOD.
Conclusions: The majority of SSc patients with 2–3 radiological features of PVOD do not develop overt PVOD. However the presence of 2–3 radiological features of PVOD is associated with high mortality.
Our results contrast sharply with those previously published in two respects. Firstly, we found that three times fewer SSc-PAH patients had 2–3 features of PVOD. Secondly, less than half as many of these patients developed pulmonary oedema following vasodilator therapy. Therefore, radiological features of PVOD may not be as common in SSc as previously thought. Moreover, the presence of these features does not confer the diagnosis of PVOD.

P5515 | BEDSIDE
Comparison of intravascular optical frequency domain imaging with intravascular ultrasound in balloon pulmonary angioplasty for the patients with chronic thromboembolic pulmonary hypertension

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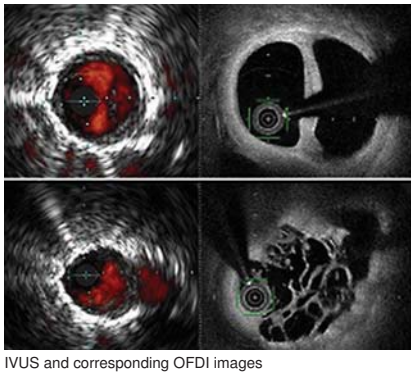
Background: Balloon pulmonary angioplasty (BPA) to the patients with chronic thromboembolic pulmonary hypertension (CTEPH) is still an evolving procedure. To comprehend the complex structures of pulmonary arteries of CTEPH, high-resolution imaging system is useful.
Purpose: The aim of this study is to evaluate the safety and feasibility of imaging pulmonary arteries of patients with CTEPH by optical frequency domain imaging (OFDI) in comparison to intravascular ultrasound (IVUS).
Methods: Eighteen consecutive attempts of OFDI and IVUS in BPA for the patients with CTEPH were evaluated. All complications related to the procedure were recorded. For the OFDI and IVUS imaging comparison, 41 regions were identified by using side branch as landmark and analyzed. Lumen area (LA) and vessel area (VA) were evaluated by two independent observers.
Results: The OFDI catheter was positioned successfully to the target lesion without any angiographical adverse event at all attempts. High-resolution OFDI images were obtained without pre-dilatation in 15 attempts. LA and VA measured by OFDI were smaller than those measured by IVUS (LA: 5.7±3.9 mm^2 vs. 9.1±6.0 mm^2, VA: 10.3±6.7 mm^2 vs. 15.1±9.7 mm^2). The correlations between the two measurements were highly significant (LA: r=0.77, VA: r=0.80). Inter and intra-observer variabilities of OFDI measurements were almost perfect and better than IVUS measurements.



IVUS and corresponding OFDI images

Conclusions: The OFDI imaging is safe and feasible in BPA for patients with CTEPH. The OFDI provided fair high-resolution images of pulmonary arteries. The correlations between OFDI and IVUS measurements were highly significant. OFDI images provided better inter and intra-observer variabilities than IVUS images, and may contribute to standardization of BPA.

P5516 | BENCH
Involvement of thrombin in vascular remodeling in chronic thromboembolic pulmonary hypertension

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Background: The precise mechanism remains unclear by which vascular remodeling progresses in chronic thromboembolic pulmonary hypertension (CTEPH). We have previously reported that platelet-derived growth factor (PDGF) plays an important role in progression of pulmonary vascular remodeling. Further, we have reported that thrombin receptor, protease activated receptor 1 (PAR1), is highly expressed in the endarterectomized tissues from patients with CTEPH. Thrombin is a part of the common coagulation cascade and has direct cellular effects through interaction with PAR1. However, the role of thrombin in vascular remodeling in CTEPH is not fully elucidated.
Purpose: To determine the significance of thrombin in vascular remodeling and evaluate whether inhibition of thrombin signaling could be a therapeutic target in CTEPH.
Methods: The endarterectomized tissues were obtained from patients with CTEPH and used to prepare cultured pulmonary vascular cells (CTEPH cells). Immunocytochemistry, PCR, Western blot analyses were performed. Cell proliferation was assessed by tetrazolium salt assay and cell migration was tested by wound healing assay. Intracellular Ca2+ imaging system was used to measure changes in cytosolic Ca2+ with fura-2.
Results: In CTEPH cells, PAR1 was expressed as well as Vimentin, smooth muscle actin, transgelin, and PDGF receptor. Thrombin treatment was associated with a rise in cytosolic Ca2+ and enhanced store-operated calcium entry, which is known to be involved in cell proliferation. Chronic treatment with a non-peptide selective inhibitor of PAR1 (SCH79797) significantly attenuates thrombin- and PDGF- induced augmentation of store-operated calcium entry (by 36.6% and 21.2%, $P<0.001$). In cell proliferation assays, thrombin- and PDGF- induced excessive cell proliferation were also significantly reduced by PAR1 inhibitor (from 111.5±0.2 to 88.5±5.9% and 109.8±2.1 to 87.7±10.1%, $P<0.05$). PAR1 inhibition significantly inhibited PDGF-induced migration of CTEPH cells and induced activation of caspase-3.
Conclusions: This study demonstrates that thrombin has direct effects on promoting vascular remodeling. Inhibiting thrombin signaling may potentially be a therapeutic target in CTEPH.
Acknowledgement/Funding: JSPS KAKENHI Grant-in-Aid for Young Scientists (B) 25860632, Takeda Science Foundation, Japan Foundation for Applied Enzymology

P5517 | BEDSIDE
Pulmonary hypertension connection formula provides a more realistic eight-year survival estimates than national institute of health and French registry equations

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National Institutes of Health (NIH) and Pulmonary Hypertension Connection (PHC) registry formulas which are based on two different equations using same hemodynamic measures, and French Registry (FR) formula based on a different equation are used for survival estimates (SE) in patients (pts) with pulmonary arterial hypertension (PAH). Although, the differences among the SEs predicted by FR, PHC and NIH are reported, the clinical relevance of these equations for long-term SE remains to be determined.
In this single-center prospective study, we aimed to compare eight-year observed survival (OS) with baseline SEs predicted by NIH, PHC and FR equations (SE-NIH, SE-PHC and SE-FR) in 204 pts (F 127, M 77, age 43.6±17.4 yrs) with PAH. Sixty seven (82%) pts were under targeted PAH treatments. Subgroups were as follows; Idiopathic PAH (n=55), PAH associated with congenital heart disease (APAH-CHD) (n=131), other subgroups of PAH (n=18). Functional class (FC) was 3,15±0,67 and six-minute walking distance was 274.45±132.2 m at diagnosis. Baseline pulmonary arterial systolic, diastolic and mean pressures and right atrial pressure (mm Hg) were 97.1±30.9, 40.9±17.9 and 62.6±21.3 and 10.4±5.5, respectively. Mean transpulmonary and diastolic pulmonary gradients (mm Hg), and cardiac index (lt/min/m^2) were 49,9±21,4, 28±18,3 and 2,5±0,83, respectively. Pulmonary vascular resistance was 11±7.9 WU. The eight-year curves of OS and SEs predicted by each equation showed that OS and SE-PHC were comparable at each time points ($p>0,05$) whereas OS was overestimated by SE - FR ($p<0,05$) and underestimated by SE - NIH along the survival curve ($p<0,05$) (Table 1).

Table 1. Survival estimates and observed survival

	1 year	2 year	3 year	4 year	5 year	6 year	7 year	8 year
NIH	0,70	0,59	0,50	0,43	0,38	0,36	0,35	0,34
PHC	0,94	0,84	0,77	0,71	0,65	0,61	0,56	0,52
FR	0,96	0,92	0,90	0,87	0,84	0,81	0,79	0,76
OS	0,87	0,81	0,75	0,67	0,59	0,51	0,50	0,46

In conclusion, eight-year follow-up in our single-center registry confirmed that PHC equation provided a more realistic SE than NIH and FR models for long-

term survival in pts with PAH. However, NIH equation underestimates and FR equation overestimates the OS, significantly.
Acknowledgement/Funding: EvalUation of Pulmonary Hypertension Risk factors AssociaTEd with Survival.

P5518 | BEDSIDE
Pulmonary arterial capacitance in heart failure with preserved and reduced ejection fraction complicated by pulmonary hypertension

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Aim: Reactive pulmonary hypertension (PH) is a severe form of PH secondary to left-sided heart failure (HF). Given the structural and functional abnormalities in the pulmonary vasculature that occurs in reactive PH, we hypothesized that pulmonary artery capacitance (PAC) may be profoundly affected, with implications on clinical outcome.
Methods and results: The studied 393 HF patients with 124 (32%) classified as passive PH and 140 (36%) as reactive PH and 91 patients with pulmonary arterial hypertension (PAH). Mean PAC was highest in patients without PH (4.5±2.1 ml/mmHg), followed by passive PH group (2.8±1.4 ml/mmHg) and lowest in reactive PH (1.8±0.7 ml/mmHg) (P=0.0001). PAC and pulmonary vascular resistance (PVR) fitted well to a hyperbolic inverse relationship (PAC=0.25/PVR, R2 = 0.70), with reactive PH patients dispersed almost predominantly on the flat part of the curve where a reduction in PVR is associated with a small improvement in PAC. The hyperbolic curves for heart failure with preserved (HFpEF) and reduced (HFrEF) ejection fraction were similar when compared by slopes (P=0.32). Elevated pulmonary capillary wedge pressure was associated with a significant lowering of PAC for any PVR (P=0.036). During a median follow-up of 31 months, both reactive PH (hazard ratio [HR] 2.59, 95% confidence interval [CI], P=0.02) and reduced PAC (HR 0.72 per 1 ml/mmHg increase, 95% CI 0.59–0.88, P=0.001) were independent predictors of mortality.
Conclusions: The development of reactive PH is associated with a marked reduction in PAC. PAC is a strong independent hemodynamic marker of mortality in HF and may contribute to the increased mortality associated with reactive PH. Modifications of the pulmonary vessels characteristics were similar in both HFpEF and HFrEF.

P5519 | BEDSIDE
The use of the diastolic pressure gradient in the diagnosis of group 2 pulmonary hypertension can identify patients at increased risk for adverse events

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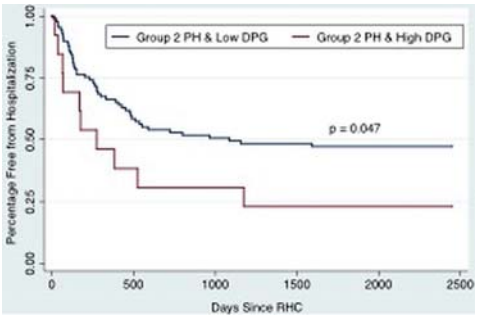
Background: The robustness of the transpulmonary gradient (TPG) in identifying a more active form of group 2 pulmonary hypertension (PH) has been criticized.
Purpose: To evaluate the prognostic risk associated with TPG and diastolic pressure gradient (DPG) in group 2 PH patients and to compare outcomes to those with pulmonary arterial hypertension (PAH).
Methods: A prospective cohort study of 261 patients with PH referred for right heart catheterization and followed for a median of 933 days. Elevated TPG and DPG were defined as >12 mmHg and ≥ 7 mmHg, respectively.
Results: Group 2 PH (n=103) patients experienced more dyspnea, fatigue, and angina compared to PAH patients (n=108), with no difference in death (9.8 vs. 9.3%; P=0.893) and a trend for greater hospitalization rates (55.9 vs. 48.2%; P=0.262). Amongst the group 2 PH patients, a high TPG (n=56) was associated with reduced 6-minute walk distance (266.8±98.7 vs. 377.8±90.1 m; P=0.001) but no difference in hospitalization (58.9 vs. 52.2%; P=0.494) or death (8.9 vs. 10.9%; P=0.751) when compared to the low TPG group. Among patients with high TPG, high DPG (n=13) was associated with worse outcomes compared to those with low DPG (n=43) on unadjusted Cox regression (hazard ratio [HR] 1.94, 95% confidence interval [CI] 0.92–4.10, $P<0.001$). When compared to patients with low DPG (n=89), those with high DPG (n=13) had greater risk of hospitalization or death on log-rank tests for equality of survival functions (P=0.047) and unadjusted Cox regression (HR 1.97, 95% CI 0.99–3.91, P=0.052).



Survival curves according to DPG status

Conclusions: Patients with group 2 PH have similar rates of adverse outcomes when compared to patients with PAH. DPG was more useful than TPG in identifying group 2 PH patients who are at increased risk of adverse events.
Acknowledgement/Funding: Mach-Gaensslen Foundation of Canada Studentship Award, University of Ottawa Heart Institute ORACLE Innovation Cluster

P5520 | BEDSIDE
Reduction in NT-proBNP and its correlation with survival in patients with CTEPH treated with riociguat: 2-year results from the CHEST-2 long-term extension study

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Background: In pts with pulmonary hypertension (PH), N-terminal prohormone of brain natriuretic peptide (NT-proBNP) is an established biomarker of disease severity. In the 16-week CHEST-1 study, riociguat significantly reduced NT-proBNP levels compared with placebo in pts with chronic thromboembolic pulmonary hypertension (CTEPH).
Purpose: We present the 2-yr NT-proBNP data from CHEST-2.
Methods: Pts with inoperable CTEPH, or persistent/recurrent PH after pulmonary endarterectomy entered CHEST-2 after completing CHEST-1 without ongoing drug-related SAEs. All pts received riociguat individually adjusted up to 2.5 mg tid. Primary endpoints were safety and tolerability; change in NT-proBNP was an exploratory efficacy endpoint.
Results: Of 243 pts completing CHEST-1, 237 (98%) entered CHEST-2. At 2 yrs, mean±SD NT-proBNP had improved by –312±1201 pg/ml (n=80) from CHEST-1 baseline in the overall population. In the inoperable and persistent/recurrent PH subgroups, NT-proBNP improved by –351±1308 pg/ml (n=60) and –194±816 pg/ml (n=20), respectively, from CHEST-1 baseline. A Cox proportional hazards regression analysis showed significant correlation between change from baseline in NT-proBNP levels and both survival (HR=0.85; 95% CI 0.79 to 0.92; $p<0.0001$) and clinical worsening-free survival (HR=0.87; 95% CI 0.83 to 0.92; $p<0.0001$), using –300 pg/ml as the unit of change for HR. Figure 1 shows the difference in survival for pts with NT-proBNP levels above and below the clinically relevant threshold of 1800 pg/ml at baseline and follow-up.

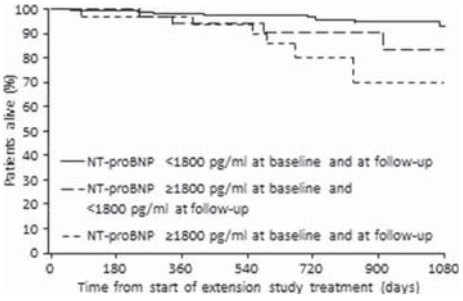

Figure 1: Survival by NT-proBNP levels

Conclusion: Reduction in NT-proBNP in pts with CTEPH treated with riociguat was sustained for up to 2 yrs in CHEST-2. Change from baseline in NT-proBNP correlated with survival and clinical worsening-free survival.
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P5521 | BEDSIDE
Left main coronary artery extrinsic compression by enlarged pulmonary artery in patients with pulmonary arterial hypertension

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Background: Extrinsic compression of the left main coronary artery (LMCA) by an enlarged main pulmonary artery (mPA) is a recognized cause of angina and sudden death in patients with pulmonary arterial hypertension (PAH).
Purpose: To evaluate prospectively the prevalence of LMCA compression in PAH patients and to identify the predictors of compression.

Methods: Consecutive patients with PAH who experience angina or angina-like symptoms underwent coronary computed tomographic angiography (CTA). Four radiologic patterns were described: 1) LMCA compression (C); 2) LMCA dislocation (D) (take-off angle <60° without compression); 3) close proximity (P) (<1 mm) of PA to LMCA; 4) normal (N) (distance PA-LMCA >1 mm). Patients with the first 3 patterns underwent coronary angiography (CA). In case of LMCA obstruction ≥50% percutaneous coronary intervention with stenting (PCI) or mPA surgical reduction (in case of planned surgical correction of congenital heart defects or urgent lung transplantation) were performed. Logistic regression and ROC curve were used for statistical analysis.
Results: The clinical evaluation of 765 patients with PAH revealed the presence of angina or angina-like symptoms in 121 patients (16%). All of them underwent CTA that showed C in 35 patients (29%), D in 49 (41%), P in 10 (8%) and N in 27 (22%). The 94 patients with C, D and P patterns underwent CA and LMCA stenosis ≥50% was found in 48 of them (48/121 = 40%); the prevalence of LMCA stenosis ≥50% at CA in C, D and P patterns was, respectively, 91%, 31% and 10%. Forty-five patients underwent PCI and stenting of LMCA and 3 underwent mPA surgical reduction without major complications. Symptomatic improvement was observed in all patients and after a mean follow-up of 23 months no deaths were observed. Logistic regression and ROC analysis identified a mPA diameter (mPAd) >40 mm assessed at the CT scan as a predictor of LMCA stenosis ≥50%.
Conclusions: The prevalence of extrinsic compression of LMCA in our population is quite high ranging from 6% of all PAH patients to 40% of those presenting with angina or angina-like symptoms. CTA is useful as a screening tool in symptomatic patients and CA is the gold standard for the final diagnosis. PCI with stenting is a safe and effective procedure. A mPAd >40 mm at CT scan is the best predictor of LMCA compression.

P5522 | BEDSIDE
RV free wall strain adds significantly to predicting functional capacity in PAH

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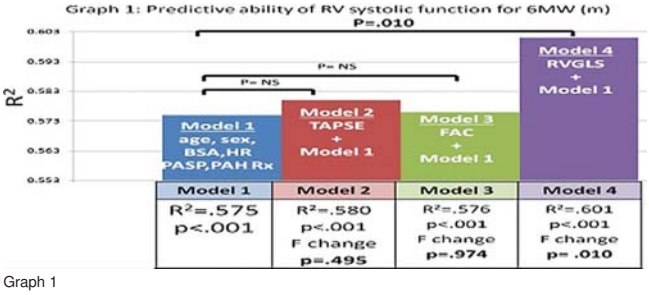
Background: Assessment of pulmonary arterial hypertension (PAH) is dependent on assessment of PA systolic pressure (PASP) and pulmonary vascular resistance (PVR), but often ignores RV function. We sought whether RV systolic functional markers including RV free wall strain (RVGLS) improved the association between PASP and functional capacity (measured as 6 minute walk, 6MW). We hypothesised that RVGLS would show a stronger relationship to 6MW than traditional markers of RV function.
Methods: Echocardiography was performed on the same day as 6MW on a PAH cohort (N=177, F:75%, 63±13.3 years; PASP 43±22 mmHg). Pts were on Rx for PAH therapy for mean 487 days (±470). Standard echo measurements were performed following ASE guidelines. RVGLS was performed using VVI. Linear regression was used to examine independent associations. Sequential models based on standard clinical variables and RV function parameters (RVGLS, FAC, TAPSE) were used to examine incremental benefit.
Results: Exercise capacity was associated with RV end-diastolic area (β –0.37 p<0.001), fractional area change (β 0.27 p<0.001), PASP (β –0.32 p<0.001), PVR (β –0.29 p<0.001) and RV GLS (β –0.48 p<0.001). The clinical model (Graph 1) consisting of age (β –0.5, p<0.001), sex (β 0.38, p<0.001), BSA (β –0.09, p=0.2), HR (β –0.28, p<0.001), PASP (β –0.23, p=0.008), PAH Rx (β –0.16, p=0.012), RVEDA (β –0.29, p=0.002) (R2=0.575, p<0.001) was improved by RV strain (β –00.21, p=0.01) (model R2=0.601, F change p=0.010). However, the clinical model was not improved by addition of TAPSE (β=0.08, p=0.27) (model R2=0.58, F change p=0.27) or FAC (β 0.035, p=0.67) (R2=0.576, F change p=0.67).



Graph 1

Conclusion: The functional status of patients with PAH is dependent on RV function (measured as RVGLS) as well as clinical factors and PASP.

P5523 | BEDSIDE
The diastolic pressure gradient and the cardiorespiratory profile during exercise in pulmonary hypertension due to left heart disease

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Background: Isolated postcapillary (Ipc) Pulmonary Hypertension (PH) is a complication of Left heart failure (LHF). A minority of LHF patients present with Combined postcapillary and precapillary PH (CpcPH), defined by a diastolic pressure gradient (DPG)≥7 and possibly associated with pulmonary vascular remodeling. The exercise pathophysiology of PH due to pulmonary vascular diseases differs from LHF for more impaired ventilatory efficiency, i.e. higher ventilation (VE) at any level of CO2 production (VCO2). It is not known if DPG influences the cardiorespiratory adaptation to exercise in PH-LHF.
Purpose: To compare cardiopulmonary exercise test (CPET) of IpcPH and CpcPH.
Methods: Retrospective data analysis (2007–2014) of PH-LHF patients who had a CPET within 1 week from a right heart cath at our PH Clinic.
Results: 42 patients (12 CpcPH) had a CPET with respiratory quotient>1.00. CpcPH and IpcPH did not differ for age, sex, height, BMI, NYHA, LHF etiology, comorbidities, treatment. Weight was slightly higher in CpcPH (p=0.05). CpcPH had higher pulmonary arterial pressures and pulmonary vascular resistance than IpcPH, and more impaired ventilatory efficiency (table).

Resting hemodynamics and CPET variables

	IpcPH	CpcPH	p
Mean pulmonary arterial pressure (mmHg)	32.8±6.2	47.3±10.0	0.000
Pulmonary arterial wedge pressure (mmHg)	21.8±3.9	21.9±4.1	0.910
Diastolic pressure gradient (mmHg)	1.8±1.9	12.5±5.4	0.000
Cardiac index (L/min/m^2)	2.3±0.6	2.3±0.6	0.850
Pulmonary vascular resistance (WU)	2.7±0.9	6.9±5.3	0.000
VO2 peak	14.7±4.8	11.8±2.6	0.056
VE/VCO2 @ AT	36.1±5.2	42.4±8.4	0.012
PetCO2 @ AT	34.3±4.8	29.9±4.7	0.022
VE/VCO2 slope	33.7±6.5	42.5±13.7	0.007

IpcPH, isolated postcapillary pulmonary hypertension; CpcPH, combined postcapillary and precapillary pulmonary hypertension; VO2, oxygen consumption; VE, ventilation; VCO2, carbon dioxide production; AT, anaerobic threshold; PetCO2, carbon dioxide partial pressure.

Conclusions: In PH-LHF, an increased DPG is associated with a more unfavorable adaptation to exercise, characterized by a greater reduction of ventilatory efficiency. This might be explained, at least in part, by the presence of pulmonary vascular disease.

P5524 | BEDSIDE
Hemodynamic effect of initial combination therapy as compared to initial monotherapy in pulmonary arterial hypertension: a single centre blinded evaluation of patients enrolled in the AMBITION study

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Background: Pulmonary arterial hypertension (PAH) is a severe disease with a complex pathogenesis, for which upfront combination therapy is an attractive option.
Purpose: To compare functional and hemodynamic changes after 6 months of first line combination therapy (C) with Ambrisentan (A) and Tadalafil (T) versus first line monotherapy (M) with A or T in subjects with PAH enrolled in a single centre in the AMBITION study.
Methods: Consecutive naïve patients with World Health Organization (WHO) functional class II-III PAH were included in the study. They were randomized to receive initial C (A and T) or M (A or T). At baseline and after 6 months of treatment 6-minute walk distance (6MWD) and right-heart catheterization were performed. Statistical analysis was performed using Student's t-test for the analysis of baseline data versus 6 months within each group and for the comparison of the absolute changes between the C and M groups.
Results: Thirty patients were randomized: 19 in the C group [53% connective tissue disease PAH (CTD-PAH) and 47% idiopathic PAH (IPAH)] and 11 in the M group [64% IPAH, 36% CTD-PAH; 6 received A, 5 received T]. No statistically significant differences were found in baseline demographic, functional and hemodynamic characteristics between C and M groups. Hemodynamic and 6MWD changes after C or M treatment are shown in the Table.

	M (±SD)		C (±SD)		p: C changes vs M changes
	baseline	6-months	baseline	6-months	
RAP (mmHg)	6±3	6±4	8±5	5±2‡	0.113
mPAP (mmHg)	53±13	42±10*	55±11	37±11†	0.042
CI (l/min/m^2)	2.6±0.5	3.2±0.7*	2.4±0.6	3.7±0.8†	0.004
PVR (WU)	10±3	6±2*	12±4	5±2†	<0.001
MVO2 (%)	69±6	73±5**	63±8	73±7†	0.005
6MWD (m)	380±76	413±101	380±64	469±71†	0.026

*p<0.01, M baseline vs M 6-months; **p=0.05, M baseline vs M 6-months; †p<0.001, C baseline vs C 6-months; ‡p<0.05, C baseline vs C 6-months. CI, cardiac index; mPAP, mean pulmonary arterial pressure; MVO2, mixed venous oxygen saturation; PVR, pulmonary vascular resistance; RAP, right atrial pressure; 6MWD, 6-minute walk distance.

Conclusions: Both initial C and initial M improved hemodynamics and exercise capacity; however initial C is associated with statistically significant larger improvements as compared with M in patients with PAH.

PULMONARY CIRCULATION, IMAGING, OTHER II

P5525 | BEDSIDE
Resistance, compliance, and the time constant of the pulmonary circulation at exercise

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Background: The resistive (pulmonary vascular resistance, Rp) and pulsatile (pulmonary arterial compliance, Cp) components of right ventricular afterload are tightly coupled in an inverse hyperbolic relationship. Across different disease populations, the product of Rp and Cp is a constant (RC-time), though apparently influenced by pulmonary arterial wedge pressure (PAWP). We examined whether RC-time was acutely modifiable during exercise.
Purpose: To describe the Rp and Cp of trained and untrained healthy adults at rest and during submaximal exercise, and the behavior of RC-time.
Methods: Sixteen sedentary subjects (10M/6F; age: 55±7 years) and sixteen athletes (16M; age: 54±6) were studied at rest and during Light (100bpm) and Moderate (sedentary, 120bpm; athletes, 130bpm) intensity cycle-ergometry exercise. Right heart catheterization was performed to measure pulmonary pressures, with simultaneous echocardiography. At each exercise intensity, pulmonary artery systolic, diastolic, mean, and wedge pressures were manually analyzed, offline, beat-by-beat. Stroke volume and cardiac output were derived from Doppler echocardiography. Rp was calculated as (transpulmonary gradient/cardiac output); Cp was calculated as (stroke volume/pulse pressure).
Results: Data are presented in Table 1. Rp was unaffected by exercise, while Cp decreased at exercise ($p<0.01$). Accordingly, RC-time decreased at exercise ($p<0.01$). PAWP increased at exercise ($p<0.01$).

Table 1. Exercise hemodynamic data

	Control		Light Ex		Moderate Ex	
	Sedentary	Athletes	Sedentary	Athletes	Sedentary	Athletes
HR (bpm)	63±8	55±9	103±3**	103±3**	122±2**‡	130±4**‡#
PAWP (mmHg)	11±2	11±3	16±4**	19±5**	14±5**	16±6**
Rp (mmHg/ml/s)	0.08±0.03	0.09±0.03	0.09±0.03	0.08±0.04	0.07±0.02	0.07±0.03
Cp (ml/mmHg)	4.8±0.9	5.9±2.1	3.3±0.5**	3.7±1.8**	3.3±0.7**	3.5±1.2**
RC-time (s)	0.38±0.08	0.46±0.18	0.28±0.08**	0.26±0.09**	0.25±0.07**	0.24±0.07**

*$p<0.05$ vs. Rest; **$p<0.01$ vs. Rest; ‡$p<0.01$ vs. Light; #$p<0.05$ vs. Sedentary. HR, heart rate; PAWP, pulmonary artery wedge pressure; Rp, pulmonary resistance; Cp, pulmonary compliance; RC-time, pulmonary time constant.

Conclusions: In healthy adults, even submaximal exercise modifies the relationship between Rp and Cp, resulting in decreased RC-time. Right ventricular pulsatile afterload increases despite stable steady-flow resistance, possibly mediated by exercise-associated increases in PAWP.
Acknowledgement/Funding: Heart and Stroke Foundation of Ontario Grant-in-aid (#T7336); Canadian Institutes of Health Research Operating Grant (#130447)

P5526 | BEDSIDE
Non-invasive evaluation of right atrial morphology and function in patients with and without pulmonary arterial hypertension

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Background: Right atrial (RA) enlargement has been depicted as a significant independent predictor of unfavourable outcome in patients with pulmonary arterial hypertension (PAH).
Aim: To detect by standard echo and by two-dimensional strain (2DSE) RA morphology and function in a population of patients with and without PAH.
Methods: The study population included 282 subjects: 92 patients with PAH (age = 55±13 years; 62% female), 105 patients with systemic sclerosis (SSc) (age = 56±15 years; 91% female) and normal resting pulmonary pressures, and 85 comparable healthy control subjects. All the patients underwent a complete clinical examination, standard Doppler echocardiography and 2DSE analysis by Vivid E9 ultrasound system (General Electrics – Horton - Norway). Analysis was performed for two-dimensional strain from the 4-chamber apical views for the basal and middle segment of RA lateral wall. The peak of RA positive strain was considered representative of "reservoir" function. All measurements were averaged on at least 3 consecutive cycles.
Results: Left ventricular dimension and function were not significantly different between the three groups. Conversely, right ventricular (RV) and RA dimensions, pulmonary artery systolic pressure (72.3±24.2 mmHg in PAH, 23.5±3.8 mmHg in SSc and 16.5±3.7 mmHg in controls; PAH vs controls and SSc both $p<0.00001$; SSc vs controls $p<0.01$) and myocardial deformation of RA lateral wall (32.3±13.2% in PAH vs. 40.2±8.9% in SSc and 57.2±8.1% in controls; PAH vs controls and SSc vs controls both $p<0.00001$; PAH vs SSc <0.01) were significantly different between the three groups. By ROC curve analysis, a RA area index ≤40% showed a sensitivity and a specificity respectively of 80.7% and 88.8% ($p<0.0001$) to predict the presence of PAH. In the overall population, by multivariable analysis, RA area index (OR: 3.1; 95% CI: 2.1– 3.9; $p<0.001$) and PAH (OR: 2.3; 95% CI: 1.1– 1.7; $p<0.001$) were powerful independent determinants of RA strain.
Conclusions: This study evaluated for the first time RA reservoir function in patients with and without PAH. RA reservoir function is severely impaired in patients with PAH. This is probably an adaptive phenomenon of RA to increased RV afterload and decreased RV function induced by PAH as suggested by the correlation of RA strain with PAH and RA area. SSc patients, compared to healthy subjects, showed an impaired RA reservoir function despite still in the limits of normal.

P5527 | BEDSIDE
Evaluation of right atrial function using speckle tracking strain in patients with pulmonary hypertension

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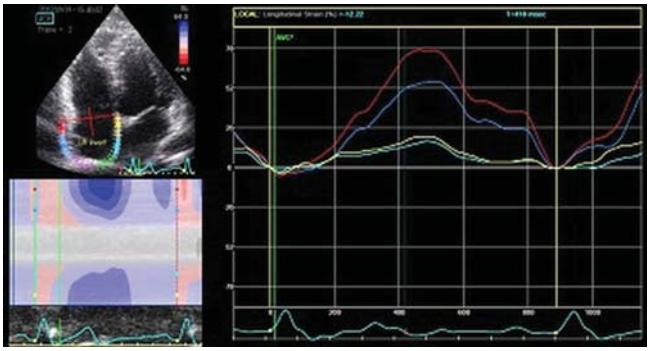
Background: Right atrial (RA) function could be a prognostic factors as well as right ventricular (RV) function in patients with pulmonary hypertension (PH), but its non-invasive evaluation is limited. Our objective was thus to evaluate RA function using two-dimensional speckle-tracking strain in PH patients.
Methods: Eighty-two PH patients with mean pulmonary artery pressure (mPAP) of 39±11mmHg (all≥25mmHg) were recruited. RA function was assessed two-dimensional speckle-tracking strain from RV-focused apical 4-chamber view. RA strain was calculated with the reference point set at the QRS onset, which enabled the recognition of the systolic peak positive RA strain (S-RAs), early diastolic strain (S-RApass), and late diastolic strain (S-RAa), corresponding to RA reservoir, conduit, and contractile function, respectively. All patients underwent right-heart catheterization for measurement of mean RA pressure (mRAP), diastolic RV pressure (dRVP), and mPAP. RV diastolic function was also evaluated using E wave from trans-tricuspid flow and E' wave from tissue-Doppler flow of tricuspid annulus. Thirty-six age- and gender-marched normal subjects were studied for comparison.
Results: S-RAs, S-RApass and S-RAa of PH patients were significantly smaller than those of normal subjects. S-RAs, S-RApass and S-RAa were significantly correlated with mRAP ($r=0.30$, $p<0.01$; $r=0.23$, $p<0.05$, $r=0.35$, $p<0.01$, respectively). S-RAs and S-RAa were significantly correlated with dRVP ($r=0.29$, $p=0.01$; $r=0.35$, $p<0.01$, respectively). Moreover, S-RAs was significantly correlated with trans-tricuspid E/E' ($r=0.25$, $p=0.03$).



Assessment of Right Atrial Strain

Conclusion: RA strain may be of a valuable additive factor for the management of PH patients, and thus have potential clinical applications.

P5528 | BENCH
The glucagon-like peptide-1 receptor agonist improves hypoxia induced pulmonary hypertension in mice model

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Background: Glucagon-like peptide-1 receptor (GLP-1R) agonist, liraglutide is an incretin hormone mimetics, a drug for diabetes mellitus. Recently, it is reported that GLP-1R agonist inhibits endothelial dysfunction, inflammation, and cell proliferation which are the major molecular findings for pathophysiology of pulmonary arterial hypertension (PAH). But the effect of GLP-1R agonist on PAH has been unclear.
Purpose: To investigate the effect of GLP-1R agonist on the development of PAH.
Methods and results: 8 weeks old C57BL6/J mice were injected liraglutide (0.3mg/kg/day) or saline for 4 weeks. 1 weeks after starting of injection, mice were placed in room air (normoxia) or exposed to chronic hypoxia (10% O2) for 3 weeks.
Right heart catheter revealed that right ventricular systolic pressure of liraglutide + hypoxia group were significantly reduced compared with that of saline + hypoxia group (30.0±1.51 mmHg vs 34.29±2.23 mmHg, $P<0.01$, n=7). Right ventricular/body weight ratio of liraglutide+hypoxia group were significantly smaller

than that of saline+hypoxia group (P<0.01). And the RT-PCR analysis showed that the expression of eNOS mRNA in the lung tissue was significantly higher in liraglutide+hypoxia group than saline+normoxia group.
Conclusion: GLP-1R agonist reduces right ventircular pressure in hypoxia induced PAH mice. This effect is suggested to be through the increased production of NO in pulmonary vessel.

P5529 | BEDSIDE
2D speckle tracking analysis of right atrium in patients with pulmonary hypertension

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Background: Right atrial (RA) strain analysis by two-dimensional speckle tracking (2DST) is a valid tool to assess RA function.
Aim: To analyze RA strain in a population of patients with pulmonary arterial hypertension (PAH) and to correlate its value with functional and haemodynamic parameters.
Methods: One hundred and three subjects (age = 57±15 years; 60% female) underwent a complete clinical examination, six minute walking distance (6MWD), standard Doppler echocardiography and 2DSE analysis by Vivid E9 ultrasound system (General Electrics - Norway) within one hour of right heart catheterization (RHC). Analysis was performed for two-dimensional strain from the 4-chamber apical views for the basal and middle segment of RA lateral wall. Right atrial systolic (RAs), right atrial early diastolic strain (RAe) and right atrial late diastolic (RAa) strain and strain rate (SR) were considered representative respectively of "reservoir", "conduit" and "contractile" function. All measurements were averaged on at least 3 consecutive cycles.
Results: At univariate analysis CI was related to 6MWD (p<0.0001; r 0.40) and RAe SR, was related to 6MWD (p<0.0001; r 0.56), pulmonary vascular resistance (PVR) (p<0.01; r 0.26), right atrial pressure (RAP) (p<0.005; r 0.32), mean pulmonary arterial pressure (mPAP) (p<0.05; r 0.23) and cardiac index (CI) (p<0.01; r 0.26). At multivariate analysis RAe SR was the only predictor of 6MWD (p>0.0001; STD error 16.4). Differently, CI, mPAP and right atrial pressure (RAP) did not correlate to 6MWD.
Conclusions: The 2DST derived strain and SR is a new tool for RA function assessment. Our findings suggest that RAe SR reflecting atrial stiffness has a key role in PAH patients functional capacity. RA functional evaluation should be included in the non-invasive follow up of PAH patients.

P5530 | BEDSIDE
Right ventricular function in patients with systemic sclerosis without pulmonary arterial hypertension

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Background: Cardiac dysfunction in systemic sclerosis (SSc) is associated with poor prognosis. Right ventricular involvement in these patients is typically associated with pulmonary arterial hypertension (PAH).
Aim: To evaluate right ventricular function and non-invasive hemodinamics by transthoracic Doppler echocardiography in SSc patients with normal ejection fraction and without known PAH, compared to controls.
Methods: Three hundred and ninety-one SSc patients without known PAH (mean age, 54.7±13.9 years) and 358 healthy age-matched controls (mean age 52.9±17 years, p=0.11) prospectively underwent a comprehensive transthoracic 2D and Doppler echocardiography, including tissue Doppler imaging analysis (TDI) of both right and left ventricle. SSc patients with significant interstitial lung disease (ILD) were excluded.
Results: SSc patients showed similar left ventricular systolic function, but worse left ventricular diastolic function parameters compared to controls. Both systolic and diastolic right ventricular function parameters were worse in SSc. Echo-derived pulmonary artery systolic pressure (PASP) values were higher in SSc patients, even without an overt diagnosis of PAH and without significant ILD (see table).

Echo variables	Controls 358 pts	SSc 391 pts	p
EF (%)	64.9±5.1	64.5±5.5	.30
Left atrium indexed volume (ml/m²)	20.2±5.8	25.2±5.2	<.0001
E/e'	6.9±2.1	7.9±2.8	<.0001
TAPSE (mm)	23.2±3.2	21.9±3.9	<.0001
RV E'/A' TDI	1.3±.4	.9±.4	<.0001
PASP (mmHg)	17±6	24±6	<.0001
PVR (W.U.)	1.4±.4	1.7±.4	<.0001
TASPE/PASP (mm/mmHg)	1.52±.65	1.01±.33	<.0001

Conclusions: SSc patients without overt cardiac dysfunction and no PAH show increased values of PASP and PVR, and borderline right ventricular involvement compared to controls.

P5531 | BEDSIDE
Assessment of systemic and pulmonary arterial remodeling in women with systemic sclerosis

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Objectives: Systemic sclerosis (SSc) leads to pulmonary circulation dysfunction. There are also some data on systemic circulation impairment. We evaluated the influence of SSc on properties of large systemic arteries wall and potential correlations between systemic and pulmonary circulation.
Methods: We examined 75 women (mean age 53,13±10,1y) with confirmed SSc (mean disease duration-DD 7,1±9,1y) and 21 age-matched women volunteers (mean age 52,6±8,3y,NS). Pulse wave velocity (PWV,Complior SR) and transthoracic echocardiography (Phillips iE33) were performed. SSc patients were divided into 2 groups according to the median of DD: ≤3 years (39pts) and >3 years (36pts).
Results: There were no differences in PWV between SSc and controls. Patients with DD>3 years had higher PWV than DD≤3 years (log PWV: 2.23±0.23 vs 2.13±0.16m/s, p=0.028). Patients with longer DD had higher PWV than controls (log PWV: 2.23±0.23 vs 2.11±0.16m/s, p=0.029). Moreover, echocardiographic indices showed impaired right ventricular function in the former (tab 1). In SSc pts with DD>3 years PWV correlated with clinical and echocardiographic parameters of pulmonary circulation: age (r=0.64; p<0.0001), AcT (r=–0.38; p=0.021), TRPG (r=0.34; p=0.04). Multiple linear regression analysis showed that PWV was independently associated with disease duration (β=0.22; p=0.02), AcT (β=–0.215; p=0.03) and age (β=0.44; p<0.001).

Ssc with DD>3 years vs controls

Parameter	SSc >3 yrs of DD (n=36)	Control group (n=21)	P value
Log PWV	2,23±0,23	2,11±0,16	0,029[a]
PWV>10 m/s	13 (36,1%)	2 (9,5%)	0,028
EF (%)	65; 53–73	66; 60–70	ns[b]
RV (mm)	25,69±3,62	23,55±2,35	0,01[a]
TRPG (mmHg)	26,83±5,32	18±3,94	<0,0001[a]
AcT (ms)	120; 65–180	130; 110–160	0,028[b]
TAPSE (mm)	18; 11–30	23; 22–30	<0,0001[b]
Tei PK	0,37±0,06	0,29±0,02	<0,0001[a]

[a]T-student test; [b]Mann-Whitney U test. TAPSE, tricuspid annular plane systolic excursion; TRPG, tricuspid regurgitation pressure gradient; AcT, acceleration time of pulmonary artery systolic flow.

Conclusions: Long lasting SSc simultaneously leads to the increased stiffness of large systemic arteries and to the progressive impairment of right ventricular function and its coupling to the pulmonary arterial bed.

P5532 | BEDSIDE
Follow-up of the pulmonary right-to-left shunt with transthoracic contrast echocardiography in patients with hereditary haemorrhagic telangiectasia

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Introduction: Pulmonary arteriovenous malformations (PAVMs) are associated with severe neurological complications in patients with hereditary haemorrhagic telangiectasia (HHT). Transthoracic contrast echocardiography (TTCE) is the first-line screening technique for the detection of pulmonary right-to-left shunts (RLS) and only moderate and large shunts seem to have clinical implications.
Purpose: Five years after the initial TTCE we evaluated the evolution of the pulmonary RLS in a single centre cohort.
Methods: All HHT patients underwent a second TTCE five years after screening. Patients with a history of PAVM embolisation were excluded. Opacification of the left ventricle was graded with a three grade scale. The TTCE after 5 years was compared to the TTCE performed at screening.
Results: In total 162 patients (55% female, 65.4% HHT type 2, age at follow-up 50.6±14.0 years) were included (expected patient number at presentation 190). The median follow-up time was 5.4 years (interquartile range 5.1–5.9 years). A pulmonary RLS was present in 93 patients (57.4%) at screening and 104 patients (64.2%) at follow-up. Increase in shunt grade was seen in 27 patients (16.7%). A significant increase was seen in 15 of these patients (55.6%) and embolisation was indicated in 6 patients (22.2%). Embolisation was feasible in 3 patients (1.9%) in whom the shunt increased within one grade but with increase of the PAVM on computed tomography. There were no complications.

Conclusions: Even in patients with no treatable PAVMs at screening, after 5 years treatable PAVMs are present in 6%. In this population there is a number-needed-to-screen of 18.

P5533 | BEDSIDE
The availability of dual-energy computed tomography for the optimal diagnosis and treatment in patients with chronic thromboembolic pulmonary hypertension

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Introduction: Balloon pulmonary angioplasty (BPA) improves clinical status and hemodynamics in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Because the success of reperfusion of occluded vessels is considered to depend on the patency of the distal vessels, the assessment of regional perfusion including collateral circulation is important for selecting the target lesions when performing BPA. Lung perfusion scintigraphy remains a widely used imaging modality for the diagnosis of CTEPH, this modality seems to lack sensitivity in spite of its high specificity and it cannot evaluate collateral circulation. Dual-energy CT (DECT) is a useful modality for evaluating lung perfusion and collateral circulation quantitatively in a single exam.
Purpose: The purpose of this study was to investigate the utility of DECT for the quantitative diagnosis of CTEPH.
Methods: A total of 59 patients (15 with CTEPH, 13 with acute pulmonary thromboembolism (APE), 15 with pulmonary hypertension (PH), and 16 controls) who underwent DECT were enrolled. Diagnosis of CTEPH and APE was established by perfusion scintigraphy and pulmonary angiography. Patients with PH were defined as those showing a tricuspid regurgitation pressure gradient greater than 40 mmHg on ultrasound echocardiography. All patients underwent DECT using the same protocols for both scanning and injection of contrast media. The iodine map on admission was analyzed, and the volume fraction in each range of CT values in the pulmonary arterial and the systemic arterial phase was investigated.
Results: The volume fraction with a CT value less than 20 Hounsfield Units (HU) was significantly higher in patients with CTEPH than in the other groups (CTEPH: 56.5±6.0%, APE: 31.0±5.3%, PH: 27.6±4.6%, control: 27.9±4.2%, $p<0.005$). Receiver-operating characteristic curve analysis showed that a volume fraction with a CT value less than 20 HU >38.1% was the optimal cut-off value for the quantitative diagnosis of CTEPH, demonstrating 86.7% sensitivity and 79.5% specificity. Volume fraction with CT values greater than 20 HU in the other groups was significantly decreased between the pulmonary arterial phase and the systemic arterial phase, but these values in patients with CTEPH remained unchanged (CTEPH: 43.5±6.0% vs. 31.9±6.7%, p=0.21, APE: 69.0±5.3% vs. 21.5±4.3%, $p<0.001$, PH: 72.4±4.6% vs. 51.2±8.3%, p=0.04, control: 72.1±4.2± vs. 30.8±6.9%, $p<0.001$).
Conclusions: DECT would be useful not only for the quantitative diagnosis of CTEPH, but also for the selection of optimal target lesions by evaluating collateral circulation when performing BPA.

P5534 | BEDSIDE
Clinical impact of treatment of atrial fibrillation in patients with pulmonary hypertension

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Purpose: Atrial fibrillation (AF) is frequently observed arrhythmia in patients with pulmonary hypertension (PH). Its prevalence and impact of treatment on prognosis of patients are not known.
Methods: We retrospectively studied the prevalence of AF and survival in 1021 patients with PH (aged 59±14 years; 454 males).
Results: AF was observed in 156 (15%) patients (42% paroxysmal AF). Patients with paroxysmal AF were in lower NYHA functional class compared to the rest of AF population (2.6±1.2 vs. 3.1±0.9; $p<0.05$). Total of 71 (46%) patients with AF died during mean follow-up of 5.1±2.3 years. Treatment strategy and mortality rates are shown in Table. Amiodarone was the most frequently used drug for rhythm control (n=49), followed by propafenone (n=29), and by sotalol (n=1). In rate control subgroup, 52 (68%) patients used beta-blockers, 15 (20%) used digoxin, 4 (5%) was on their combination and rest of patient was not treated by bradycardic therapy. Higher mortality was observed in patients stayed on rate control strategy ($p<0.05$).

Treatment strategy and mortality

Treatment strategy	N	Mortality rates
Rhythm control	79 (51%)	27 (34%)
Rate control	77 (49%)	44 (57%)

$p<0.05$ for comparison between mortality rates.

Conclusion: Patients with PH had high prevalence of AF. Permanent AF is associated with worsening of functional class. Rhythm control strategy seems to have lower mortality rate in PH population.

CARDIOVASCULAR RISK: PREMATURE AGEING AND ELDERLY

P5535 | BEDSIDE
Accelerated atherosclerosis in systemic lupus erythematosus patients with secondary antiphospholpid syndrome

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Introduction: Patients with antiphospholipid syndrome (APS) have been evaluated in the context of accelerated atherosclerosis in numerous studies, bringing this concept into the focus regarding proper treatment of this population of patients. Carotid intima-media thickness (cIMT) has been established as a distinguished marker of cardiovascular risk. The aim of this study was to evaluate relationship between presence of more than one antiphospholipid antibody (aPL) and cIMT values in SLE patients with secondary APS.
Materials: We analyzed 80 patients with systemic lupus erythematosus (SEL) and secondary APS 74 female (92.5%) and 6 male (7.5%), average age 49.4±13.1 years. In all patients presence of lupus anticoagulans (LA), anticardiolipin (aCL IgG/IgM) and anti-β2 glycoprotein-I (anti-β2GPI IgG/IgM) antibodies has been established, and they were classified into group with only one or more than one aPL present in any combination. Measurement of cIMT has been performed on common carotid artery (CCA), its bifurcation (CCAbiff) and internal carotid artery (ICA) on both sides. We defined cIMT values 1.1mm and higher as plaque presence.
Results: There were 63.8% patients with more than one aPL present. Prevalence of standard atherosclerotic risk factors was below 40%. Age, hypertension, presence of diabetes mellitus and hyperlipidemia resulted in higher values of cIMT in studied group patients. Average values of cIMT were significantly higher in patients with more than one aPL present for almost all segments of carotid trunk (CCA right, p=0.009, CCA left, p=0.034, CCAbiff right, p=0.093, CCAbiff left, p=0.632, ICA right, p=0.027, ICA left, p=0.544). After adjustment for age, current cigarette smoking, diabetes, hypertension and hyperlipidemia, the relative odds for atherosclerotic plaque presence on carotid arteries in SLE patients with APS and more than one aPL present was 4.19 (95% confidence interval 0.09 to 0.95, p=0.041).
Conclusion: Presence of more than one aPL in SLE patients with APS is independent predictor of premature atherosclerosis. In this subgroup of APS patients more aggressive approach towards prevention and control of standard atherosclerotic risk factors is crucial.

P5536 | BEDSIDE
Advanced atherosclerosis in rheumatoid arthritis: the role of von willebrand factor activity

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Objective: To evaluate association between von Willebrand factor (vWF) activity, inflammation markers, disease activity, cardiovascular risk scores, and advanced subclinical atherosclerosis in patients with rheumatoid arthritis (RA) and low cardiovascular risk.
Methods: Abovementioned parameters were determined in blood samples of 74 nondiabetic, normotensive, normolipemic, female subjects (42 patients and 32 matched healthy controls, age 45.3±10.0 vs. 45.2±9.8 years). Framingham, Reynolds, and QRISK2–2013 cardiovascular risk scores were calculated in all subjects. Intima-media thickness (IMT) was measured at common carotid, bifurcation, and internal carotid arteries. Subclinical atherosclerosis was defined as IMT above IMTmean+2SD in controls at each carotid level and atherosclerotic plaque as IMT>1.5 mm. Majority of RA patients were on methotrexate (83.3%), none on steroids >10 mg/day or biologicals.
Results: Subclinical atherosclerosis was more frequent in RA patients than in controls (35.7% vs. 3.1%, $p<0.01$). RA patients with subclinical atherosclerosis had higher vWF activity than those without (133.5±69.3% vs. 95.3±36.8%, $p<0.05$). Predictive value of vWF was confirmed by logistic regression analysis. vWF activity correlated significantly with inflammation markers, disease activity, rheumatoid factor concentration, anti-CCP antibodies, Framingham, Reynolds, and QRISK2–2013 risk scores. vWF activity was higher in participants with subclinical atherosclerosis (130±68% vs. 97±38%, $p<0.05$) or atherosclerotic plaques (123±57% vs. 99±45%, $p<0.05$) than in those without.
Conclusions: We demonstrated association of vWF activity and advanced subclinical atherosclerosis in low-risk RA patients as well as its correlation with inflammation markers, disease activity, and Framingham, Reynolds, and QRISK2–2013 cardiovascular risk scores. Therefore, vWF might be a valuable marker of early atherosclerosis in RA patients.

P5537 | BEDSIDE

Evaluation of early cardiovascular involvement in young patients with psoriatic arthritis

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Background: Psoriatic arthritis (PA) is a cardiovascular risk factor but data regarding scope and time of cardiovascular involvement (including atherosclerosis) are scarce so further studies are required. The aim of the study was evaluation of early cardiovascular involvement in young patients with psoriatic arthritis.
Methods: Cross-sectional study included 39 consecutive patients with psoriatic arthritis (PAGroup) diagnosis on the basis of ASAS criteria and modified CASPAR criteria. The study included men and women aged 23–60 years with disease duration <10 years. There were 90 patients in control group (CG) with performed CT coronary angiogram, who corresponded to PAG by age, gender, hypertension, hiperlipidemia, smoking, BMI. Cardiovascular assessment was performed using clinical and laboratory exams, echocardiographic examinations, carotid arteries ultrasound and CT coronary angiogram.
Results: Mean age of PAG was 45.1, 25–60 years, (53.9% women) and CG: 42.4, 23–59 years (46.7% women). The mean duration of disease was 18 months. Inflammatory disease activity assessed with the scales: BASDAI and ASDAS was considered as high. PAG patients had significantly lower HDL cholesterol values: 51.2±14.5 vs. 59.2±15.9 mg/dL (p=0.0257) and significantly higher triglycerides (TG) concentrations: 117 vs 91.6 mg/dL (p=0.026). There was a strong correlation between elevated C-reactive protein, index of inflammation, and HDL cholesterol lowering. Ultrasound examination of carotid arteries in PAG compared with the CG showed marked thickening of intima-media complex (CIMT): 0.90±0.21 vs. 0.64±0.16mm, p<0.0001. Coronary atherosclerotic lesions were observed significantly more often in PAG than in the CG, p<0.0001. Strong correlation of atherosclerotic plaques presence was observed with traditional cardiovascular risk factors. There was also a significant correlation between the presence of atherosclerotic lesions in both carotid and coronary artery and elevated concentrations of TG and lowered concentrations of HDL, which indirectly may indicate a role of inflammation in the pathogenesis of atherosclerosis in patients with PA. In echo exams thickened septum in PAG was observed, p=0.0025, despite a comparable incidence of hypertension in the study group and the control.
Conclusions: In patients with PA structural changes in the cardiovascular system, including atherosclerosis of coronary and carotid arteries are significantly increased in comparison with the control group. It confirms possible inflammatory etiology in the development of early changes in the circulatory system in these patients.

P5538 | BEDSIDE

Association of insulin resistance and subclinical atherosclerosis in patients with rheumatoid arthritis

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Background: Accelerated atherosclerosis in rheumatoid arthritis (RA) is well established during the last decade.
Purpose: To investigate the prevalence of insulin resistance in RA pts with normal glycoregulation and its association with carotid intima-media thickness (IMT) and therapy exposure.
Methods: Our study included 90 RA pts (age 52.4±9.9 yrs, 86.7% females, disease duration 9 yrs, range 4–13). We determined body mass index (BMI), waist circumference (WC), blood pressure, smoking habits, and disease activity score (mDAS28-SE). IMT was measured bilaterally, at common carotid (CCA), bifurcation (BF), and internal carotid arteries (CI). All pts were treated with disease modifying antirheumatic drugs, 65.6% were on steroids (<10 mg/day), and 27.8% were on biological therapy. IR was calculated using the updated-computer Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and serum specific insulin concentrations (measured by ELISA). IR was defined as HOMA2-IR>1.
Results: IR was detected in 74.4% of pts with median value of 1.4 (range 1.0–2.3). Pts with IR compared with those without IR had increased IMT (mm) at all levels of carotid arteries. CCA max: 0.841±0.144 vs. 0.762±0.105 (p=0.018); CCA mean 0.740±0.129 vs. 0.653±0.097, p=0.004; BF max: 1.059±0.169 vs. 0.920±0.124, p=0.001; BF mean: 0.908±0.141 vs. 0.782±0.126, p=0.000; CI max: 0.678±0.085 vs. 0.620±0.121, p=0.014; CI mean: 0.599±0.077 vs. 0.553±0.091, p=0.020. Both groups were comparable regarding RA duration and duration of all anti-inflammatory treatment including glycocorticoids. In multivariate logistic regression adjusted for age, BMI, WC and triglycerides we found that statistical significance disappeared for CCA and CI but stil persisted for BF (e.g. for age BF max β coef. 4.479, p=0.030; BF mean: β coef. 6.516, p=0.017). In univariant regression analysis, we revealed predictive value of logHOMA2-IR for IMT BF max: β coef. 0.253, p=0.001; BF mean: β coef. 0.178, p=0.006; CI max: β coef 0.097 p=0.026; while for other levels statistical significance was borderline (for CImean and CCAmean p=0.052, and for CCAmax p=0.064). On the other hand we found significant association of logHOMA2-IR with disease activity: DAS28 β coef 0.034, p=0.037.
Conclusions: RA pts with IR had significantly increased carotid IMT at all evaluated levels. Significant difference persisted for carotid BF even after adjustment for well known risk factors for atherosclerosis. Significant association of IR and disease activity may indicate the important role of RA itself in the interplay of IR and atherosclerosis.

P5539 | BENCH

Testosterone deprivation accelerates cardiac dysfunction and cardiac mitochondrial impairments in obese-insulin resistant rats

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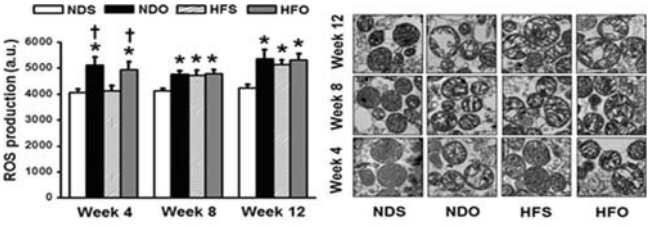
Background: Low testosterone level is associated with increased risks of cardiovascular diseases (CVD). Since obese-insulin resistance subjects have been shown to have impaired cardiac function and that the incidence of obesity is increased in ageing men, a condition of testosterone deprivation may aggravate the cardiac dysfunction in obese-insulin resistant subjects. However, the mechanism underlying this hypothesis is unclear.
Purpose: We hypothesized that obese-insulin resistance accelerates and aggravates the impairment of metabolic parameters, heart rate variability (HRV), left ventricular (LV) function and cardiac mitochondrial function in testosterone-deprived rats.
Methods: Orchiectomized or sham operated male Wistar rats (n=36/group) were randomly divided to receive either normal diet (19.77% fat) or high-fat diet (57.60% fat) for 12 weeks. Metabolic parameters, HRV, LV function by echocardiography and cardiac mitochondrial function were determined at 4, 8 and 12 weeks.
Results: Insulin resistance was seen at 8 weeks in high-fat diet sham (HFS) and high-fat diet orchiectomized (HFO) rats, whereas insulin resistance was not observed in normal diet sham (NDS) and normal diet orchiectomized (NDO) rats. The development of HRV depression, LV contractile dysfunction and increased cardiac mitochondrial ROS production was observed earlier in orchiectomized (NDO and HFO) rats at week 4, whereas HFS rats exhibited these impairments later at week 8 (Figure). NDO rats did not have impaired insulin sensitivity. However, HFO rats had markedly higher cholesterol level and diastolic blood pressure than HFS rats.



NDS = Normal diet +Sham, NDO = Normal diet +ORX, HFS = High fat diet +sham, HFO = High fat diet +ORX
*p < 0.05 vs. NDS, †p < 0.05 vs. HFS
Testosterone level and Mitochondrial ROS

Conclusion: Testosterone deprivation accelerates the impairments of cardiac autonomic function, LV function and cardiac mitochondrial function in obese-insulin resistant rats.

P5540 | BEDSIDE

Low testosterone and high pulse pressure are complementary predictors of cardiovascular events in erectile dysfunction patients

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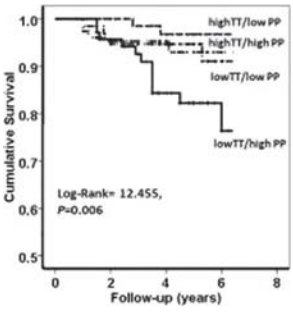
Purpose: It has been shown that decreased concentrations of testosterone and high pulse pressure (PP) are predictors of cardiovascular (CV) events in erectile dysfunction (ED) patients. We investigated, whether testosterone and PP have an independent or a complementary prognostic value in ED patients.
Methods: Serum total testosterone (TT) and PP were measured in a cohort of 425 ED patients followed six years for the occurrence of CV events (CV death, coronary artery disease, stroke). We prospectively stratified patients into groups, on the basis of the tertiles of the measured TT and PP and cardiac event-free survival curves were constructed by Kaplan–Meier analysis.
Results: Among 425 enrolled ED patients, 23 patients demonstrated a CV event. Baseline TT levels were significantly lower and PP was higher in CV-event group than the event-free survival group (all P<0.01). Kaplan–Meier analysis showed that patients with TT in the lower tertile (≤4.0 ng/mL) had a worse prognosis than

patients with TT >4.0 ng/mL (log rank: 6.37, P=0.008), and that patients with PP in the upper tertile ≥60 mmHg had a greater risk of adverse events than patients with PP <60 mmHg (log rank: 5.32, P=0.021). Figure shows Kaplan–Meier survival curves for patients with combinations of low or high TT (≤ or >4.0 ng/mL) and high or low PP (≥ or <60 mmHg) values. The event-free rate in patients with combined low TT and high PP is significantly lower than that in patients with either low TT or high PP alone.



Testosterone, pulse pressure and CV risk

Conclusion: In patients with ED, the combination of low TT and high PP was associated with a shorter event-free period compared with either decreased TT or elevated PP levels alone. Measurement of testosterone concentration may be useful to further stratify the risk of ED patients who have high peripheral PP.

P5541 | BEDSIDE
Association between endogenous serum testosterone concentrations and aortic pressures and pulse wave amplification indices in erectile dysfunction patients

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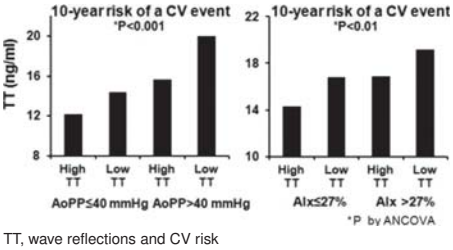
Purpose: Erectile dysfunction (ED) is an independent predictor of future cardiovascular (CV) events. Aortic pressures (central) and low testosterone independently predict future CV events and mortality. The relationship between testosterone, central pressures and wave reflection indices in ED patients is unknown.
Methods: Total testosterone (TT) levels were measured in 407 consecutive ED patients (55±8 y/o) without CVD. Central (aortic) systolic and pulse pressure, augmentation index (AIx) and augmented pressure (AP) as indices of pulse wave amplification across the arterial tree were measured with SphygmoCor device (AtCor Medical).
Results: TT levels were inversely correlated with systolic and pulse central pressures (r=–0.195 and r=–0.249, respectively) and wave reflection indices (AIx: r=–0.208 and AP: r=–0.168) (all P<0.001). In multivariate regression models adjusting for age and risk factors, TT was an independent predictor of central pressures and wave reflection indices (all P<0.001). The combination of low TT level (<4.0ng/ml) with higher central pulse pressure (>40 mmHg) and AIx (>27%) values showed greater effect on 10-year risk of a CV event (figure).



TT, wave reflections and CV risk

Conclusions: Our study is the first, to the best of our knowledge, to demonstrate in ED patients the independent association of low testosterone with central pressures and indices of pulse wave amplification across the arterial tree. This observation highlights the role of testosterone as a marker of arterial disease and predictor of CV events and imply a pathophysiological contribution of testosterone deficiency to age and blood pressure-related processes associated with generalized arterial disease.

P5542 | BEDSIDE
Impact of ages on fibrinogen levels and its relationship with coronary artery disease: a single-centre study

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Background: Previous reports have suggested an association between elevated fibrinogen and CAD. Few studies so far have investigated the impact of age on fibrinogen levels and its association with coronary artery disease (CAD) as evaluated by coronary angiography in elderly patient, that are therefore the aims of the current study.
Methods: We measured fibrinogen in 3637 consecutive patients undergoing coronary angiography. Blood samples were collected at admission for fibrinogen levels assessment. CAD was defined for at least 1 vessel stenosis>50% as evaluated by QCA.Severe CAD was defined by the presence of at least a 50% stenosis involving the left main or a 3 vessel disease.Elderly were≥75 years old.
Results: A total of 1796 out of 3637 were elderly patients, which were more often females, with higher prevalence of hypertension, previous MI or CABG, renal failure, but less often smokers (p<0.001, respectively),with lower prevalence of hypercholesterolemia (p=0.035) and family history of CAD (p<0.001). Elderly patients were more frequently on ACE-inhibitors (p=0.001), ARBs (p=0.002), calcium-antagonists, diuretics, nitrates (p<0.001, respectively).Elderly patients displayed higher creatinine, HDL cholesterol (p<0.001, respectively), uric acid (p=0.03), C reactive protein, (p=0.02), but lower total cholesterol, LDL cholesterol, triglycerides, PLT, haemoglobin (p<0.001, respectively) and WBC levels (p=0.002). Elderly patients displayed higher fibrinogen levels as compared to younger patients (464.4±153.4 mg/dl vs 422.1±12.21 mg/dl, p<0.0001). Among elderly patients higher fibrinogen levels were associated with the prevalence of CAD (adjusted OR [95% CI]=1.317 [1.118–1.460], p=0.0001). Similar results were found for severe CAD (adjusted OR [95% CI]=1.146 [1.052–1.248], p=0.002).
Conclusions: This study shows that elderly patients display higher fibrinogen levels as compared to younger patients. Among elderly patients, elevated fibrinogen is associated with the prevalence and extent of CAD.

P5543 | BEDSIDE
The prognostic values of hypoalbuminemia in patients with ST-segment elevation myocardial infarction

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Background: Hypoalbuminemia is a marker of frailty and it is associated with a poor prognosis in patients (pt) with ST-segment elevation myocardial infarction (STEMI).
Purpose: The aim of this study was to examinate the impact of hypoalbuminemia on prognosis of STEMI according to the age of the pt.
Methods: STEMI pt enrolled in the prospective "Cardio-STEMI Sanremo" registry (February 2011 - June 2014) were divided on the base of the values of albumin at admission: albumin >3 g/dl (normA group) and albumin ≤3 g/dl (hypoA group). Age was considered for a sub-analysis at a cut off of 75 years old. The endpoints were hospital MACE (cardiovascular death, MI, stroke) and long term survival.
Results: Out of 519 pt, 21.2% (110) had albumin values ≤3 g/dl. HypoA pt were older (71 vs 65 years old; p<0.01), mainly female (39.1% vs 24.0%; p<0.01) and with a lower body mass index (BMI 25 vs 27; p<0.01). There were no significant differences for cardiac risk factors or previous cardiac disease between the two groups. The incidence of initial TIMI grade 0 flow was higher in HypoA (57.7% vs 45.4%; p=0.03) whereas final TIMI grade 2–3 flow was achieved in the same proportion of pt. The incidence of BARC bleeding ≥2 was not different in the two groups, but HypoA experienced a higher rate of blood transfusion (5.5% vs 1.7%; p=0.04) and had a longer median in-hospital stay (6 vs 4 days, p<0.01). Hospital MACE were nominal more frequent in HypoA (7.4% vs 3.7%, p=0.11). At long term follow-up (median 741 days, [IR 443–1079]) all-cause mortality and cardiovascular mortality were higher in HypoA (respectively 21.8% and 16.4% vs 8.6% and 5.4%). In the Cox proportional hazard model [considering sex, ejection fraction, BMI, diabetes, glomerular filtration rate and hemoglobin values], pt younger than 75 years old showed no differences in mortality according to albumin values (Hazard Ratio 1.43, 95% confidence interval 0.77–2.65, p=0.26). Conversely analyzing pt over 75 years old, hypoalbuminemia resulted as an independent predictor of mortality (Hazard Ratio 2.80, 95% confidence interval 1.32–5.94, p<0.01). In older patients all-cause mortality and cardiovascular mortality were respectively 50.3% vs 23.5% (Log Rank p=0.01) and 39.6% vs 22.9% (Log Rank p=0.03) in HypoA group vs normA group.
Conclusion: Low albumin values (≤3 g/dl) at admission are associated with a worse in-hospital outcome in STEMI pt. Focusing on pt over 75 years old, hypoalbuminemia is a strong independent predictor of long-term mortality.

P5544 | BEDSIDE
3-year health related quality-of-life outcomes after percutaneous coronary intervention in elderly patients

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Background: Health-related quality-of-life (HRQoL) is an important but often neglected outcome measure for elderly undergoing percutaneous coronary intervention (PCI).
Purpose: We aim to evaluate long-term impact of PCI on health status in elderly patients.

Methods: We analyzed 998 consecutive patients undergoing PCI at our institution from September 2009 to January 2011. EuroQoL-5D (EQ-5D) health survey was used to assess HRQoL. Baseline, 6- 12-, 24 and 36-month HRQoL were compared among 3 age groups (<60, 60–79 and ≥80 years). Utility score improvement of 0.11 was considered a minimal clinically important difference (MCID)
Results: Patients aged <60, 60–79 and ≥80 years accounted for 32.5%, 59.5% and 8.0% of all patients undergoing PCI, respectively. Patients aged ≥80 years had highest 3-year all-cause mortality rates compared to patients 60–79 and <60 years of age (20% vs. 9.4% vs. 5.9%, respectively, p<0.01) Mean EQ-5D scores improved from 0.55 at baseline to 0.87 at 36-month follow-up in patients aged <60 years, 0.56 to 0.84 in patients aged 60–79 years and 0.56 to 0.83 in patients aged ≥80 years (All p<0.01). EQ-5D VAS scores at baseline (48.3±20.0 vs. 49.9±19.0 vs. 47.6±20.4, p=0.568) and 36 month (72.9±13.6 vs. 71.6±15.4 vs. 75.0±19.3, p=0.311) were similar among three age groups. Quality-adjusted-life-years gained after 3 years were comparable between age groups (0.96 vs. 0.84 vs. 0.80, p=0.24). Proportion of patients who experienced MCID improvement in HRQoL at 36-months were similar among age groups (82.6% vs. 81.5% vs. 82.5%, p=0.84).
Conclusion: Elderly patients who underwent PCI experienced similar improvement in quality-of-life compared to younger patients up to 3 years follow-up. Our findings suggest that age per se should not deter against revascularization because of potential benefits in quality-of-life.
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P5545 | BENCH
Decreased six-minute walk distance at hospital discharge is an independent predictor for poor instrumental activities of daily living after discharge in elderly patients with chronic heart failure

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Background: Elderly patients with chronic heart failure (CHF) are well known to have poor instrumental activities of daily living (IADL) after hospital discharge. Decreased six-minute walk distance (6MWD) was reported to be a strong predictor of rehospitalization and mortality in them. This study aimed to investigate whether decreased 6MWD measured at hospital discharge reflected poor IADL after discharge in elderly CHF patients.
Methods: We recruited 333 elderly patients, 203 males and 130 females, who were ≥65 years and admitted to our hospital because of heart failure. We assessed patients' characteristics, plasma brain natriuretic peptide, left ventricular ejection fraction and 6MWD at hospital discharge. IADL was evaluated using the Frenchay activities index (FAI) 3 months after discharge, while FAI score of ≤21 in males and ≤27 in females indicated poor IADL. We used multivariate logistic regression analysis and the area under the receiver operating characteristics (ROC) curve to determine significant predictors affecting poor IADL and their cut-off values.
Results: Of all patients, 129 male and 93 female patients had poor IADL. The multivariate logistic regression analysis identified 6MWD as a significant independent predictor for poor IADL in male and female patients (P<0.001, respectively). The odds ratio of poor IADL with each 10-meter decrease of 6MWD and its cut-off value were 1.10 (95% confidence interval: 1.05–1.17, P<0.001) and 350 meters in males, and 1.22 (95% confidence interval: 1.14–1.44, P<0.001) and 300 meters in females (figure).

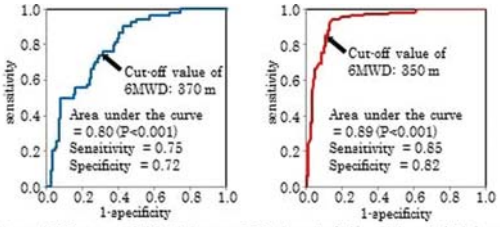

Figure: ROC curves of 6MWD for poor IADL in male (left) and female (right) patients

Conclusion: Decreased 6MWD at hospital discharge was identified as an independent strong predictor for poor IADL after discharge, and its cut-off value was 350 meters and 300 meters in male and female elderly patients with CHF, respectively.

P5546 | BEDSIDE
Unexpected senile cardiac amyloid in 5% of severe aortic stenosis patients undergoing surgery

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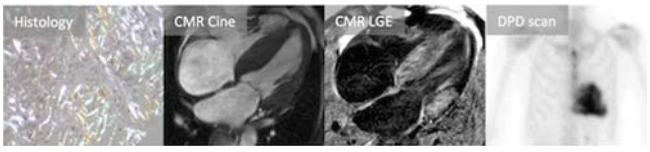
Background: Aortic stenosis (AS) affects 3% of people aged >75 and treatment is offered to increasingly older patients. Autopsy studies have found senile cardiac amyloid (ATTR) in 25% of octogenarians.
Aim: To investigate the prevalence of myocardial amyloid in patients with severe AS.
Methods: 130 patients with severe AS awaiting valve replacement (AVR) underwent cardiovascular magnetic resonance (CMR) and intra-operative myocardial biopsies (screened for amyloid with congo red). If positive, tissue was sub-typed by immunohistochemistry, and patients were referred for DPD scintigraphy (Figure 1).
Results: 97 patients had calcific AS (cAS) [73±8 years; 57% male]; the remainder had bicuspid (n=31), rheumatic or unicuspid AS (1 each). Myocardial amyloid (all ATTR) was found in 5 cAS patients (5.2% of >65 years; Table 1); none in the other cohorts. CMR detected 3 of 5, but missed 2. 1-year post-op, 3 of 5 affected patients had died compared to 5% in the whole cohort.

Patients with AS and ATTR amyloid

Age/gender	73F	69M	80F	85M	84M
AVAi (cm^2/m^2)	0.33	0.52	0.60	0.34	0.35
CMR (Δ amyloid)	+ve	+ve	suggestive	–ve	–ve
DPD (Perugini grade)	II	II	not done	I	not done
Status	alive	dead	dead	alive	dead



Diagnosis of senile cardiac amyloidosis

Conclusion: 5 of 97 patients undergoing AVR for cAS had senile cardiac amyloid on biopsy - these had a poor outcome. Screening elderly with AS may be warranted in the light of new amyloid therapies and to aid risk stratification.

PHARMACOTHERAPY AND ELECTROPHYSIOLOGY ISSUES IN THE ELDERLY

P5547 | BENCH
Vitamin K supplementation inhibits cardiovascular calcification in a murine model of chronic kidney disease

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Background: Biological aging and diseases like diabetes mellitus or chronic kidney disease are characterized by cardiovascular calcification associated with enhanced morbidity and mortality. Matrix Gla protein (MGP) is a key calcification inhibitor within the arterial tunica media. Its activity is critically dependent on activation by vitamin K (VK)-dependent carboxylation.
Hypothesis: Vitamin K supplementation may prevent cardiovascular calcification in a murine model of extraosseous calcification.
Methods: Experimental extraosseous calcification was induced by a 5/6-nephrectomy in combination with a high phosphate diet in Wistar rats (n=28). Animals received high VK (CKD-K) or low VK diet (CKD). 20 sham-operated rats served as controls receiving both diets (Co;Co-K). Up to 12 weeks, we assessed longitudinally vital parameters, serum chemistry, creatinine clearance and cardiac function (echocardiography). After 12 weeks we investigated cardiovascular calcification (atomic absorption spectrometry) as well as structural alterations (elastic fibre breaking points, alkaline phosphatase staining) and mRNA expression of calcification regulating proteins.
Results: As expected, nephrectomy with high phosphate diet induced aortic (1,3 fold;p<0,05) and myocardial (2,4 fold;p<0,05) calcification. In parallel, these animals exhibited increased vascular deposits of alkaline phosphatase (ALP) (2,2 fold;p<0,01) indicative of osteblastic transdifferentiation. VK supplementation prevented extraosseous calcium deposits in aorta and myocardium as well as increased aortic ALP tissue concentrations in the CKD-K group. Tissue mRNA expression was affected by VK supplementation with increased MGP induction (20,1 fold;p<0,05). Both interventional groups (CKD;CKD-K) exhibited similar hypertension with secondary cardiovascular structural alterations as myocardial hypertrophy (1,6 fold septum diameter;p<0,001) and increased elastic fibre breaking points in the arterial tunica media (3,4 fold;p<0,001).
Conclusion: VK supplementation rescues cardiovascular calcification in a

murine model of extraosseous calcification. The protective influence of VK on tissue calcium content may be related to inhibition of secondary mineralisation of damaged vascular structures and mediated via activation of MGP and alteration of MGP gen regulation.

P5548 | BEDSIDE
The association between antihypertensive drug use, mortality, and hospital admissions related to medication in community dwelling elderly of 80 year and older: a retrospective cohort study

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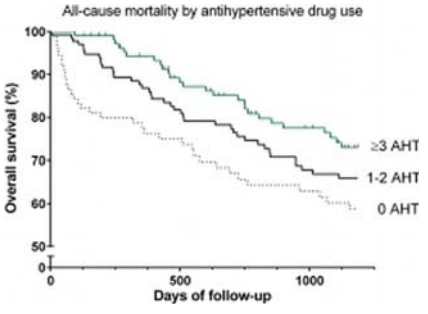
Introduction: Blood pressure (BP) treatment in the elderly is much debated. Although ESH/ESC hypertension (HT) guideline advises to leave treatment decisions for frail elderly at the discretion of the treating physician, it still remains a challenge to select those patients who will benefit from antihypertensive drugs (AHD) and those in whom AHD may be harmful.
Purpose: We performed a real life survey on the association between AHD, mortality and potential Hospital Admissions Related to Medication (HARMs) in the light of polypharmacy and multimorbidity in the very old.
Methods: All 336 community dwelling elderly from our Academic General Practice who were ≥80 years on 1 January 2011 were included. Retrospective chart review was performed on baseline characteristics, incidence of acute hospital admissions, and death in the following years. Polypharmacy was defined as ≥5 separate drugs, multimorbidity as >1 chronic disease.
Results: Baseline characteristics were: age 85 (82–88) years, 28% male, 67% HT, 42% CVD, 30% CHF, 55% polypharmacy, 86% multimorbidity. A recent BP was documented in only 62% (146±24/77±14 mmHg). AHD were used in 73% (33% ≥3 AHD). Mortality was 10% per year. In 2 year follow-up, 34% were admitted to a hospital least once (8% CVD, 2% CHF, 20% potential HARM, 4% other). AHD use was associated with lower mortality: HR (95% CI) 0.51 (0.33–0.79) after adjustment for CVD, multimorbidity, polypharmacy, and CHF. None of these were associated with hospital admissions or HARMs.



Conclusion: In this retrospective study, AHD use was highly prevalent in community dwelling elderly and associated with lower mortality. Surprisingly, AHD were not associated with HARMs. One explanation may be that AHD are already withheld or discontinued in the most sick and vulnerable.

P5549 | BEDSIDE
Antiplatelet therapy in the very elderly: should tolerability of therapy after percutaneous coronary intervention guide patient and device selection?

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Introduction: Compliance and tolerability of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) have been poorly studied in the very elderly greater than 85 years old. The elderly have high rates of bleeding, need for urgent procedures and cognitive issues, all of which could impact DAPT duration. This study investigates outcomes and duration of DAPT in patients greater than 85 years old undergoing PCI at our institution.
Methods: A registry of consecutive patients over the age of 85 years old undergoing PCI at 2 sites in Australia between Jan 2010 and March 2013 was analysed. All patients undergoing stent implantation or receiving balloon angioplasty were studied. The treating cardiologist nominated a recommended period of DAPT at the time of PCI at their discretion. Patients were reviewed at 30 days and one year after implantation.
Results: We studied 254 consecutive patients and all received follow up at 30 days and one year. A total of 90 (35%) patients received bare metal stents, 152 (60%) received drug eluting stents and 12 (5%) received balloon angioplasty. In the entire cohort, 163 (64%) patients reached the physician target DAPT duration and 137 (54%) reached one year of DAPT or equivalent. Of the patients receiving drug eluting stents, 94 (62%) reached one year of DAPT equivalent (68% if deaths are excluded). In total, 37 patients (14%) died in the follow up period. Major bleeding had occurred in 10 patients at 30 day follow up and in 23 at 1 year follow up. Of the 22 patients who died between 30 days and one year, 11 did not complete 30 days of DAPT. Their risk ratio for death at one year compared to patients who completed 30 days of DAPT was 3.8 (95% CI 1.7 to 8.2). Their risk ratio for cardiac mortality at one year was 3.3 (95% CI 1.2 to 9.2).
Conclusion: DAPT is poorly tolerated in the elderly and there is an association between early cessation and mortality at our institutions. Further study to predict the best candidates for PCI in the very elderly may improve outcomes.

P5550 | BEDSIDE
New oral anticoagulants: perioperative bridging therapy versus no bridging therapy

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Background: Perioperative management of anticoagulation is not well established in patients with new oral anticoagulants. The purpose of this study was to evaluate the current strategies of perioperative anticoagulation in a large cohort of patients and to assess the risk of bleeding.
Methods: 851 consecutive bridging episodes were collected in the German BNK online bridging registry (BORDER 2). The incidence of bleeding and ischemic events was assessed and risk factors for bleeding events determined.
Results: 300 patients (pts) (35%) had a Vitamin K antagonist and 549 pts (65%) had a new oral anticoagulant, (apixaban N=82, dabigatran N=95, rivaroxaban N=372). In 2 pts the medication was missing. 499 pts (59%) did not receive perioperative bridging therapy. 352 pts (41%) received perioperative bridging therapy (13 pts received new oral anticoagulants, 6 pts unfractionated heparin and 333 low molecular weight heparin). Major surgery was performed in 144 cases and minor surgery in 707 pts. Clinical relevant bleeding occurred in 32 (3.8%) pts and major bleeding in 5 (0.6%) of pts. Independent risk factors for bleeding were major surgery, a HASBLED score >2 and bridging therapy.

Variable	Odds ratio	95% CI	P
Bridging therapy	1,7	1,2–2,5	0.003
Major surgery	2,5	1,2–5,5	0.02
HASBLED >2	2,4	1,0–5,7	0.05

Conclusions: Perioperative bridging therapy is uncommon in patients with new oral anticoagulants. Independent risk factors for clinical relevant perioperative bleeding are major surgery, an increased clinical risk score for bleeding (HASBLED >2) and bridging therapy.
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P5551 | BEDSIDE
Long-term effect of antihypertensive drugs on the risk of new onset osteoporotic fractures in the elderly - A population-based longitudinal cohort study

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Background: Antihypertensive drugs have been linked to new-onset osteoporotic fractures (NOF); however, data on the effect of these drugs on the development of NOF in hypertensive patients has not been well determined.
Purpose: To investigate the association between antihypertensive drugs and NOF.
Methods: Our data were taken from claim forms provided to our National Health Insurance from January 2002 to December 2012. Prescriptions for antihypertensive drugs before the index date were retrieved from a prescription database. We estimated the hazard ratio (HR) of NOF associated with antihypertensive drug use; non- NOF subjects served as the reference group.
Results: A total of 128 NOF cases were identified among 1144 elderly hypertensive patients during the study period. The mean age of NOF group was 78.9 years and that of non-NOF was 75.6 years. There was a significant difference in age between the two groups of patients ($P<0.0001$). The risk of NOF after adjusting for sex, age, comorbidities, and concurrent medication was higher among users of angiotensin- converting enzyme (ACE) inhibitors diuretics (HR, 1.64; 95% confidence interval (CI), 1.01–2.66) than among non-users. Patients who take calcium channel blockers (HR 0.70; 95% CI 0.49 – 1.00) are at a lower risk of developing NOF than non-users. Diuretics, beta-blockers, angiotensin receptor blockers, and alpha-blockers were not associated with risk of NAF.
Conclusions: The results of this study suggest that hypertensive patients who take calcium channel blockers are at lower risk of NOF. ACE inhibitors were associated with a significant increase in the risk of NOF.

P5552 | BEDSIDE

The dynamics of velocity parameters of cardiac electrical activity in healthy males aged 1 to 64 years

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Objective: To investigate the dynamics of velocity parameters of heart electrical activity in healthy males aged 1 to 64 years.
Methods: Healthy males of different age groups were randomly sampled: children population aged 1 to 16 years (n=324), divided into age groups 1–3 (n=47), 4–6 (n=95), 7–10 (n=94), 11–16 (n=88), and adult population aged 18 to 64 years (n=99), divided into age groups 18–24, 25–34,35–44,45–54,55–64 years old. Velocity parameters of cardiac electrical activity were measured by the ventricular activation rate (VAR), detected by using ECG and first ECG derivative methods.Statistical analysis was performed using t-test for independent samples, Pearson's correlation,nonparametric Spearman rank correlation. Results are performed as M±SD.
Results: In healthy boys the dynamics of VAR was age-related, it had a form of undulating curve with the nadirs in the age of 7–8 years and 14–16 years. Data did not reveal statistical differences in VAR between age groups 1–3 years old and 4–6 years old (53,4±0,4 sec^{-1} vs. 52,4±0,28 sec^{-1}, NS). VAR in 1–3 years old group was statistically higher in comparison with age groups 7–10 years old and 11–16 years old (51,4±0,26 sec^{-1}, $p<0,01$ and 48,8±0,23 sec^{-1}, $p<0.001$ respectively). Boys with arterial hypertension aged 11 to 16 years had lower VAR than healthy boys of same age (VAR 45,8±0.9sec^{-1} vs. 48,8±0,23 sec^{-1}, $p<0.001$), their VAR didn't differ from adults aged 25 to 34 years. Data revealed negative correlation between age and VAR in pediatric population ($r=-0,57$, $p<0,05$), between age and heart rate ($r=-0,6$, $p<0,001$). Data revealed positive correlation between VAR and heart rate ($r=0.33$, $p<0,001$). In adult population VAR was significantly lower than in pediatric population, VAR gradually lowers with ageing with peak in age groups 18–24 and 25–34 years old (47,4±0,42 sec^{-1} and 46,6±0,54 sec^{-1} respectively) and nadir in age group 55–64 years old (41,3±0,83 sec^{-1}, $p<0,001$). Data demonstrated negative correlation between age and VAR ($r=-0,73$, $p<0,001$). Data showed positive correlation between VAR and heart rate ($r=0,45$, $p<0,0001$).
Conclusions: Data establish the pattern of lowering cardiac velocity parameters with ageing, in boys with arterial hypertension velocity parameters demonstrate premature cardiovascular ageing. In childhood there was found a tendency to heterochrony due to the heterogeneous heart development. Absence of a strong correlation between velocity parameters of cardiac electrical activity and the heart rate confirms that ventricular activation rate is an independent significant marker of the electrical activity of the heart.

P5553 | BEDSIDE

Electrophysiological study is required for the prognosis evaluation of preexcitation syndrome in patients aged 60 and over

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Background: Management of preexcitation syndrome (PS) in elderly patients is unknown. The purpose of study was to look for the influence of age ≥60 on clinical, electrophysiological data and long-term follow-up of patients with a PS.
Methods: 953 patients, 62% males, aged from 5 to 85 years, mean 33±17, were referred for PS. Clinical, electrophysiological and exercise testing data were collected. Patients were followed from 3 months up to 10 years (5.4±5 years).
Results: 71 patients were aged from 60 to 85 years (mean age 68.4±6); 882 were <60 (mean 30.5±14). Heart disease (HD) was more frequent in patients ≥60 (20%vs6.7%) ($p<0.0001$). Gender did not differ. Accessory pathway (AP) location did not differ except for right lateral, anteroseptal, nodoventricular AP only noted in patients <60. Patients ≥60 were more frequently symptomatic than patients <60 (80 vs 63%) ($p<0.007$). No arrhythmia was induced in patients ≥60 at exercise testing but PS pattern disappeared in 20 patients. At EPS, maximal rate conducted over AP was similar in patients ≥60 and <60 in CS (181±58.5 vs 190±65 bpm) (0.55) or after isoproterenol (230.5±59 vs 232±69). The number of induced reciprocating tachycardia was lower in patients ≥60 (39.4%vs54.6%) (0.014), but induced AF (28%vs23.6%) and malignant forms (14%vs15%) did not differ significantly in patients ≥60 and <60. During follow-up AP ablation was indicated as frequently in patients ≥60 (42%) and in patients <60 (48%). Failure or recurrence requiring a 2nd procedure was similar in patients ≥60 (20.6%) and in patients <60 (18%). Late occurrence of AF predicted by AF induction was more frequent in patients ≥60 than in patients <60 (respectively 13%,3.5%,$p<0.001$). In untreated patients by AP ablation late poorly-tolerated tachycardia was more frequent in patients ≥60 (4.3%) than in patients <60 (0.5%,$p<0.0001$). Effects of age at multivariable analysis on AF occurrence and spontaneous poorly-tolerated arrhythmias adjusted on previous HD, gender and induction of AF at EPS indicated that only age ≥60 was associated with the risk of adverse events (0.000) and that age ≥60 (0.01) and AF induction (0.000) were predictors of the risk of AF.
Conclusions: Despite the low prevalence of preexcitation syndrome in patients ≥60 years (7.5%), elderly patients have a higher risk of AF and of poorly-tolerated tachycardia than younger patients. Exercise testing was not useful but the risk of AF risk was predicted by electrophysiological study. Therefore elderly patients with a preexcitation syndrome require the same management as younger patients.

P5554 | BEDSIDE

Prevalence and prognosis of Brugada electrocardiogram patterns in an elderly Han Chinese population: a nation-wide community-based study (HALST cohort)

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Background: The exact world-wide prevalence of Brugada electrocardiogram (ECG) pattern is still unclear, especially in adults aged 55 years and older.
Methods: The study was conducted as part of the Healthy Aging Longitudinal Study (HALST) in Taiwan. Using a stratified random sampled method, a sample of community-dwelling subjects was recruited from seven community-based regions across Taiwan. All enrolled subjects were follow-up annually and cause of death was documented by citizen death records.
Results: A total of 5214 subjects were enrolled (male/female: 2530/2684) with a mean age of 69±8 years. The overall prevalence of Brugada ECG patterns was 3.32%. Four subjects carried spontaneous type 1 Brugada ECG pattern, 68 carried type 2, and 101 carried type 3. Compared to the world-wide average prevalence of Brugada ECG patterns, the prevalence of spontaneous type 1 Brugada ECG pattern in subjects from the HALST cohort was similar (0.077% vs. 0.07%) and the combined prevalence of type 2 and type 3 Brugada ECG pattern was 10 times higher (3.24% vs. 0.28%) even the mean age of study subjects was significantly higher (69±8 vs 35±8, $P<0.001$). However, all-cause and cardiovascular mortality rates were not significantly different between subjects with or without Brugada ECG patterns during the 4-year follow-up (log-rank test, P=0.21, 0.24, respectively).
Conclusion: The prevalence of Brugada ECG pattern in adults aged 55 years and older in Taiwan was higher than the average world-wide prevalence but was not associated with increased mortality.

P5555 | BEDSIDE

The natural history of multifocal atrial rhythms in elderly outpatients. Prospective data from the 'Ikaria study'

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Purpose: Multifocal atrial tachycardias confer an adverse prognosis in hospitalized patients. We assessed the prognostic impact of multifocal atrial rhythms (MARs - either chaotic atrial rhythm or multifocal atrial tachycardia/bradycardia) in very elderly individuals enrolled in the "Ikaria study".
Methods: The "Ikaria study" is a prospective epidemiological survey, carried out in the province of Ikaria island, in which 1420 permanent inhabitants participated voluntarily. Using a random number generator, and after the exclusion of 18 subjects due to poor quality of ECG recording, a number of 110 subjects aged 60 to 74 years, 112 aged 75 to 89 years and 61 over 90 years old, was enrolled and prospectively evaluated. ECGs interpretation was performed independently by 2 expert cardiologists and in case of disagreement, a third expert was consulted to reach consensus. The ECG diagnosis of MARs was established according to the recommendations for the Standardization and Interpretation of the Electrocardiogram of the American Heart association. Individuals with atrial fibrillation-flutter were excluded. In June of 2013, the four years follow-up of the cohort of the study was performed.
Results: At baseline examination, a high prevalence of MARs was detected in the study population (namely 6%), which in subjects >90 years was even higher (15%). Individuals with MARs were older, more often female and less active. In multivariate analysis, independent predictors of MARs were age (OR=1.07, 95% CI: 1.02–1.13, p=0.01) and female sex (OR=4.77, 95% CI: 1.23–18.48, p=0.02). The mortality rate during the follow-up period was 8.4% without differences between age groups (p=0.209). Mortality rate was 6% in individuals with MARs and 9% in those without (p=0.72). Mortality was associated with age (OR 1.07, 95% CI: 1.02–1.12, p=0.005) and history of cardiovascular disease at baseline (OR 4.57, 95% CI: 1.87–11.2 p=0.001).
Conclusions: Contrary to hospitalized patients with multifocal atrial tachycardias, MARs were not associated with increased mortality in elderly outpatients in 'Ikaria study'.

P5556 | BEDSIDE
Prognosis of the elderly patients after implantation of bradycardia pacemaker

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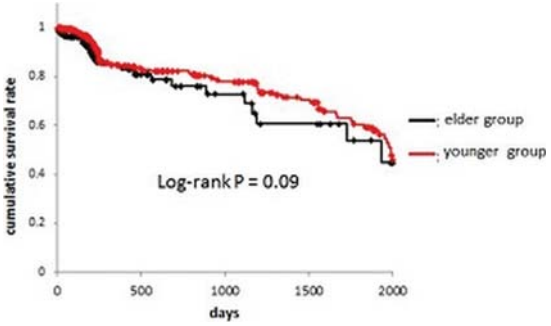
Purpose: The aim of the present study was to assess the prognosis of the elderly patients (aged ≥85 years) needed for the implantation of bradycardia pacemaker (PM).
Methods: A total of 869 patients (men 49.0%, 76.6±10.6 years) receiving a first bradycardia PM between January 2006 and June 2013 were enrolled, and the clinical outcome was compared between the elderly group (201 patients, 88.6±3.2 years) and the younger group (667 patients, 73.0±9.3 years).
Results: At the end of a mean follow-up of 430±556 days, 128 patients (14.7%) died, mostly of non-cardiac cause (73%). The mortality rate was similar between the elderly group and the younger group (15.4% vs. 14.5%, P=0.09). The mortality rate was similar regardless of the indication for implantation (atrio-ventricular conduction disturbance or sick sinus syndrome, P=0.59), initial rhythm (sinus bradycardia or atrial fibrillation with slow ventricular response, P=0.62), pacing mode (dual chamber or single chamber, P=0.70), and the position of the leads (septum or apex, P=0.38). Predictors for all-cause mortality were history of myocardial infarction, stroke, and heart failure.



Kaplan-Meier curve for survival rate

Conclusions: The mortality rate of the elderly patients receiving PM was not inferior to the younger patients. The prognosis was determined not by age, indication for implantation, initial rhythm, pacing leads and mode but by the comorbid diseases.

P5557 | BENCH
Osteopontin-deficient mice are protected against age-related myocardial dysfunction, structural remodelling and senescence

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Background: Aging induces osteopontin (OPN) expression in skeletal muscle and vasculature that compromises function and ability for renewal. Whether OPN has an impact on myocardial aging, contractility and structure is currently unknown.
Purpose: To explore whether OPN deficiency is able to prevent age-related cardiac abnormalities.
Methods: OPN KO (n=10) and wild-type C57BL6 (WT, n=10) mice were followed up until the age of 14 months. To explore if OPN deficiency impacts on age-related cardiac dysfunction, myocardial function was monitored by echocardiography in non-sedated mice and explored by left ventricular ejection fraction (LVEF, %) and deformation parameters such as myocardial strain rate (SR, s^{-1}) within the anterior and posterior walls. Cardiac structural remodelling was evaluated by heart weight to tibia length (HW/TL), wheat-germ agglutinin (cardiomyocyte size) and Sirius red staining (fibrosis). Myocardial senescence was estimated by p21 and p16 expression. Oxidative stress was measured by malondialdehyde levels, whilst apoptosis rate by TUNEL-assay. All data were collected at a young (2–3 months) and old age (13–14 months).
Results: As shown in the table, young WT and OPN KO did not differ in terms of myocardial function. With age, LVEF and SR values remained in the range of young values in OPN KO hearts, but significantly declined in WT ($p<0.05$ vs. young WT and aged OPN KO). Whilst HW/TL, cardiomyocyte size and fibrosis increased with aging in WT hearts, they were preserved around young levels by OPN deficiency. Induction of p16 and p21 in WT hearts with aging was rescued in OPN KO hearts. Myocardial malondialdehyde levels as well as TUNEL positivity were elevated by aging but without any difference between WT and OPN KO hearts.
Conclusions: OPN deficiency protects against age-dependent cardiac remodelling and dysfunction, independent of age-related oxidative stress or apoptosis. These results raise the possibility of OPN inhibition as cardioprotective strategy against myocardial aging.

Basic cardiac parameters in young and aged WT and OPN KO mice

	Young WT	Young OPN KO	Aged WT	Aged OPN KO
HW/TL, mg/mm	6.5±0.3	6.2±0.2	8.6±0.2	7.3±0.4
LVEF, %	74.8±1.7	82.3±2.0	78.8±4.1	83.4±2.0
Anterior SR, s^{-1}	25.4±0.93	25.8±1.2	19.6±0.8	23.4±0.6
Posterior SR, s^{-1}	29±0.8	27.2±0.9	19.2±0.8	23.9±0.6

P5558 | BENCH
Increased expression of the aging related splice variant progerin in patients with cardiomyopathy

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Objective: Defined mutations in the human lamin A gene or in enzymes processing the important nuclear membrane protein LMNA (e.g. Zmpste24) are causally involved in premature aging syndroms like progeria. The most prevalent and recurrent point mutation is depicted by a single C to T (1824) nucleotide substitution in exon 11 of the lamin A gene. This results in the activation of a cryptic splice donor site and production of a truncated prelamin A protein (LMNA Δ50 aa), also called progerin. Besides, low levels of progerin also play a prominent role in the process of aging in healthy individuals. Since LMNA mutations are associated with dilated cardiomyopathy, we aimed to address whether progerin and Zmpste24 play a role in patients with cardiomyopathy.
Methods: To quantitatively analyze the expression of progerin and Zmspte24, blood and endomyocardial biopsies (n=6) were obtained from non-ischemic cardiomyopathy patients. For controls, blood samples from age matched healthy individuals as well as biopsies from healthy transplanted hearts (n=6) were analyzed. Total mRNA was extracted and quantitative RT-PCR analyses were performed. Total LMNA expression was determined utilizing primers spanning exon 8 to 9. To specifically quantify progerin expression, we designed optimized primers spanning the splice junction site between exon-11 and 12. Progerin expression was related to total LMNA expression. Zmpste24 expression was related to housekeeping genes rpl32 and polr2a.
Results: Progerin mRNA levels were not significantly different in blood samples from controls and DCM patients (0.84±0.14 vs. 0.81±0.33; p=0.67). In contrast, progerin levels were significantly upregulated in failing hearts compared to heart biopsies derived from healthy controls after heart transplantation (1.66±0.56 vs. 1.06±0.07; p=0.01). Zmpste24 mRNA level were not significantly different between patient and control blood samples (1.31±0.23 vs. 1.11±0.15, p=0.12) and hearts (1.05±0.13 vs. 1.00±0.20, p=0.62).
Summary and conclusion: In conclusion, our preliminary data suggest that elevated levels of the aging related splice variant progerin are involved in human heart failure.

CARDIOVASCULAR MORTALITY IN ELDERLY

P5559 | BEDSIDE
Heart failure mortality in the elderly in Brazil: time trend analysis from 1996 to 2012

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Background: Heart failure (HF) presents epidemic characteristics with considerable impact on morbidity and mortality, especially among the elderly. In Brazil, HF is responsible for high mortality rates.
Objective: To evaluate the HF brut mortality rate variation trend in the elderly in Brazil, comparing with the variability of population growth by age group in the last decades.
Methods: Information was obtained from data published by the Informatics Department of Brazilian Health System (Datasus) regarding brut mortality rates. We

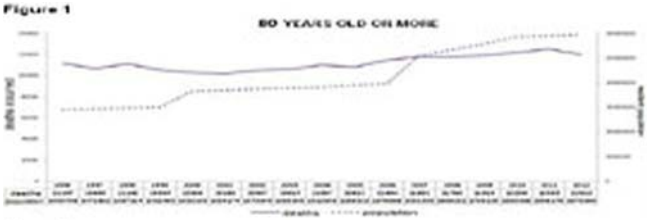
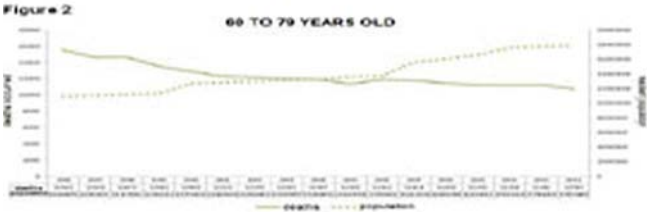
Figure 1


Figure 2


performed data analysis to determine the mortality rates for HF per 100 thousand inhabitants and by age groups of 60–79 years and ≥80 years, comparing with the variability of growth of the correspondent age groups in the general population, from 1996 to 2012, based on data collected in the Brazilian Geographic and Statistics Institute (IBGE).
Results: Analysis of death due to HF in the group over 80 years of age in 1996 presented a rate of 770.2/105 inhabitants and showed a significant drop in 2012, with 403.6/105 inhabitants, amounting to a decrease of 47.6% per 105 inhabitants. By contrast, in the same period, the population of this age group increased by 104.7% (fig.1). Analysis of death due to HF in the group over 60–79 years in 1996 presented a rate of 142.2/105 inhabitants and showed a significant drop in 2012, with 60.2/105 inhabitants, amounting to a decrease of 57.7% per 105 inhabitants. By contrast, in the same period, the population of this age group increased 63.7% (fig.2).
Conclusion: The study results demonstrate a downward trend in HF mortality rates among the elderly in Brazil in recent decades. The trend is more pronounced in the ≥80 year age range.

P5560 | BEDSIDE
Trend in mortality rates from acute coronary syndrome in octogenarian patients during the period 2000-2006 compared to 2008-2013

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Background: Few data are available regarding the outcome of octogenarians with acute coronary syndrome (ACS).
Methods: We evaluated 30-day and 1-year clinical outcome of 1477 patients ≥80 years old (mean age 85±4, females 43%), by analyzing data from ACS patients hospitalized in all coronary care units in Israel during two-month periods/year during the period 2000 to 2006 ("early period", n=1033) and compared to the period of 2008 to 2013 ("late period", n=444).
Results: In the late period ACS octogenarian patients were older (85±4 vs 84±4 years; $p<0.01$), had higher incidence of hypertension (85% vs 74%, $p<0.01$), diabetes (39% vs 30%, $p<0.01$), dyslipidemia (75% vs 41%, $p<0.01$) and family history of CAD (8% vs 4%, $p<0.01$), had more prior myocardial infarctions (MI) (41% vs 36%, $p<0.02$), percutaneous coronary interventions (PCI) (37% vs 16%, $p<0.01$) and prior chronic renal disease (30% vs 24%, $p<0.01$) compared to those in the early period. Time from chest pain onset to hospitalization and PCI were similar in both groups. Octogenarians from the early period had higher frequency of anterior wall MI (39% vs 25%, $p<0.01$), higher Killip class on hospital admission, while left ventricular ejection fraction was similar among patients from the 2 period groups. Significantly more patients in the late period underwent PCI compared to the early period (94% vs 55%, $p<0.01$), received more dual antiplatelet therapy (84% vs 42%, $p<0.01$), beta blockers (80% vs 67%, $p<0.01$), angiotensin-converting enzyme inhibitors (74% vs 69%, $p<0.02$) and statins (91% vs 53%, $p<0.01$). Mean hospital duration was significantly higher in patients from early compared to the late period (8±7 vs 7±6 days, $p<0.01$). In-hospital, 7-day-, 30-day- and 1-year mortality rate were significantly higher in octogenarians from the early compared to the late period (12% vs 8%, $p<0.02$; 11% vs 8%, $p<0.05$; 17% vs 13%, $p<0.02$; 32% vs 26%, $p<0.01$; respectively). Major adverse CV events (30-day mortality, hospitalization for unstable angina, MI) were also significantly more frequent in those from the early compared to the late group (31% vs 21%, $p<0.01$). Multivariate Cox regression analysis demonstrated better 1-year survival in octogenarians with ACS from the late compared to the early period with HR 1.17, 95% CI 0.87 to 1.57 (p=0.03).
Conclusion: In-hospital, 30-day and 1-year survival rates of ACS octogenarian patients during the period 2008 to 2013 significantly improved compared to those in the earlier period between year 2000 to 2006.

P5561 | BEDSIDE
Four-year (2009-2013) all cause and cardiovascular disease mortality in older adults and its determinants

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Aim: Ikaria Island, Greece, has joined "Blues Zones", a National Geographic project, which includes places with high life expectancy. This work aimed to examine risk factors in relation to 4-years all cause and cardiovascular disease events, in the Ikaria Study participants.
Methods: From June to October of 2009, 330 men and 343 women, aged 65 to 100 years, were enrolled; in June-July 2013, were re-evaluated. Multivariable analysis, using the proportional hazards Cox model with all cause and cardiovascular disease death as end points, and various socio-demographic, clinical and lifestyle characteristics, as predictors, were fitted.
Results: Age-standardized gender-specific CVD incidence was 520 cases per 10,000 men inhabitants and 320 cases per 10,000 women, (21% of death causes). Other causes of death were: cancer (21%), infection (10%), respiratory (3%) and other causes (26%). Age, male gender (Hazard Ratio 2.85, 95% CI 1.75, 7.55), heart rate (1.02, 95% CI 1.01, 1.05), urea levels per mg/dl (1.02, 95% CI 1.01, 1.04), left atrial maximum volume per ml (1.09, 95%C1.008, 1.031), left ventricular hypertrophy (1.947, 95% CI 1, 3.922), thyroid stimulating hormone (1.06, 95% CI 1.006, 1.11), and depression (1.076, 95% CI 0.99, 1.17) were positively associated with mortality. Coffee consumption (0.99, 95% CI 0.99, 1.00), tea (0.992, 95% CI 0.985, 0.998), fruit intake (0.995, 95% CI 0.991, 0.999), olive oil (0.97, 95% CI 0.951, 0.989) and left ventricular ejection fraction (0.932, 95% CI 0.895, 0.97) were inversely associated with CVD.
Conclusion: Common CVD factors were not associated with CVD incidence in older individuals; whereas other biological and nutritional factors were placed in this aetio-pathological puzzle.

P5562 | BEDSIDE
Identifying the last year of life in patients presenting with acute coronary syndrome: a multicentre prospective study (FATE-ACS study)

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Introduction: Acute Coronary Syndromes (ACS) are common in elderly and frail populations. An accurate and reliable tool to identify ACS patients approaching end-of-life remains to be determined.
Methods: This is a multicentre study of consecutive unselected patients admitted between May 2012 and July 2013 with a diagnosis of ACS. Patients were assessed during admission using the Gold Standards Framework prognostic indicator guide (GSF) and clinical risk scores including GRACE, ACEF and New York PCI risk score. Pre-specified primary outcome was all-cause mortality at one-year; secondary outcomes were cardiovascular death, non-cardiovascular mortality, re-hospitalization for ACS and re-hospitalization for non-ACS causes.
Results: Six hundred and twenty nine (629) ACS patients were enrolled and one-year follow-up data were available for 626 patients. Fifty-two (8.3%) met GSF criteria (GSF(+)) for end-of-life care. GSF(+) patients were more likely to be older, female and with lower BMI compared to GSF negative (–) patients. GSF(+) patients underwent angiography and coronary intervention less frequently (95% vs 75%, $p<0.001$ and 77% vs 59,6%, p=0.005). Compared with GSF(–) patients, GSF(+) patients had higher 12 month all-cause mortality (42.3% vs. 4.5%; $p<0.001$), cardiovascular mortality (15.4% vs. 2.8%; $p<0.001$) and non-cardiovascular mortality (26.9% vs. 1.7%; $p<0.001$), with AUCs for all-cause mortality above 0.80. Multivariate analysis confirmed the independent correlation of GSF with all-cause and non-cardiovascular death.
Conclusion: The GSF used in a hospital setting identifies those ACS patients who are at high risk of death within 12 months. The GSF or a similar tool should be used to screen ACS patients for end of life care.

P5563 | BEDSIDE
Factors, associated with in-hospital mortality of acute myocardial infarction: results from the single-center registry in Ukraine

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Purpose: To evaluate in-hospital mortality of acute myocardial infarction (MI) patients (pts) and examine its predictors in the single-center registry in Ukraine (herein – the Center).
Methods: Retrospective analysis of 548 pts prospectively enrolled in the Center's MI registry between 2010 and 2014 (mean age 72±10,9 ys; 306 males (67,0%); 345 STEMI pts (63,0%); 175 recurrent MI pts (31,9%)). Group 1 (G1) included 449 (81,9%) survived pts, group 2 (G2) – 99 (18,1%) pts who dead in hospital. Some registries were selected as comparators: Ukrainian (UR, n=262), RECORD (Russia, n=796), Polish Registries (PR) STEMI (n=31298) and NSTEMI (n=2663), ACS-I registries STEMI (n=4431) and NSTEMI (n=5367).
Results: In-hospital mortality rate for the Center's MI pts (18,1% [95% confidence interval (CI) 14,9–21,6]) was higher than that in the UR (6,2% [95% CI 3,5–10,0]) and ACS-I (4,9%: 518 of 10484 pts). The same was observed for the Center's STEMI pts (26,1% [95% CI 21,5–31,1]), comparing with the UR (7,4% [95% CI 4,0–12,4]) and PR (9,3%). In-hospital mortality rate for NSTEMI pts was comparable among studied registries. In-hospital mortality for the Center's MI pts was associated with more advanced age (72 (63–78) and 80 (74–85) ys in G1 and G2, respectively; $p<0,001$), higher STEMI (56,8% and 90,9%, respectively; $p<0,001$) and recurrent MI frequencies (26,5% and 56,6%, respectively; $p<0,001$), without gender differences. According to generalized boosted model, age was the most significant independent in-hospital mortality predictor. The Center's MI pts were older (72 [95% CI 71–73] ys) than those in the UR (64 [95% CI 62–65] ys), RECORD (65±12,4 ys), PR STEMI (64±12,4 ys), PR NSTEMI (68±11,8 ys), ACS-I STEMI (63±13 ys) and ACS-I NSTEMI (66±12 ys). The frequencies of the Center's MI pts with age ≥75 ys (44,3% [95% CI 40,1–48,5]) ≥85 ys (13,7% [95% CI 10,8–16,6]) were higher than those in PR STEMI (22,8% and 3,8%, respectively) and PR NSTEMI (33,3% and 5,4%, respectively).
Conclusions: The pts with MI, included in the Ukrainian single-center registry, were older than those in the national and some European MI registries. In-hospital mortality rate for the Center's STEMI pts was higher than those for STEMI pts in the studied registries. In-hospital mortality was associated with age, STEMI

and recurrent MI, with the age as the most significant independent predictor. The higher the Center's MI cases in-hospital mortality rate could be partially related to the higher prevalence of comorbidities in the elderly pts.

P5564 | BEDSIDE
Residual lesion in left anterior descending artery is associated with 3-year mortality in super-elderly patients with acute coronary syndrome

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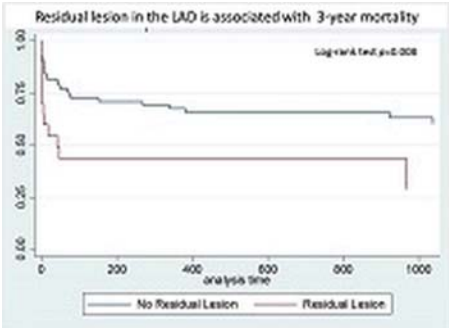
Background: Super-elderly patients, defined as those aged ≥85 years, often present with multiple lesions in clinical setting of acute coronary syndrome (ACS). Non-culprit lesions sometimes seem not to be treated with percutaneous coronary intervention (PCI) only because of their advanced age.
Purpose: The purpose of this study is to reveal whether PCI for non-culprit lesions is beneficial for super-elderly patients.
Methods: This study included consecutive 91 patients with ACS. We calculated SYNTAX score to evaluate the complexity. The associations of residual lesions and complexity with 3-year mortality were investigated using Cox regression.
Results: In 91 patients (mean age, 88.2±3.0, 52% male), culprit lesions were as below: left anterior descending artery (LAD): 50, Left circumflex artery (LCx): 29, right coronary artery (RCA): 31. The median of SYNTAX score was 14 (interquartile range, 8–22). Complete vascularization was not performed in 43 patients during hospitalization. Residual lesions were as below: LAD: 20, LCx: 22, RCA: 21. Residual lesion in the LAD was associated with higher 3-year mortality (p=0.04), but residual lesion in the LCx or RCA was not (p=0.27 and 0.77, respectively). The Cox regression model demonstrated that those with residual lesion in the LAD had increased risk of 3-year mortality in relation to those without the one (HR: 2.43, 95% CI 1.21–4.87, p=0.01). A 1-unit increase in SYNTAX score was associated with 1.07-fold increased risk for 3-year mortality (95% CI 1.03–1.10, p<0.001).



Three-year mortality

Conclusions: Even though the most of the super-elderly patients with ACS presented with less complicated lesions, no treatment with PCI for residual lesion in the LAD might be associated with higher 3-year mortality.

P5565 | BEDSIDE
Predicting clinical outcomes in elderly patients with acute myocardial infarction undergoing primary percutaneous coronary intervention

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Background: Consistent with the aging population in the Western world, there is a growing number of elderly patients with ST-elevation myocardial infarction (STEMI). Validated risk models to determine which of these patients are prone to have poor clinical outcomes are essential.
Purpose: The purpose of this study is to identify risk factors for both serious adverse events (SAE) and minor adverse events (AE) in elderly STEMI patients undergoing primary percutaneous coronary intervention (pPCI).
Methods: All STEMI patients (aged ≥70 years) treated with pPCI in 2013–2014 were assessed. The safety management system (SMS) score to identify frail elderly patients was used in the risk model in addition to established risk factors. The primary endpoint was a combination of 30-days mortality, re-infarction, revascularisation, major bleeding, cerebrovascular accidents and major peri-procedural events. The secondary endpoint combined minor adverse events with the primary endpoint. Logistic regression analysis was used to identify predictors.
Results: A total of 151 patients were included with a mean age of 78.2±5.9 years and 91 (60.3%) were male. Median SMS score was 0 [IQR 0–1]. Primary and secondary endpoint rates were 24.8% and 43.9% respectively. SMS score was an independent predictor of serious adverse events [OR 1.3, p=0.029]. A trend was observed that the SMS score was associated with increased occurrence of the secondary endpoint [OR 1.4, p=0.056].
Conclusion: The rate of SAE 30 days after admission in STEMI patients ≥70 year is 24.8%. The SMS score for frail elderly patients is an independent predictor of the combined endpoint of mortality and other major events.

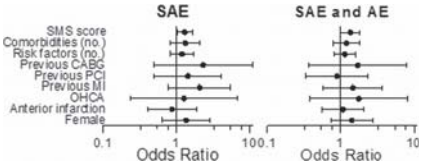

Figure 1. Predictors of 30-days SAE and combined endpoint of SAE and minor AE in elderly STEMI patients.

P5566 | BEDSIDE
Performance of Euroscore II compared to additive and logistic Euroscore in predicting hospital and midterm mortality, ICU and hospital lenght of stay in octagenarians undergoing cardiac operation

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Background: Euroscore II is a very useful tool in predicting mortality in cardiac surgery procedures. However, its use is suggested for patients below the age of eighty years old.
Purpose: Our intention is to assess the performance of Euroscore II in comparison to additive and logistic Euroscore in predicting hospital and midterm mortality, as well as ICU and hospital length of stay (LOS) in octogenarians undergoing cardiac operation.
Methods: We evaluated prospectively collected data for 508 octogenarians (mean age 83±2.6 years, n=231 females), who underwent isolated CABG (n=146), isolated non-CABG (n=97), 2 procedures (n=219) and 3 procedures (n=46) from March 2008 to April 2013. Midterm follow-up was 34.1±19.9 months. Logistic and Cox regression analyses were used to calculate odds ratios and hazards ratios, while C statistic (ROC curve), Hosmer-Lemeshow test and Extreme Quartile Odds Ratio (EQuOR) were used to assess the discriminatory ability and calibration of the algorithms.
Results: There were 33 (6.5%) hospital deaths and 159 (31.3%) midterm deaths. The mean ICU LOS was 4.3±10 days and the mean hospital LOS 15.7±25.1 days. Mean Euroscore II was 8.6±8.7, additive Euroscore 9.4±2.5 and logistic Euroscore 16.9±13.5. Euroscore II had the best discriminatory ability, as measured by C statistic in predicting hospital mortality (0.77 vs. 0.74 and 0.75), ICU LOS (0.70 vs. 0.67 and 0.67) and hospital LOS (0.69 vs. 0.64 and 0.64), while it showed good calibration in these outcomes (P=0.140, P=0.587 and P=0.140 respectively). Euroscore II was an independent predictor of midterm mortality (HR=1.042, 95% CIs:1.030–1.055, P<0.001) and had the best discriminatory ability as measured by EQuOR (2.67 vs. 2.60 and 2.50).
Conclusions: Euroscore II showed the best performance in predicting hospital and midterm outcomes in octogenarians undergoing cardiac operation as compared to the previous versions.

P5567 | BEDSIDE
Laboratory tests combined into a frailty index predict mortality and cardiovascular events in hypertensive older adults

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Background and introduction: Older adults suffering from hypertension are at increased risk of cardiovascular events/mortality and risk increases with increasing frailty. Few longitudinal data are available in such older adults despite high prevalence of hypertension and an ageing population. Methods to identify those at highest risk, the frailest, vary from scales to indices. One such is the Frailty Index (FI). The FI counts the "deficits"(symptoms/signs/disease eg diagnosis of diabetes or uric acid>900 or<100) dividing by the total number to give a value between 0–1, higher values mean greater frailty. The FI robustly predicts mortality but can be challenging to use in clinical practice. Recent research suggests that an FI based solely on routine laboratory (lab) data may allow the identification of older adults at risk of death and be more practical in clinical settings (1). The HYpertension in the Very Elderly Trial (HYVET) was a double blind placebo controlled trial of antihypertensives which showed benefit of treatment and collected data on cardiovascular events/mortality. The HYVET data present an opportunity to investigate the utility of a lab-FI in this population.
Purpose: To investigate the utility of a lab-FI in the HYVET population.
Methods: To enter the HYVET trial participants had to be≥80 years with a systolic pressure of ≥160mmHg. Blood pressure and lab values for creatinine, glucose, haemoglobin, potassium, sodium, urea, haematocrit, uric acid, total and HDL cholesterol were collected at baseline and combined into a lab-FI. Incident cardiovascular events and mortality were collected and validated by an independent blinded committee. Cox proportional hazard regression was used to examine the relationship between the baseline lab-FI and subsequent events.
Results: The HYVET trial randomised 3845 participants and had a mean follow

up of 2 years. There were 431 deaths, of which 220 were cardiovascular, and 329 cardiovascular events (fatal + non-fatal). The lab-FI ranged from 0.03 to 0.5 with a median value of 0.19 Baseline lab-FI was associated with increased risk of death (HR1.024 95% Confidence Interval (CI): 1.012:1.036), increased risk of cardiovascular death (HR1 0.021 95% CI 1.004:1.039) and increased risk of cardiovascular events (HR1 0.021 95% CI 1.007:1.035).

Conclusion: Initial analysis of a lab-FI calculated using the HYVET data suggests that it may be useful for assessing risk of mortality and cardiovascular events in an elderly hypertensive population.

Reference:

Howlett S, et al. Standard laboratory tests to identify older adults at increased risk of death.

Acknowledgement/Funding: This work did not receive funding. The HYVET trial was funded by grants from the British Heart Foundation and Servier International

P5568 | BEDSIDE

Incidence and prognosis of incident disability in older patients hospitalized for acute cardiac conditions

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Background and purpose: Cardiac disease is the main cause of hospitalization in elderly people. Hospitalization is frequently associated with physical deconditioning and new disability that often persists after discharge. We aimed to asses the incidence and impact of a new disability in elderly patients hospitalized by acute cardiac conditions.

Methods: We analyzed 197 patients over 75 years admitted to one cardiology department. Six basic activities necessary for independent daily living (ADL) were evaluated at admission and discharge. New disability was defined as the loss of independence to perform at least one ADL. Risk factors, comorbidity, other geriatric conditions, diagnosis on admission, and interventions during hospitalization were recorded. 12-month adjusted mortality, readmission and need for new social help risks were assessed by multivariate logistic regression analyses.

Results: New disability was observed in 32 patients (16.2%), which was related to male gender (75.6% vs 46.1%, p=0.003), prior geriatric conditions, such as frailty (62.5% vs 37.0%, p=0.007) or depression (12.9% vs 3.4%, p=0.026), and diagnosis on admission (p=0.004). After adjusting for age and comorbidity, incident disability during hospitalization was associated with an increased risk of mortality at 1 month (OR=4.01, 95% CI: 1.15–13.95, p=0.029). Of those with new disability, 18.8% died at 1 month and 34.4% died at 12 months. Of survivors, 57.7% had chronic disability after 12 months, needing new social help 46.7%.

Differences in 1-month and 12-month outcomes in elderly patients hospitalized for acute cardiac conditions according to the development of new disability at discharge

	New disability	No new disability	p value
1-month mortality	6 (18.8%)	7 (4.3%)	0.003
1-month readmission	4 (17.4%)	20 (14.5%)	0.718
Need for new help at 1 month	9 (50.0%)	42 (32.8%)	0.152
12-month mortality	11 (34.4%)	28 (17.1%)	0.025
12-month readmission	12 (54.5%)	68 (47.9%)	0.561
Need for new help at 12 months	7 (46.7%)	46 (37.1%)	0.471

Conclusion: New disability developed during hospitalization for acute cardiac conditions occurs frequently and increases the risk of mortality and permanent dependency.

P5569 | BEDSIDE

Outcome of acute coronary syndrome octogenarian patients in Israel

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Background: While patients ≥80 years old constitute the fastest growing segment of the population and have a high prevelance of coronary artery disease (CAD), few data are available regarding the outcome of octogenarians with acute coronary syndrome (ACS).

Methods: We evaluated in-hospital and 30-day clinical oucome of 1,896 patients [250 (13%) ≥ and 1,646 (87%) <80 years old] from the ACS Israel Survey (ACSIS), by analyzing data from ACS patients hospitalized in all coronary care units in Israel during a two-month period in 2013.

Results: ACS patients ≥80 years (mean age 85±4) had higher incidence of CAD risk factors, prior cardio-cerebrovascular events, chronic renal failure and cardiac medication use compared to patients <80 years (mean age 61±11). Time from chest pain onset to hospitalization and myocardial infarction (MI) location were similar in both groups. Killip class on admission was higher, while left ventricular ejection fraction was lower in ACS ≥ compared to <80 years. ST elevation MI (STEMI) on admission was more common in ACS patients < than ≥80 years (41% vs 31%).

The in-hospital and 30-day mortality rates were significantly lower in ACS patients ≥80 years who underwent any percutaneous coronary intervention (PCI) during hospitalization compared with those who did not (4.8% vs 13% and 7.2% vs 22.8%, p<0.01) and the use of IIb/IIIa antagonist did not increase major bleeding and/or mortality. Seventy-seven patients ≥80 years had STEMI: 48 (62%) underwent primary PCI (18 patients with and 30 without IIb/IIIa), while 29 (38%) patients did not. No significant major bleeding was observed between the groups (Table 1).

Table 1

	Age <80 (n=1646)	Age ≥80 (n=250)	P value
Any PCI during hospitalization	1185 (72%)	127 (51%)	<0.001
IIb/IIIa antagonist use during PCI	773 (47%)	72 (29%)	<0.001
In-hospital mortality	21 (1.3%)	16 (6.4%)	<0.001
In-hospital major bleeding	12 (0.7%)	25 (10%)	<0.001
30-day MACE	179 (12%)	66 (27%)	<0.001
30-day mortality	35 (2.8%)	17 (9.7%)	<0.001

Conclusion: Octogenarians ACS patients have significantly worse in-hospital and 30-day outcome compared to those <80 years.

AGEING: COGNITIVE, VASCULAR AND AUTONOMIC IMPAIRMENT

P5570 | BEDSIDE

Central aortic reservoir-wave analysis predicted 20-year all-cause and cardiovascular mortalities independently of wave reflection and arterial stiffness: a community-based study

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Central aortic pressure waveforms contain incremental prognostic value in addition to traditional cardiovascular risk factors. Recently, pressure wave propagation theory and its derived parameters, pulse wave velocity (PWV) and backward wave amplitudes (Pb) has been demonstrated to provide incremental value in addition to currently accepted biomarkers in various study population. Subsequently, parameters calculated based on the reservoir-wave concept, combining elements of wave transmission and Windkessel models of arterial pressure generation, has been shown to predict clinical outcomes in elderly patients with hypertension. However, the comparative utility of the above parameters in prediction of cardiovascular events is unknown. Carotid blood pressure waveforms were measured in a community-based survey of 1172 patients (47% women, mean age 52±13 years old, range 30–79 years), which were decomposed into their forward wave amplitudes (Pf), backward wave amplitudes (Pb), and a reflection index (RI, = [Pb/(Pf+Pb)]). Reservoir-wave analysis was performed and indices of arterial function, including the systolic and diastolic rate constants, were derived. During a median follow-up of 19.8 years, 315 (26.9%) deaths occurred, including 84 (7.2%) cardiovascular origins. In multivariate analysis accounting for age, sex, body mass index, systolic blood pressure, fasting glucose, HDL cholesterol, LDL cholesterol, smoking, PWV and Pb, reservoir-wave parameters: systolic rate constant (Wald X2 =14.60, p<0.0001), diastolic rate constant (Wald X2 =20.25, p<0.0001), and reservoir pressure integral (Wald X2 =17.26, p<0.0001), could independently predict cardiovascular mortality. Moreover, to predict cardiovascular and total mortality, the addition of diastolic rate constant to the above multivariate model resulted in significant net incremental improvement in the risk assessment (net reclassification index = 0.14; p=0.01 and 0.04, p=0.003, respectively). In conclusion, reservoir-wave approach could predict long term outcomes in general population independently of arterial propagation parameters.

P5571 | BEDSIDE

Predictors of aortic pulse wave velocity in the very elderly with severe aortic stenosis

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Background: Aortic stiffness increases with age and is associated with increased mortality in patients with severe aortic stenosis (AS). Aortic pulse wave velocity (AoPWV) is a robust method to detect increased aortic stiffness in the elderly, with previously determined normal reference values in Europeans. It is unknown if severe AS in the very elderly (>70 years) is associated with increased AoPWV. Predictors of AoPWV in this population were not studied.

Aim of study: Compare the AoPWV in the very elderly with severe AS with age; gender, and coronary artery disease (CAD) matched controls and to study the predictors of AoPWV in this population.
Methods: We measured the AoPWV invasively during cardiac catheterization in 40 patients with severe AS and 20 matched control subjects referred for cardiac catheterization. In every case, we used femoral artery arterial access through 6 French sheath and we placed a 4 French pigtail catheter in ascending aorta above the aortic valve. We recorded pulse pressure waves simultaneously from the pigtail catheter and side arm of the femoral artery sheath on a calibrated paper and measured pulse wave transit time in 10±2 consecutive waves using foot to foot method. Pulse travel length was the length of pigtail catheter Segment inside the Patient. AoPWV was determined by dividing travel length/transit time.
Results: AoPWV in AS group (13.3 (10.9, 15.9) m/s) was not significantly different from control group (14.2 (12.4, 17.5) m/s), p=0.198. Central systolic blood pressure (SBP) (adjusted ß= 0.45, p=0.001) and glomerular filtration rate (GFR) (adjusted ß= –0.29, p=0.023) were independent predictors of AoPWV in AS group. AoPWV was not related to aortic valve area. Central SBP ≥141 mmHg predicted abnormal AoPWV (≥14.6 m/s) with 100% sensitivity and 70% specificity, area under the curve = 0.87, p<0.001, and GFR ≤48 ml/min/1.73 m^2 predicted abnormal AoPWV with 69% sensitivity and 82% specificity, area under the curve is 0.77, p=0.006 in AS group.
Conclusion: AoPWV is not increased in the very elderly with severe AS compared to controls and is best predicted from the central SBP.

P5572 | SPOTLIGHT
Cardiovascular risk factors over the adult life course: associations with carotid intima-media thickness and carotid-femoral pulse wave velocity in older British men

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Background: It is increasingly recognized that cardiovascular disease (CVD) and cardiovascular ageing are processes which may begin well before later life. However, few prospective epidemiological studies have distinguished the influence of key cardiovascular risk factor exposures at different stages of the life course to relevant markers of cardiovascular disease and ageing in later life.
Purpose: We aimed to examine the associations between established cardiovascular risk factors at three points during adult life (median 45, 65 and 78 years) on carotid intima media thickness (cIMT) and carotid-femoral pulse wave velocity (CFPWV) at 78 years.
Methods: The British Regional Heart Study is a prospective study of cardiovascular disease originally based on 7735 men aged 40–59 years from 24 British towns. Men took part in cardiovascular risk assessments providing information on cigarette smoking, body mass index [BMI], SBP, DBP, total, HDL-cholesterol, non-HDL cholesterol, plasma glucose) at median ages 45, 65 and 78 years and had measurements of cIMT (ultrasound) and CFPWV (Vicorder) at 78 years. Life course modelling approaches were used to define models of accumulation, sensitive period and mobility for the development of risk.
Results: Among 3137 surviving men, 1696 men (54%) had cIMT measurements and 1577 had CFPWV measurements at 78 years. cIMT was positively associated with BMI levels at 45, 65 and 78 years (stronger at 45 and 65), with SBP at 45, 65 and 78 years (stronger at 45 and 65), with plasma glucose and HDL-cholesterol (inversely) at 78 years and with cigarette smoking at 45 years. Life course models suggested risk accumulation over all three age points for BMI and SBP but were inconclusive for the other risk factors. CFPWV was positively associated with SBP at 45, 65 and 78 years (strongest at 78 years), with DBP at 65 and 78 years (stronger at 78 years) and with non-HDL cholesterol at 78 years only. Life course models suggested a sensitive period at 78 years for both SBP and DBP but were inconclusive for the other risk factors. These results were not materially affected by adjustment for blood pressure and lipid lowering medications.
Conclusion: Established CVD risk factors (particularly blood pressure) are strong influences on these markers of cardiovascular disease and ageing. The influence of BP on cIMT appeared to be cumulative, while the influence of BP on CFPWV mainly reflected recent BP. Cardiovascular ageing is likely to be influenced both by longer-term risk accumulation and by recent risk factor exposures.

P5573 | SPOTLIGHT
Incidence of carotid plaque components: a 4-year follow-up study using serial magnetic resonance imaging

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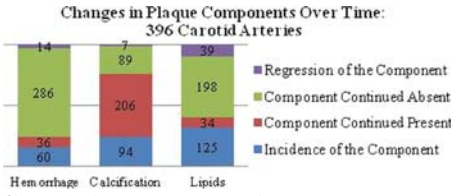
Background: Carotid atherosclerotic plaque components such as intraplaque hemorrhage (IPH), calcification and lipid-cores are important markers of plaque vulnerability. How these components change over time and which factors lead to the development of each component remain unknown.
Methods: 198 participants (mean age 67.5±10.6yrs) from a population-based study, all with carotid wall thickening on ultrasound, underwent two magnetic resonance imaging scans for carotid plaque characterization (mean interscan interval of 4.1±0.2yrs). Presence of IPH, calcification and lipid-core was assessed in both sides on baseline and follow-up scans. The association between cardiovascular risk factors and incidence of each carotid plaque component was assessed.
Results: In the 396 arteries, incidence of IPH, calcification and lipid-core was, respectively, 17.3%, 51.4% and 38.7%. The factor most strongly associated with incidence of IPH was use of antihypertensive drugs (multivariate adjusted OR 2.5 [1.2–5.2]). Incidence of calcification was associated with total cholesterol levels (multivariate adjusted OR per SD increase in cholesterol 1.5 [1.1–2.2]) and hypertension (multivariate adjusted OR 2.2 [1.1–5.1]). Higher cholesterol levels were also associated with incidence of lipid-cores (multivariate adjusted OR per SD increase in cholesterol 1.3 [1.1–1.7]).



Changes in plaque components over time

Conclusions: In community-dwelling subjects, hypertension and its treatment, and serum cholesterol levels were the main risk factors for the incidence of atherosclerotic plaque components over time.
Acknowledgement/Funding: This study was supported by The Netherlands Heart Foundation, (grant no. 2009B044) and the Netherlands Organization for Scientific Research

P5574 | SPOTLIGHT
Ankle-brachial Index: an ubiquitary available marker of cognitive impairment in low-income countries- the EPIDEMCA study

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Background: Some epidemiological studies in high income studies suggest an association between cardiovascular diseases (CVD) and the the development of cognitive, but data are in low- and middle-income countries, where live two-thirds of the individuals affected by dementia.
Purpose: Our aim was to investigate the association between the ankle brachial index (ABI), a marker of atherosclerosis, and cognitive function, using an extensive neuropsychological battery in African urban and rural population in two countries in Central Africa: Republic of Congo (ROC) and Central African Republic (CAR). We hypothesized that both low (<0.90) and very high (>1.40) ABI are associated with increased risk of cognitive impairment in these populations.
Methods: This cross-sectional study (Epidemiology of Dementia in Central Africa), was performed in two predefined districts representative of Brazzaville (ROC) and Bangui (CAR) (sampling proportional to the size of the main subdivisions) and by exhaustive door-to-door sampling in two rural areas (Gamboma in ROC) and Nola in CAR). All individuals ≥65 years living in these areas were invited to participate. Socio-demographic data, medical history, medication, clinical and biological data were collected. Cognitive impairment was defined according to the DSM-IV criteria.
Results: Among the 1662 participants (age 72.9±6.5 years, 59.3% females), the prevalence of cognitive impairment was 13.6%, higher in subjects with ABI≤0.9 and ABI≥1.4 than those with 0.9<ABI<1.4, p=0.0024). 1.03–2.25; CI: 95% 1.52; (OR: ABI (≤0.90) low and 1.06–2.23; 95% CI: 1.78; smoking p<0.0001), 1.59–3.49; 2.36; gender female 1.07–1.12; 1.09; age with associated significantly was impairment Cognitive intake. alcohol factors risk cardiovascular occupation, status, marital education, depression, anxiety, areas, rural or urban country, gender, age, for adjustments after analysis, multivariate a in observed also cognitive between association significant This 12%, vs. 17% (20.1%/>.
Conclusion: This is the first large epidemiological study showing the interest of the ABI, an accessible marker of CVD in these low-income countries, to identify also patients at risk of cognitive impairment.
Acknowledgement/Funding: French National Agency (ANR) for funding this study through the ANR-09-MNPS-009-01 grant; Universities of Bangui (CAR) and Marien Ngouabi in Brazzavil

P5575 | BEDSIDE

Cognitive aging and the incidence of cardiovascular events and diabetes: a meta-analysis of the HPS, SEARCH and HPS2-THRIVE studies

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Purpose: Cognitive aging has been linked to stroke and vascular risk factors, such as diabetes, but small study sizes have limited inference. The relationship of cognitive aging to the incidence of cardiovascular events and diabetes is investigated among >45 000 individuals at high vascular risk who participated in the HPS, SEARCH and HPS2-THRIVE studies.
Methods: Participants in the studies were followed-up for the incidence of events during a mean of 5 years (>11 000 major vascular or diabetic events). Cognitive function at the end of follow-up was assessed via a modified Telephone Interview for Cognitive Status (TICS-m) test. In each study the associations of standardized cognitive function Z-scores with incident events were assessed by a linear regression adjusting for years of follow-up and baseline predictors of cognitive function. Results were then combined in a meta-analysis. The relationship between Z-scores and age was used to convert Z-score differences to years of cognitive aging.
Results: The strongest baseline predictors of cognitive function were age, shorter height, prior stroke and diabetes. The incidence of stroke was associated with 7 years greater cognitive aging and incidence of transient ischemic attack (TIA), myocardial infarction (MI), new onset diabetes and diabetic complications requiring hospitalisation were each associated with 2–3 years greater cognitive aging. In contrast, undergoing CABG, PTCA or non-coronary revascularisation procedures was not associated with greater cognitive aging (Figure).

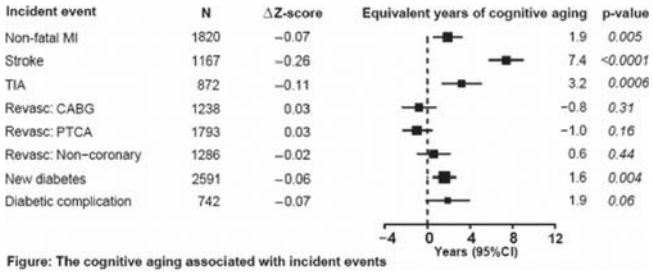

Figure: The cognitive aging associated with incident events

Conclusions: Clinical events were associated with 2–7 years of cognitive aging whereas undergoing a revascularisation procedure was not associated with cognitive aging, highlighting the value for cognition of vascular disease prevention.
Acknowledgement/Funding: Grants from Merck, the Medical Research Council and the British Heart Foundation for studies conducted and reported independently of funding sources

P5576 | BEDSIDE

A combined cognitive-exercise training improves endothelial function in patients with mild cognitive impairment: the train the brain study

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Introduction: Vascular factors are possibly involved in development of cognitive decline, related both to vascular and Alzheimer dementia.
Purpose: To evaluate the effects on cognitive and vascular function of a combined cognitive-exercise training in patients with mild cognitive impairment (MCI) or mild Alzheimer Disease (AD).
Methods: 121 patients with MCI or mild AD were recruited and randomized to a combined 7-month cognitive (6h/week) and exercise training (3h/week) or standard care. 94 patients (75±5 years, 48% men, 56% hypertensives), 36 in the non-training group and 58 in the training group, agreed to participate in the vascular function substudy. Endothelium-dependent (flow-mediated dilation, FMD) and independent (response to glyceryl trinitrite – GTN) vasodilation of the brachial artery (BA), and pulse wave velocity (PWV) were measured. Cognitive impairment was evaluated by means of the ADAS-cog scale.

Variable	Non training (n=36)		Training (n=58)		P interaction time × treatment arm
	T0	T7	T0	T7	
Systolic BP (mmHg)	140±18	134±16	141±16	135±15	0.97
Diastolic BP (mmHg)	73±10	68±9*	73±8	70±10*	0.59
BA diameter (mm)	4.16±0.87	4.35±0.75	4.36±0.83	4.32±0.73	0.04
FMD (%)	3.21±2.00	2.41±1.70	2.87±2.17	3.40±1.78#	0.007
Baseline shear rate (1/s)	295±114	250±116	316±195	304±246	0.44
Hyperemic shear rate (1/s)	889±408	764±297	1187±715	1014±661	0.77
Response to GTN (%)	6.96±3.03	6.96±4.14	6.67±3.94	6.91±3.71	0.82
PWV (m/s)	10.5±2.6	9.5±1.6	10.7±2.7	10.3±1.9	0.29

*p<0.05 vs T0; #p<0.05 vs non training.

Results: Blood pressure (BP) was significantly reduced after 7months both in the training and in the non-training group (see Table), whereas in the non-training group more patients increased the number of BP-lowering drugs (16% vs 2%, p=0.007). There was a significant interaction between time and treatment arm for BA diameter. FMD was increased only in the training group. No significant changes in PWV, shear rate and response to GTN were observed over time. ADAS-cog was significantly worsened only in the non-training group (p for interaction time*treatment arm 0.008).
Conclusions: A combined 7-month cognitive and exercise training is able to improve endothelial function as well as cognitive function in individuals with MCI or mild AD.
Acknowledgement/Funding: Fondazione Pisa

P5577 | BEDSIDE

Extent and characteristics of atherosclerotic plaques and their relation to cerebral grey matter atrophy in asymptomatic patients with non-obstructive carotid lesions

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Introduction - Presence of carotid plaques has been recently associated with cognitive decline, presumably on a vascular basis, in apparently asymptomatic patients without previous cerebrovascular events.
Purpose: IMPLAC (imaging della placca carotidea) is a prospective study designed to investigate the clinical value of carotid computed tomography (CT) and contrast enhanced ultrasound (CEUS) for the prediction of ischemic cerebral burden and cerebral atrophy measured by longitudinal magnetic resonance imaging (MRI). Here we present the baseline data of this study concerning the relationship between carotid plaque characteristics and brain volumes.
Methods: Between 4/2012 and 6/2014 we screened 218 patients. Of these 161 was excluded due to potential causes of cerebral damage such as overt neurological disorder and atrial fibrillation. Carotid CEUS, CT and brain MRI were performed in 60 asymptomatic patients with carotid stenosis <70% based on Doppler flow velocity. Common carotid artery [CCA], carotid bulb, external and internal carotid artery [ICA] were examined bilaterally. Brain volumes (total brain, grey matter [GM] and white matter [WM] volumes) were measured.
Results: Mean age of the study population was 69±8 years (56% males) and had an average Framingham risk score at 10 years of 9%. Based on ultrasound duplex examination, median carotid artery stenosis in the most affected district was 54% and on CT scan was 50% as estimated by ECST criteria, and 4 carotid segments were involved on average in each patient.
Measure of GM atrophy correlated with some carotid characteristics. Since, as expected, GM volumes inversely correlated with age, all correlations were age-adjusted. Degree of plaque stenosis was not associated with GM volumes whereas markers of extent of carotid atherosclerotic disease, such as mean intimal-media thickness and total plaque area, were associated with decreased GM volumes. GM atrophy also correlated with increased grey-scale scoring (r=–0.50, p<0.0001) and increased levels of Hounsfield unit (r=–0.32, p=0.02), suggesting a higher calcium content in the plaque. No association was found with total brain and WM volumes.
Conclusions: A larger total plaque area and higher calcification of the carotid plaques were specifically associated with the decrease of the brain GM volume in asymptomatic patients with non-obstructive lesions. This findings underline the need to consider the carotid atherosclerotic disease not only as a potential risk factor for ischemic stroke but also as a significant marker of GM atrophy and possibly vascular cognitive decline.
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P5578 | BEDSIDE

Cognitive impairment predicts future cardiac events in elderly patients with heart failure

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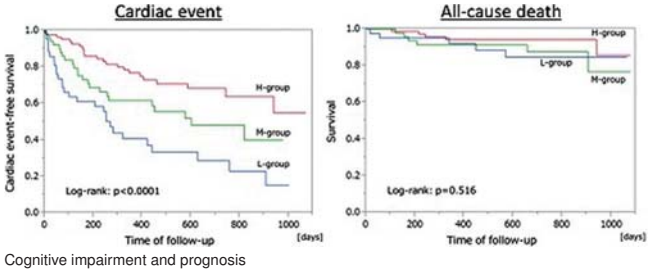
Background: Cognitive impairment is a common condition among elderly patients. Recently, data have been published on the relation of cognitive impairment to increased risk of mortality in elderly patients with heart failure (HF). However, little is known about the association between cognitive dysfunction and long-term cardiac prognosis.
Purpose: We hypothesized that the risk of mortality or future cardiac events is associated with cognitive impairment in HF patients.
Methods: We enrolled consecutive 180 patients (98 males) with hospitalized HF over the age of 65 in this study. The Mini-Mental State Examination (MMSE) was administered to assess global cognitive function. All patients were divided into 3 groups based on MMSE; the High-group (27–30 pts), the Middle-group (22–26 pts), and the Low-group (0–21 pts). All patients were followed up at the average period of 567 days.

Results: The mean age, left ventricular ejection fraction, and plasma brain natriuretic peptide level at discharge were 78.4 years old, 48.8%, and 312pg/mL. As for cardiac events, Kaplan-Meier survival analysis revealed that composite end-points (cardiac related death and hospitalization due to worsening HF) were significantly higher in the Low-group (Figure; left panel). In addition, composite cardiac events were higher in the sub-group without social and/or family support availability in Low-group. On the other hand, there was no difference between 3 groups in all-cause deaths (Figure; right panel).



Cognitive impairment and prognosis

Conclusions: Global cognitive function assessed by the MMSE predicts future cardiac events in elderly patients with HF. Individualized social and/or family supports are required especially for the HF patients with severe cognitive impairment.

P5579 | BEDSIDE

Skeletal muscle atrophy is associated with presymptomatic hippocampal atrophy in elderly patients with heart failure

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Background: Cognitive impairment is increasingly prevalent in elderly patients with heart failure (HF), and is associated with frequent rehospitalization and increased mortality because of reduced adherence to optimal medications and self-care regimens. On the other hand, age-related atrophy of skeletal muscle, known as a sarcopenia, is also common in elderly HF patients and is closely related to poor prognosis in these disease states. Alternatively, exercise training has been shown to increase cognitive function as well as improve exercise capacity in elderly adults. These findings suggest that cognitive impairment and skeletal muscle atrophy seen in HF could be closely associated with each other. However, structural alterations between skeletal muscle and hippocampus in elderly HF patients has never been well characterized. The purpose of this study is to investigate the association between cross-sectional area (CSA) of thigh muscle and that of hippocampus by using magnetic resonance (MR) imaging. Furthermore, we also performed quantitative evaluation of presymptomatic atrophic change in hippocampus by using voxel-based specific regional analysis system (VSRAD) in these patients.

Methods and results: Ten stable elderly HF patients without dementia (5 females, 76±11 years old, NYHA functional class I-III) were studied. CSA of thigh muscle was 86±23 cm^2, and that of hippocampus was 1.7±0.4 cm^2. Z score of VSRAD was 1.1±0.7, indicating the mild degree of hippocampal atrophy compared to normal limit (<1.0). Six minutes walking test (6MWT) distance was 306±103 m. By univariate analysis, there was a significant positive correlation between thigh muscle area and hippocampus area (r=0.748, p=0.013). Muscle CSA and 6MWT distance were also negatively correlated with Z score (r=–0.644 and –0.638, respectively, p<0.05). By multivariate analysis, CSA of thigh muscle was identified as an independent determinant of hippocampal atrophy after adjusted for age and gender (β-coefficient 0.017, 95% CI 0.003–0.032, p=0.027).

Conclusions: Skeletal muscle atrophy and exercise intolerance are associated with the presymptomatic hippocampal atrophy in elderly HF patients. These results suggest that early intervention of cardiac rehabilitation program is required to preserve cognitive function as well as exercise capacity in elderly HF patients.

P5580 | SPOTLIGHT

Impaired orthostatic blood pressure stabilization is highly prevalent and a novel risk factor for unexplained falls in older adults: Findings from a prospective national cohort study

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Background and introduction: Impaired orthostatic blood pressure stabilization is highly prevalent in older adults, but it is unknown if it is an independent risk factor for incident all-cause or unexplained falls in older adults.

Purpose: To determine if impaired orthostatic blood pressure stabilization is an independent risk factor for incident all-cause and/or unexplained falls in older adults.

Methods: Data were analysed from the first two waves of a prospective, randomly sampled, national cohort study of older community dwelling adults. Continuous beat-to-beat blood pressure recordings measured during active standing were analysed. Impaired blood pressure stabilization (OH(40)) was defined as a systolic blood pressure drop of ≥20mmHg and/or diastolic blood pressure drops ≥10mmHg below resting values at 40 seconds after standing. Relationships with the number of all-cause and unexplained falls were assessed using negative binomial regression and modified Poisson regression respectively after covariate adjustment.

Results: 4128 participants were included in analyses (mean age 61.5 years, 54.2% female, mean (SD) time between waves 743 (83.9) days). At baseline, OH(40) was present in 15% of the population and symptomatic in 42%. When accompanied by hypertension and dizziness, those with OH(40) were at increased risk of an unexplained fall (Relative risk: 3.04, 95% CI: 1.5–6.0; P<0.001), but not of more all-cause falls (Incidence rate ratio: 1.25, 95% CI: 0.78–2.01; P<0.356).

Conclusion: Impaired orthostatic BP stabilization 40 seconds after standing is common and is a novel risk factor for future unexplained in older adults, especially in the presence of hypertension and symptoms. Impaired BP stabilization is an easily measurable, early physical sign of cardiovascular ageing in older adults and should be considered in the future assessment of falls risk in older adults.

P5581 | BEDSIDE

Age and outcome of head-up tilt table testing in syncope patients

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Background: The head-up tilt test (HUTT) is a useful diagnostic tool for syncope. We described the outcome of HUTT in syncope patients and identified the relationship between age and different hemodynamic outcomes.

Methods: In this cross sectional study, we prospectively enrolled consecutive patients who presented with syncope and underwent HUTT with clinical suspicion of neurocardiogenic syncope after excluding orthostatic hypotension cases. HUTT consisted of consecutive passive and active phases. In the passive phase, patients were tilted at 70° for 20 minutes; and if negative, the test was repeated with 400 micrograms sublingual TNG for another 20 minutes. Positive responses were classified according to the Vasovagal Syncope International Study (VASIS) classification and compared for age and gender.

Results: A total of 498 patients were enrolled [age= 44.93±18.77 years; male=271 (54.4%)]. Overall, 291 (58. 4%) patients had a positive HUTT while 256 (88.5%) patients had a positive result during the active phase. The test results were as follows: 107 (36.7%) mixed type (VASIS I), 103 (35.3%) cardioinhibitory (VASIS IIA=44 [15.1%]; VASIS IIB=59 [20.2%]), and 80 (27.4%) vasodepressive (VASIS III). There was no relationship between gender and the type of syncope. The trend of HUTT result significantly changed by age and the rate of cardioinhibitory syncope decreased after middle-ages (p-value for trend=0.02).

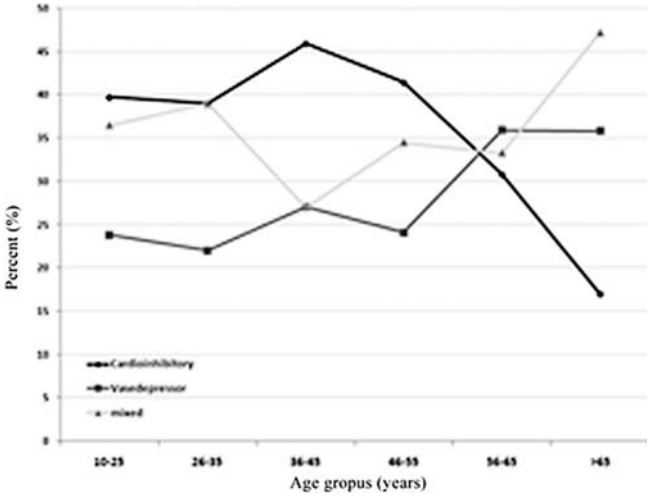

Figure 1. Age & HUTT

Conclusion: Hemodynamic response to tilt test depended on age. Cardioinhibitory response became less frequent with aging due to exaggerated vagal activity in the younger patients as compared with the older subjects.

ASSESSING CARDIOVASCULAR RISK AND INCIDENCE ACROSS THE LIFESPAN

P5582 | BENCH
Avoidable deaths from cardiovascular diseases: 40-year follow-up of 19,000 London Civil Servants

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Purpose: Death rates from cardiovascular diseases (CVD) have declined substantially in the UK over the last half-century. We examined trends in proportional mortality from CVD and the major causes of CVD (ischaemic heart disease [IHD], stroke and other vascular causes) in a 40 year follow-up of a prospective study of 19,019 male London Civil Servants.
Methods: The participants in the Whitehall study were men aged 40–69 years who worked in central London when first examined between 1967 and 1970. All participants were flagged with the Office for National Statistics who provided the date and cause of death. Deaths were classified by cause into CVD and non-CVD and CVD deaths were further classified into IHD, stroke and other vascular causes. Deaths were also classified by decade of follow-up (1970's, 1980's, 1990's, 2000's) and logistic regression was used to adjust for age at death.
Results: Among the 15,006 deaths with a known cause of death, 7020 died from CVD (47% of all deaths) of which, 4285 were from IHD (29%), 1400 from stroke (9%) and 1335 from other vascular causes (9%). The mean age at death was 75 years for IHD, 80 years for stroke and 78 years for other vascular causes. Hence, IHD accounted for a higher proportion of premature deaths before 70 years compared with deaths from stroke or other vascular causes (39% IHD, 5% stroke and 7% other vascular causes). The proportion of all deaths due to CVD declined progressively by increasing decades of follow-up (54%, 51%, 45% and 41%). Most of the decline in CVD deaths was due to a decline in IHD deaths (42%, 34%, 27% and 20%), respectively. In contrast, the proportion of all deaths due to stroke increased (6%, 9%, 10% and 12%), as did the proportion due to other vascular causes (7%, 9%, 9% and 10%). After adjusting for age at death, the odds of IHD declined by 19% per calendar decade, whereas there were no significant trends over calendar time in stroke (–1%, p=0.75) or other vascular causes (2%, p=0.65).
Conclusions: Consistent with UK national mortality statistics, CVD death rates declined progressively over the last four decades. However, CVD remained the single most important cause of death. Most of the decline in CVD deaths reflected reductions in IHD deaths, which still account for a substantial burden of premature deaths.
Acknowledgement/Funding: British Heart Foundation

P5583 | BEDSIDE
Correlation of ankle brachial index measurement: all the techniques are valid?

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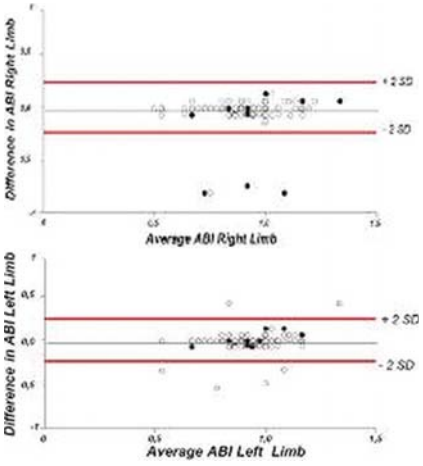
Objective: The ankle-brachial index (ABI) is a tool for the diagnosis and management of peripheral arterial disease, and a marker of atherosclerosis. The objective of this study is to determine the correlation of ABI measured by a pocket Doppler device compared to ABI determination at the echo Doppler vascular laboratory.
Methods: We evaluated the ABI in patients referred to the echo Doppler vascular laboratory for an arterial and/or venous lower limb study between March 2014 to December 2014. Resting ABI was determined with a pocket Doppler (continuous Doppler) and then by Doppler at the echo vascular laboratory (pulsed Doppler).



Bland-Altman plot

All measurements were made by two examiners. Reproducibility was assessed by the use of the reproducibility coefficient and correlation coefficients between measurements.
Results: 410 patients, 69% were men, mean age 58 years were included. The mean resting ABI with pocket Doppler was 1.01 and the ABI registered with pulsed Doppler at the vascular laboratory was 1.04. The reproducibility coefficient showed no significant difference between measurements ($p>0.1$) and the correlation coefficient showed high agreement between inter-observer reproducibility (0.79–0.97).The Bland-Altman method was used to demonstrate the correlation between the two measurements. The mean difference between the two measurement methods was 0.003 in the right side (p=0.1) and in left of 0.002 (p=0.6) (see Figure 1).
Conclusions: Our study demonstrates that ABI measurements with pocket Doppler and pulsed Doppler at the vascular laboratory are consistent and can be replaced with each other. When used properly, the ABI remains an invaluable tool for assessment not only of peripheral arterial disease, but also a great prognostic marker for cardiovascular disease.

P5584 | BEDSIDE
Phytate (IP6) and age-related cardiovascular calcification

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Purpose: Cardiovascular calcification is not just a degenerative process linked to the ageing by itself; there is growing evidence of the molecular aspects of both processes. Myo-inositol hexaphosphate (phytate, IP6), a natural component of the Mediterranean diet has been shown to prevent cardiovascular calcification in experimental animals. We aim to identify whether a difference IP6 levels may be involved in cardiovascular calcification in elder humans.
Methods: An elderly patient population of 178 consecutive patients (mean 68 years, 81 female) referred for echocardiography was studied. These were grouped according to IP6 urinary levels in low (LIP6) <0.61 μM, moderate (MIP6) 0.61–1.21 0 μM and high (HIP6) >1.21 μM. Valve calcification was estimated by echocardiography (Rosenheck score) post acquisition and data on concomitant diseases, pharmacological treatment and diet were collected.
Results: Mitral annulus calcification was present in 24% HIP6 group, 36% MIP6 and 40% LIP6 group (p=0.015). Patients without mitral calcification had significantly higher phytates levels (1.30±1.24 μM urinary IP6, n=117) than patients with mitral anuluscalcification (0.89±0.68 μM IP6, n=61). A trend to present moderate to severe aortic calcification with less urinary phytates (35% LIP6, 34% MIP6 and 28% HIP6 respectively) was observed. Furthermore patients with lower IP6 showed a higher prevalence of diabetes, hypercholesterolemia, chronic kidney disease and peripheral vascular disease ($p<0.05$).
Conclusions: An inverse correlation between the level of IP6 urinary levels and calcium estimation by echocardiography was found and the presence of traditional cardiovascular risk factor also kept this relation. Further studies are needed to determine the role of phytates enhancing cardiovascular aging and its potential in the treatment and preventing disease.

P5585 | BEDSIDE
Temporal trends in the prevalence of ischaemic heart disease in Catalonia

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Background: An increase in the incidence and attack rates of definite and possible acute myocardial infarction (AMI) was observed in a well delimited geographical area of 1,000,000 plus inhabitants through a population AMI disease registry during a ten year period. The objective of the present study was to analyze the trends in the prevalence of ischaemic heart disease during the same period from population surveys.
Methods: Data from the initial and third MONICA population surveys, separated by a period of ten years carried out in independent random samples of the general population (n=2571 and n=3484 men and women aged 25 to 64 years (response rates 74% and 72%) respectively) were used. Survey methods followed the WHO-MONICA protocol. Effort angina and possible acute myocardial infarction were assessed by the Rose questionnaire and a resting 12-lead electrocardiogram which was coded manually with the Minnesota code by two independent observers. Data was analyzed with SPSS-13.
Results: Prevalence of effort angina as assessed by the Rose questionnaire remained stable: 2.6% and 2.2% in men and 3.1% and 2.1% in women (p NS). However, prevalence of definite Q waves (Minnesota codes 1.1 and 1.2) or ischemic changes (ST-T alterations in the electrocardiogram (Minnesota codes 4.1–3 or 5.1–3) increased from 5% (95% CI 4–7) to 7% (6–8) in men and from 7% (6–9) to 13% (11–15) in women. Prevalence of ischemic signs alone (ST-T) were more prevalent in women 12% (10–14) versus 6% (4–7) in men. Prevalence of ischaemic changes (ST-T) significantly doubled in women aged 45–54, 6.8% (4.2–9.5) to 13.6% (10.3–16.8) while remained non-significant in younger women and were nearly significant in men 4% (3–5) to 6% (4–7).
Conclusions: Prevalence of ischemic signs in the electrocardiogram were more prevalent in women. Chronic objective forms of ischemic heart disease increased

in women and tended to increase also in men. These findings corroborate the existence of an increasing epidemic of coronary heart disease during the studied period, as it was previously shown with the increase in the incidence of AMI.
Acknowledgement/Funding: Funded by the Department of Health of Catalonia

P5586 | BEDSIDE
Is the extent of coronary arterial plaque associated with non-coronary vascular outcomes in asymptomatic type 2 diabetics? A prospective CT angiography based 7 year outcomes study

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Background: Extent of coronary arterial plaque predicts coronary heart related events in asymptomatic type 2 diabetics (DM) but its relation to non-coronary vascular events (NCVE) is unclear. We examined this relationship in a prospective 7 year outcomes study.
Methods: A population based cohort of DM (N=630) underwent baseline risk assessment by United Kingdom Prospective Diabetes Study coronary heart disease risk score (UKPDS). Maximal treadmill exercise tolerance (METS) (N=526), coronary artery calcium (CAC) scoring (Agatston method) and total coronary plaque length (CPL) on coronary CT angiography (CTA) were assessed. NCVE (stroke/transient ischemic attack, carotid or peripheral vascular intervention/amputation, diabetic ulcer, retinopathy or renal failure) were measured over 6.5±1.0 yr.
Results: Coronary plaque was found in 500 (79.4%) of pt and NCVE occurred in 96 (15.2%). CAC and CPL were univariate but not independent predictors of outcome. UKPDS score, maximal exercise tolerance and baseline retinopathy were independent outcome predictors and their combination improved discrimination of NCVE on ROC analysis (C-statistic) (Table). Addition of METS to combined baseline risk from prior retinopathy and UKPDS resulted in continuous event net reclassification improvement (NRI) of 34.2%, non-event NRI 17.7%.

Outcome predictors

Baseline variable	Univariate		Multivariate		C-statistic
	Hazard ratio	p-value	Hazard ratio	p-value	
UKPDS*	1.3 (1.2–1.4)	<0.001	1.3 (1.2–1.5)	<0.001	0.628
Retinopathy	4.0 (2.7–6.1)	<0.001	3.6 (2.1–5.9)	<0.001	(0.640)
Insulin treated	2.2 (1.4–3.3)	<0.001	1.2 (0.70–1.9)	0.56	
Exercise tolerance (METS)	0.86 (0.79–0.94)	0.001	0.89 (0.81–0.97)	0.009	0.639
Log (CAC+1)#	1.4 (1.1–1.6)	0.001	1.2 (0.82–1.6)	0.41	
Total plaque length#	1.2 (1.1–1.5)	0.012	0.99 (0.68–1.4)	0.94	
UKPDS + retinopathy + METS					0.762$

*Per 10% 10 yr risk: #per quartile: $p=0.018 vs UKPDS + retinopathy combined.

Conclusion: In DM with no history of CAD independent predictors of NCVE were: 1. UKPDS risk score, baseline retinopathy and maximal effort tolerance. 2. Coronary calcium and plaque extent were univariate but not independent predictors of NCVE. 3. Maximal exercise tolerance improved discrimination and reclassification when added to other baseline risk predictors.
Acknowledgement/Funding: European Foundation for the Study of Diabetes

P5587 | BEDSIDE
The prevalence of cardiovascular events and short-term mortality increase in the elderly with stable coronary artery disease and hospitalization for acute lower respiratory tract infection

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Background: Earlier studies for the relationship between respiratory infection and the risk of CVD did not address cardiac comorbidities in the patients suffered from infection at the baseline.
Purpose: We try to investigate the prevalence of CVEs and mortality in the elderly with sCAD after hospitalization 90 days for acute lower respiratory tract infection (ALRTI).
Methods: This is a prospective, controlled cohort study. Participates were collected from the elderly patients with sCAD and hospitalized for ALRTI and sCAD without ALRTI as the controls. The CVEs and all-cause mortality after admission were followed up and recorded during 90 days.
Results: The researchers compared 257 cases (infection group) with 169 age-matched controls (No infection group), mean age 88±5 years. In the subsequent 90 days, of 257 subjects in infection group, 82 CVEs (31.9%) and 34 all-cause death (13.2%) were occurred; of 169 controls in no infection group, 23 CVEs (13.6%) and all cause mortality (1.8%) were recorded. Within 90 days, sCAD patients with ALRTI had a 2.3 fold increased risk for CVEs (31.9% vs 13.6%, $p<0.001$), and 7.6 fold increased risk for all cause mortality (13.2% vs 1.7%, $p<0.001$) compared with controls. The risk of CVEs was highest during the first 2 weeks in infection group, but not in no infection group. The association between ALRTI and subsequent risk for CVEs and all cause mortality was adjusted for multiple potential confounders, ALRTI (OR 2.162, 95% CI 1.023–4.569) is an independent risk factor for the increment of CVEs and all-cause mortality.
Discussion: We found that elderly patients hospitalized for ALRTI had a higher risk of CVEs and all cause mortality within the 90 days. Our results also suggested that the infection could have consequences on CV outcome and death for several months after ALRTI, and hinted that patients who got over the acute event still had an increased risk for CVE events and all cause mortality during 90 days after infection, persistent inflammation might explain risk increase.
Conclusion: Hospitalization for ALRTI was associated with an increased risk for CVEs and all cause mortality in elderly patients with sCAD during 90 days. ALRTI should be considered an independent risk factor for adverse outcome after respiratory infection. So, monitoring and stratifying for future risk of CVEs and all cause mortality in elderly patients with sCAD after ALRTI were of important clinic meaning. Adding pneumonia and flu vaccination to elderly patients with sCAD, may help to prevent CVEs and decrease death rate as well as acute infection.

P5588 | BEDSIDE
Association between dynamic penile peak systolic velocity and major adverse cardiovascular events in men with arterial hypertension

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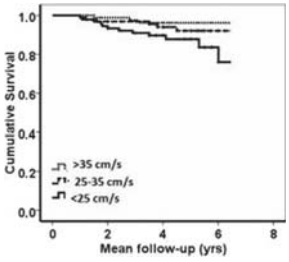
Purpose: Hypertension is associated with an approximately two-fold increase in the likelihood of having an abnormal penile blood flow. Reduced penile peak systolic velocity (PSV) correlates with adverse cardiovascular outcomes. Aim of this study is to investigate whether low PSV predicts major adverse cardiovascular events (MACE) in hypertensive males.
Methods: Penile PSV was measured in 298 hypertensive males (55±9 y/o) without known cardiovascular disease by Doppler ultrasound after intracorporal injection of prostaglandin E1.
Results: During the mean follow-up period of 4.9 years, a total of 22 MACE occurred. Compared to patients who did not experience MACE, subjects who developed MACE had lower PSV (28±10 vs 32±8 cm/s, $p<0.01$). The whole population was divided into tertiles according to PSV (low tertile <25 cm/s; middle tertile 25–35 cm/s; high tertile >35 cm/s). PSV was associated with MACE and the differences between the tertiles were significant (log-rank test: 6.54; $p<0.01$, figure). A Cox model showed that subjects with arterial insufficiency (low tertile) had an approximately 3-fold higher MACE risk compared to those with arterial sufficiency (high tertile) and mild arterial insufficiency (middle tertile) after adjustment for age, systolic pressure, metabolic parameters, smoking, C- reactive protein and testosterone (HR 2.9, 95% CI 1.35 to 7.12, p=0.02). A PSV value of 38.6 cm/sec was associated with a negative predictive value (ability to rule out MACE) of 97.5%.



Penile PSV and MACE in hypertensive men

Conclusions: Our study is the first to investigate the prognostic role of penile blood flow in hypertensive patients. The principal finding is that low PSV predicts MACE in long-term follow-up independent of hypertension severity and decreased testosterone that is often present in such patients.

P5589 | BEDSIDE
Decreasing incidence of cardio-vascular events or deaths in CAD patient cohorts 2004-2011. Results from the disease management program (DMP) for coronary artery disease (CAD)

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Background and purpose: In 2004 the DMP CAD was initiated primarily to improve secondary prevention among patients with CAD. Principally the DMP CAD should help to increase the medication rates but it was also intended to reduce morbidity and mortality. The purpose of this study was to analyse differences in the incidence of myocardial infarction, acute coronary syndrome, apoplexy or death in cohorts of CAD patients inscribed 2004–2011.
Methods: Data from all patients inscribed 2004–2011 were analysed retrospectively (n=302390, 63.3% male, 68.5±10.7 yrs.). Composite endpoint was documented until 2013 in 50442 (16.7%) patients. Total incidence and incidence of the composite endpoint within the first two years after inscription in the DMP were calculated for the patient cohorts of 2004/05, 2006/07, 2008/09, and 2010/11. Risks were calculated using separate logistic regression models (odds ratios, 95% confidence intervals) for 1, total incidence, and 2, incidence within first two years.
Results: Between 2004/05 and 2010/11 incidence of composite endpoint within the first two years in the DMP decreased from 911 to 505 cases per 10000 pa-

Table 1

Risk factor	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Sex (male vs. female)	0.78	0.76–0.79	0.79	0.77–0.81
Age (≥76 vs. ≤65 yrs)	1.30	1.26–1.34	1.33	1.29–1.38
Heart failure	0.94	0.92–0.97	0.98	0.95–1.01
Diabetes	1.14	1.12–1.16	1.10	1.07–1.13
COPD	1.29	1.26–1.33	1.15	1.11–1.19
Cohort 2006/07 vs. 2004/05	1.04	1.01–1.07	1.43	1.38–1.48
Cohort 2008/09 vs. 2004/05	0.44	0.43–0.45	0.63	0.60–0.65
Cohort 2010/11 vs. 2004/05	0.22	0.21–0.23	0.45	0.43–0.47

Number of patients in model 1: 170,024, model 2: 145,363.

tients (2006/07: 1138, 2008/09: 653). Risks of incident composite endpoint are given in table 1.

Conclusions: Apart from the patients inscribed 2006/07 incidence of MI, ACS, apoplexy or death shows a continuous decrease. Although a selection bias of the patients inscribed in the DMP cannot completely be excluded, this effect mirrors a tendency of decreasing death rates of patients suffering from CAD or heart failure which has been demonstrated for the last 10 to 15 years in Germany and worldwide.

P5590 | BEDSIDE
Association of polymorphisms of FURIN and ZPR1 with metabolic syndrome in Japanese individuals

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Purpose: Although genome-wide association studies (GWAS) have identified various genes and loci in predisposition to metabolic syndrome or each component of this condition, the genetic basis of metabolic syndrome in Japanese individuals remains to be identified definitively. Various genes and loci that confer susceptibility to coronary artery disease (CAD) or myocardial infarction (MI) have also been identified for Caucasian populations by meta-analyses of GWASs. Given that metabolic syndrome is an important risk factor for CAD, we hypothesized that certain polymorphisms may contribute to the genetic susceptibility to CAD through affecting the susceptibility to metabolic syndrome. The purpose of the present study was to examine the possible association of metabolic syndrome in Japanese individuals with 29 polymorphisms previously identified as susceptibility loci for CAD or MI by the meta-analyses of GWASs in Caucasian populations.

Methods: The study population comprised 1822 subjects with metabolic syndrome and 1096 controls. Subjects with metabolic syndrome had three or more of the five components of the diagnostic criteria for metabolic syndrome, whereas control individuals had none or one of the five components. The genotypes for 29 polymorphisms were determined by the multiplex bead-based Luminex assay.

Results: Comparisons of allele frequencies by the chi-square test revealed that rs17514846 (A→C) of the furin (paired basic amino acid cleaving enzyme) gene (FURIN, P=0.0006), rs599839 (G→A) of the proline/serine-rich coiled-coil 1 gene (PSRC1, P=0.0486), and rs964184 (C→G) of the ZPR1 zinc finger gene (ZPR1, P=0.0078) were significantly ($P<0.05$) associated with the prevalence of metabolic syndrome. Multivariable logistic regression analysis with adjustment for age, sex, and smoking status revealed that rs17514846 of FURIN (P=0.0016; odds ratio 0.76; dominant model) and rs964184 of ZPR1 (P=0.0164; odds ratio 1.21; dominant model) were significantly associated with metabolic syndrome. The minor A allele of rs17514846 of FURIN was significantly related to a decrease in the serum concentration of triglycerides (P=0.0293) and an increase in the serum concentration of high density lipoprotein (HDL)-cholesterol (P=0.0460). The minor G allele of rs964184 of ZPR1 was significantly related to increases in the serum concentration of triglycerides ($P<0.0001$) and fasting plasma glucose (P=0.0028) and a decrease in the serum concentration of HDL-cholesterol (P=0.0105).

Conclusion: FURIN and ZPR1 may be susceptibility loci for metabolic syndrome in Japanese individuals.

P5591 | BEDSIDE
Design and recruitment of the ROBINSCA trial: screening for cardiovascular disease

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Background: ROBINSCA (Risk Or Benefit IN Screening for CArdiovascular disease) is the only large-scale population-based RCT designed to investigate whether screening for a high risk of cardiovascular disease by means of 1. the Systematic COronary Risk Evaluation (SCORE) model or 2. coronary artery calcium (CAC), is effective for reducing morbidity and mortality due to coronary heart disease (CHD) with at least 15%.

Purpose: To give an overview of 1) the first recruitment results of 1 out of 3 regions in the Netherlands in which ROBINSCA is conducted and 2) the study protocol.

Methods: Based on the population registry 135,872 men (aged 45–74 years) and women (aged 55–74 years) were invited to fill in a risk questionnaire and measure their waist circumference in the first region. Persons with an expected high risk of cardiovascular disease based on the questionnaire were considered eligible. Exclusion criteria were: 1) previously diagnosed CVD, 2) previous cardiovascular surgery, 3) calcium score measured last year, 4) use of cholesterol-lowering and anti-hypertensive medication, 5) incomplete informed consent form. Inclusion criteria were: 1) BMI≥30, 2) waist circumference ≥88 cm (women) or ≥102 cm (men), 3) current smoker, 4) family history of CVD.

The aim is to randomise 39,000 eligible respondents in all 3 regions to be able to detect a 15% reduction in CHD with a power of 80%. Based on the study protocol, eligibles will be randomised (1:1:1) to the control arm, screen arm A (screening by SCORE), or screen arm B (screening by CAC scoring). Participants in the intervention group with a high risk for CHD will be referred to their general practitioner for treatment by cardiovascular risk management.

Results: Circa 33,000 persons responded (25%) in the first region. Of the first 10,004 respondents 3,027 were excluded based on exclusion criteria. Thereafter, another 1,669 respondents were excluded because of not meeting inclusion criteria. Finally, 5,308 respondents (53,1%) were eligible for randomisation.

Conclusions: The first part of the recruitment phase of the ROBINSCA study is promising. Forthcoming years, screening results should show if population-based screening for a high risk of cardiovascular disease can be (cost-)effective and which screening method is the most appropriate.

Acknowledgement/Funding: European Research Council grant

P5592 | BEDSIDE
Prevalence of abnormal glucose regulation 7 years after a ST-elevation myocardial infarction in patients without known diabetes at baseline: results of repeated oral glucose tolerance testing

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Background: Screening for undetected type-2 diabetes (DM) in patients with myocardial infarction, including an oral glucose tolerance test (OGTT), has been recommended in current guidelines.

Purpose: The aims of the present study were: 1) to study the long-term progression of glucometabolic abnormalities in ST-elevation myocardial infarction (STEMI) patients without known DM and 2) to evaluate the use of OGTT in STEMI patients in order to identify patients at risk of developing DM.

Methods: Stable patients with a primary PCI treated STEMI without known DM, age <85 years or s-creatinine <200 umol/l, were included. A standardised OGTT was performed in 140 STEMI patients during the acute phase (baseline, 17 h after PCI) and repeated after 3 months and 7 years follow-up and patients were classified according to the OGTT results.

Results: OGTT 7 years after STEMI: 16 (11.5%), 25 (18%) and 11 (8%) of the patients had criteria for DM, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), respectively. The prevalence of abnormal glucose regulation (DM + IGT+ IFG) was 37, 22 and 37% at baseline, 3 months and 7 years, respectively, however, about 50% of the patients were reclassified during follow-up. Four patients fulfilled the DM criteria at all time-points, additionally, 12 patients were classified with DM at 7 years.

OGTT at baseline vs. 7 years: Of the 13 patients diagnosed with DM at baseline, only 4 had criteria for DM after 7 years and only 6 of the 34 patients classified with IGT at baseline fulfilled criteria for DM.

OGTT at 3 months vs. 7 years: All 5 patients classified with DM after 3 months remained in this category after 7 years. Of the 17 patients classified with IGT at 3 months only 2 patients fulfilled criteria for DM 7 years later and 5 of these patients were reclassified as having normal glucose tolerance. Five of the 109 patients with normal glucose tolerance at 3 months were classified with DM after 7 years.

Conclusions: Results of a very early OGTT during the acute STEMI do not provide reliable information about long-term glucometabolic abnormalities and should not be recommended. A DM diagnosis 3 month after index STEMI, was confirmed in all patients 7 years later. On the contrary, only 2 of 17 patients diagnosed with IGT at 3 months developed DM during 7 years follow-up. Follow up of STEMI patients without known diabetes revealed that relatively few patients developed DM during 7 years follow-up. Results from early testing of STEMI patients with OGTT should be interpreted with caution.

P5593 | BEDSIDE

Association of genetic variants of the alpha-kinase 1 gene with type 2 diabetes mellitus in a longitudinal population-based genetic epidemiological study

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Purpose: We previously identified nine genes and chromosomal region 3q28 as susceptibility loci for myocardial infarction, ischemic stroke, or chronic kidney disease in Japanese by genome-wide and candidate gene association studies. Given that diabetes mellitus (DM) is an important risk factor for these diseases, we hypothesized that certain polymorphisms in the 10 loci may contribute to genetic suscep-tibility to them by affecting the susceptibility to type 2 DM. The purpose of the present study was to examine the possible association of 13 polymorphisms in the 10 loci with the prevalence of type 2 DM in community-dwelling Japanese.
Methods: Study subjects comprised 6027 individuals (797 subjects with type 2 DM, 5230 controls) who were recruited to the Inabe Health and Longevity Study, a longitudinal genetic epidemiological study of atherosclerotic, cardiovascular, and metabolic diseases. The subjects were recruited from individuals who visited the health care center at Inabe General Hospital for an annual health checkup, and they are followed up each year (mean follow-up period, 5 years). Subjects with type 2 DM had a fasting plasma glucose level of $\geq$6.93 mmol/L or a blood hemoglobin A1c content of $\geq$6.5%, or were taking antidiabetes medication. The control individuals had a fasting plasma glucose level of $<$6.05 mmol/L and a blood hemoglobin A1c content of $<$6.2%, and had no history of DM.
Results: Longitudinal analysis with a generalized estimating equation and with adjustment for age, sex, and body mass index revealed that rs2116519 (C$\rightarrow$T) of the family with sequence similarity 78, member B gene (FAM78B, P=0.0188) as well as rs2074379 (G$\rightarrow$A, P=0.0121) and rs2074388 (A$\rightarrow$G, P=0.0053) of the alpha-kinase 1 gene (ALPK1) were significantly (P$<$0.05) associated with the prevalence of type 2 DM. Longitudinal analysis with a generalized linear mixed-effect model and with adjustment for age, sex, and body mass index among all individuals revealed that rs2116519, rs2074379, and rs2074388 were significantly related to fasting plasma glucose level (P=0.0352, 0.0017, and 0.0010, respectively) and to blood hemoglobin A1c content (P=0.0065, 0.0090, and 0.0079, respectively). Similar analysis among individuals not taking antidiabetes medication revealed that rs2074379 and rs2074388 were related to fasting plasma glucose level (P=0.0073 and 0.0042, respectively) and blood hemoglobin A1c content (P=0.0142 and 0.0126, respectively), whereas rs2116519 was related to blood hemoglobin A1c content (P=0.0470).
Conclusion: ALPK1 may thus be a susceptibility locus for type 2 DM in Japanese.

STROKE

P5594 | BEDSIDE

Endovascular Treatment in Ischemic Stroke: A Meta-analysis of 11 Randomized Trials with Trial Sequential Analysis

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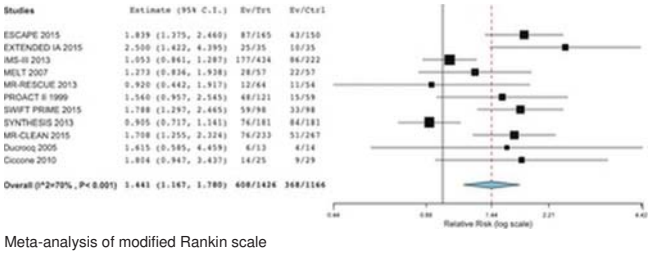
Aim: Endovascular treatment (ET) has been increasingly used in patients with ischemic stroke. However, there is controversial data about its efficacy and safety. Therefore we performed meta-analysis (MA) to compare efficacy and safety of ET plus intravenous thrombolysis (IVT) and IVT alone. Also, we performed trial sequential analysis (TSA) to differentiate conclusive vs inconclusive results and to demonstrate presence or absence of futility.
Methods: We searched PubMed, Embase and Scopus and international congress until February 2015. Eleven randomized controlled trials (RCTs) included to MA. The primary endpoint was independent outcome assessed by modified Rankin scale 0–2 at 90 days. Secondary endpoints were symptomatic intracerebral hemorrhage (ICH) and death. Our assumptions for TSA included two-sided testing, type 1 error=5%, power=80% and 20% relative risk reduction (RRR).



Meta-analysis of modified Rankin scale

Results: Eleven RCTs with 2592 patients comparing ET+IVT (n=1426) and IVT (n=1166) were included in the meta-analysis. In ET plus IVT arm, significantly more patients achieved independent outcome than IVT alone (42.6% vs 31.5%; RR=1.441; 95% CI, 1.167 to 1.780; p$<$0.001). However, there were no significant differences between ET plus IVT and IVT alone arms in terms of death (15.6% vs 16.6%; RR=0.881; 95% CI, 0.738 to 1.052; p=0.161) and ICH (8.6% vs 6.0%; RR=1.300; 95% CI, 0.968 to 1.748; p=0.081). TSA analysis results showed that to draw firm conclusion, the optimal information size would be 3780 and the cumulative effect size measure did not entered the futility area.
Conclusions: This meta-analysis indicates that ET plus IVT seems to be associated with improved independent outcome. However, there are similar safety outcomes between groups. To draw firm any conclusion, we need new RCTs.

P5595 | BEDSIDE

Early recurrence and cerebral bleeding in patients with acute ischemic stroke and atrial fibrillation: effect of anticoagulation and its timing. The RAF study

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Background: Anticoagulation timing in acute cardioembolic stroke remains controversial. In a prospective cohort of patients with acute stroke and atrial fibrillation (AF), we evaluated: 1) the risk of recurrent ischemic event and severe bleeding; 2) the risk factors for recurrence and bleeding; 3) the risk of recurrence and bleeding associated with anticoagulant therapy and its starting time after the acute stroke.
Methods: The primary outcome of this multicenter study was the composite of stroke, transient ischemic attack (TIA), symptomatic systemic embolism, symptomatic cerebral bleeding and major extra-cranial bleeding within 90 days from acute stroke.
Results: Of the 1,029 patients enrolled, 123 had 128 events (12.6%): 77 (7.6%) ischemic stroke or TIA or systemic embolism, 37 (3.6%) symptomatic cerebral bleeding and 14 (1.4%) major extra-cranial bleeding. High CHA2DS2-VASc score, high NIHSS, large ischemic lesion and type of anticoagulant were predictive factors for primary study outcome. Patients treated with oral anticoagulants alone had a better prognosis compared to those treated with low molecular weight heparins (LMWHs) alone or followed by oral anticoagulants. At adjusted Cox regression analysis, initiating anticoagulants 4 to 14 days from stroke onset was associated with a significant reduction in primary study outcome, compared to initiating treatment before 4 or after 14 days: Hazard Ratio 0.53 (95% CI 0.30–0.93).
Conclusions: Acute stroke in AF patients is associated with high rates of ischemic recurrence and major bleeding at 90 days. Anticoagulant treatment administered between 4 and 14 days from the acute event was associated with improved functional outcome.
Acknowledgement/Funding: No financial support

P5596 | BEDSIDE

Comparison of antiplatelet regimens in secondary stroke prevention: a nationwide cohort study

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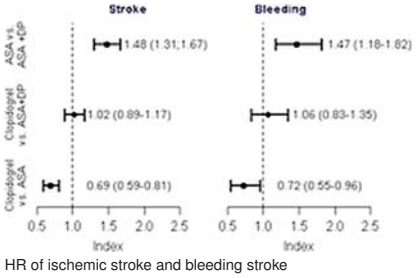
Purpose: The purpose was to determine whether acetylsalicylic acid, clopidogrel or combination of acetylsalicylic acid and dipyridamole was superior in preventing recurrent stroke and bleeding.
Methods: From Danish nationwide registries, patients discharged with first-time ischemic stroke in the period 2007–2010, and no history of atrial fibrillation were identified. Hazard ratios and 1-year risk of recurrent ischemic stroke and bleeding were calculated according to antiplatelet regimen.
Results: A total of 3043 patients were treated with acetylsalicylic acid, 12,295 with acetylsalicylic acid and dipyridamole combined, and 3885 with clopidogrel. Adjusted hazard ratios (HR) for clopidogrel versus combination of acetylsalicylic acid and dipyridamole were 1.02 (95% confidence interval (CI); 0.89–1.17) for ischemic stroke and 1.06 (95% CI; 0.83–1.35) for bleeding. Adjusted HRs (see Figure) comparing acetylsalicylic acid versus combination of acetylsalicylic acid and dipyridamole was 1.48 (95% CI; 1.31–1.67) for stroke and 1.47 (95% CI;



HR of ischemic stroke and bleeding stroke

1.18–1.82) for bleeding. Clopidogrel versus acetylsalicylic acid yielded a HR of 0.69 (95% CI; 0.59–0.81) and 0.72 (95% CI; 0.55–0.96) for stroke and bleeding, respectively. For acetylsalicylic acid, acetylsalicylic acid and dipyridamole, and clopidogrel one-year predicted risk of ischemic stroke was 11.1 (95% CI; 10.2–12.2), 7.7 (95% CI; 7.3–8.3) and 8.0 (95% CI; 6.9–8.7), respectively, and 3.4 (95% CI; 2.8–3.9), 2.4 (95% CI; 2.1–2.7) and 2.4 (95% CI; 1.9–2.9) for bleeding, respectively.
Conclusion: The combination of acetylsalicylic acid and dipyridamole, and clopidogrel were associated with similar risk of recurrent ischemic stroke and bleeding, whereas acetylsalicylic acid was associated with higher risk of stroke and bleeding.

P5597 | BEDSIDE
Thrombectomy for acute ischemic stroke: retrieval of larger thrombi is associated with improved neurological recovery

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Background and introduction: In the Multicenter Randomized clinical trial of endovascular treatment for acute ischemic stroke in The Netherlands (MR CLEAN), thrombectomy restored flow and led to improved functional outcome. We hypothesize that the characteristics of the retrieved thrombi reflect disease etiology and therefore may predict clinical outcome.
Purpose: To study macroscopy of thrombi retrieved during thrombectomy and correlate this with AIS baseline characteristics and changes in AIS severity between presentation and discharge.
Methods: 35 thrombi were collected from AIS patients undergoing thrombectomy. Thrombi were fixed in 4% buffered formaldehyde and calibrated images were taken. Length, width, area and numbers of particles were measured. An linear regression analysis was used to associate thrombus characteristics with patient characteristics and clinical outcome. Clinical parameters used in our analysis were, National Institutes of Health Stroke severity Scale (NIHSS), stroke etiology (modified TOAST-score), location of occlusion on CT-Angio, cardiovascular risk factors and the use of rtPA. Results were considered statistically significant if $p<0.05$.
Results: Most patients included in this study had a severe stroke, with median NIHSS of 17 (IQR 11–19). 17 (49%) patients had a stroke of cardiac origin and 7 (20%) due to large vessel atherosclerosis. CTA revealed that 32 (91%) of the occlusions were present in the middle cerebral artery. 28 (80%) of our patients received intravenous treatment with rtPA. We saw no association between macroscopy and gender, cardiovascular risk factors (except a history of symptomatic atherosclerosis) and TOAST criteria after adjustment for baseline NIHSS. Patients with atherosclerotic disease had longer and larger thrombi (p=0.0035 and p=0.045 respectively.) With increasing thrombus length (β=–1.42; p=0.03) and width (β=–2.28; p=0.04) a significantly improved NIHSS outcome was observed after IAT at discharge. Interestingly, an increased number of particles retrieved during thrombectomy showed a trend (p=0.079; β=0.71) towards a worse NIHSS at discharge.
Conclusions: Retrieval of a large thrombus during thrombectomy is associated with improved neurological recovery: size matters!

P5598 | BEDSIDE
Stroke, major bleeding and mortality in newly diagnosed atrial fibrillation with moderate-to-severe chronic kidney disease: results from GARFIELD-AF

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Purpose: To study outcomes in atrial fibrillation (AF) patients with moderate-to-severe chronic kidney disease (CKD; NKF-KDOQI stage≥3) vs mild/no CKD (stage<3).
Methods: GARFIELD-AF enrolled 17,168 patients with newly diagnosed non-valvular AF and ≥1 additional investigator-defined stroke risk factor in 2010–13. Hazard ratios (HR) were adjusted for CHA2DS2-VASc, ethnicity, antithrombotic therapy, smoking and AF type.
Results: 17,165 patients had data on renal function and 1-y outcomes. Stage≥3 patients (n=1757) were older than stage<3 patients (n=15,408) and more often female. They had more comorbidities and higher CHA2DS2-VASc and HAS-BLED. Despite more frequent use of anticoagulant±antiplatelet in stage≥3 patients (66.4% vs 60.1%), the risk of stroke/systemic embolism (SE), all-cause death and cardiovascular death was higher than in stage<3 patients (HR [95% confidence interval], 1.68 [1.15–2.46], 1.94 [1.59–2.37], 1.78 [1.34–2.35]). The HR for major bleeding was 2.19 (1.39–3.45).

Table 1

	Stage ≥3 CKD (n=1757)	Stage <3 CKD (n=15,408)
Women, n (%)	870 (49.5)	6649 (43.2)
Age, mean (SD), y	76.5 (9.1)	69.0 (11.4)
Medical history, n (%)		
Congestive heart failure	519 (29.5)	3020 (19.6)
Coronary artery disease	487 (27.7)	2933 (19.0)
Acute coronary syndromes	270 (15.4)	1352 (8.8)
Hypertension	1483 (84.4)	11922 (77.4)
Diabetes	522 (29.7)	3237 (21.0)
CHA_2 DS_2 -VASc score, mean (SD)	4.2 (1.5)	3.1 (1.6)
HAS-BLED score, mean (SD)	2.6 (0.8)	1.3 (0.8)
1-year outcomes, events/100 person-years (95% CI)		
All-cause death	10.20 (8.74, 11.89)	3.39 (3.10, 3.70)
Cardiovascular death	5.29 (4.27, 6.55)	1.74 (1.54, 1.97)
Stroke/systemic embolism	2.49 (1.82, 3.40)	1.24 (1.07, 1.44)
Major bleeding	1.91 (1.33, 2.72)	0.72 (0.60, 0.88)

CKD, chronic kidney disease; SD, standard deviation; CI, confidence interval.

Conclusion: Moderate-to-severe CKD is linked to a higher rate of stroke/SE, major bleeding and death, including cardiovascular death in AF patients.
Acknowledgement/Funding: The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG

P5599 | BENCH
A preclinical study of honeycomb microporous covered stents for the treatment of large wide-necked cerebral aneurysms

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Background: The treatment of large wide-necked cerebral aneurysms is extremely difficult, and carries a high risk of rupture, even when surgical or endovascular methods are available. The covered stent is one of the most promising advances in the treatment of complicated intracranial aneurysms (e.g., giant or very large wide-necked aneurysms), which have a high tendency to rupture. This treatment strategy is very simple, as the aneurysm neck is shielded with a cover film to stop the flow of blood into the aneurysm cavity. In this study, the in vivo performances of the newly developed microporous covered stents with a fine-tuned pore design (which provided a honeycomb pattern mesh-like cover film) were evaluated in the 3 animal models.
Methods and results: The microporous covered stents were prepared using specially designed balloon-expandable stents (diameter 3.5–5.0 mm; length 16–28 mm), which were prepared by dip-coating to completely cover their struts with polyurethane (thickness 20 μm) and microprocessing to form the honeycomb pattern after expansion. 1) In an internal carotid artery canine model (diameter 5 mm, n=12), all stents that were mounted on the delivery catheter passed smoothly through the tortuous vessel with minimal arterial damage. 2) In a outer-sidewall aneurysm canine model (n=15), almost all parts of the aneurysms had embolized immediately after stenting, and histological examination at 1 month revealed neointimal formation with complete endothelialization at all stented segments and entirely organized aneurysms. 3) In a perforating artery rabbit model (diameter 3 mm, n=15), the lumbar arteries remained patent, with minimal change in the vascular flow pattern for over 1 year, even after placement of a second, overlapping stent. At 2 months after stenting, the luminal surface was covered with complete thin neointimal formation.
Conclusion: Based on the results obtained from these experimental models, the following successful outcomes were observed: 1) easy navigation of the covered stent delivery system into the 3-D tortuous arteries, 2) instant occlusion of large aneurysms, even those that were located at the outer-sidewall of the curved arteries, and 3) preserved patency of the perforating arteries after stenting. Based on these successful preclinical results (additional details will be published shortly), an investigator-initiated first-in-human clinical trial of the honeycomb microporous covered stents will be conducted in 2015.

P5600 | BEDSIDE
Usual blood pressure and risk of vascular dementia

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Purpose: Vascular dementia is the second most common form of dementia and poses a significant clinical and economic burden. The association between blood pressure and risk of vascular dementia is unclear.
Methods: A cohort of 4.28 million individuals, free of vascular disease and de-

mentia, was identified from linked electronic health records. Cox models were used to analyse time to initial presentation of physician-diagnosed vascular dementia, adjusted for age, BMI, gender and smoking status. Models were further adjusted for incidence of stroke and transient ischemic attack, to estimate what proportion of the association between systolic blood pressure (SBP) and risk of vascular dementia was mediated by clinically diagnosed cerebrovascular disease.
Results: Over a median follow up of 7.0 years, 11 114 initial presentations of vascular dementia were observed after exclusion of the first four years of follow up. The association between 20 mm Hg higher usual SBP and risk of vascular dementia declined with increasing age, from an HR of 1.62 (CI 1.13, 2.35) in the age group of 30 to 50, to an HR of 1.26 (CI 1.18, 1.35) in the age group of 51 to 70, to an HR of 0.97 (CI 0.92, 1.03) in the age group 71 to 90 (p trend = 0.006). 30% of excess risk of vascular dementia associated with higher SBP in the age group 30–70 was mediated through incident stroke and transient ischemic attack.
Conclusions: Although blood pressure is positively associated with risk of vascular dementia, the association declines with increasing age. Previously reported inverse associations between blood pressure and vascular dementia in old age are likely due to reverse causality. Assuming causality, individual and population-level efforts to reduce blood pressure and prevent stroke and transient ischemic attack may reduce the incidence of vascular dementia.

P5601 | BEDSIDE
Atrial fibrillation is associated with stroke in veteran endurance athletes

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Background: Atrial fibrillation (AF) is associated with a five-fold increased risk of stroke in the general population, but AF in absence of co-morbid conditions (lone AF) has been suggested to have a favourable prognosis. Prolonged endurance exercise seems to increase the risk of AF, but stroke risk has previously not been investigated in veteran endurance athletes with AF.
Purpose: To study the associations between AF, lone AF and stroke among Norwegian veteran cross-country skiers.
Methods: All 3114 male veteran cross-country skiers aged ≥40 years who completed the 54-kilometre Birkebeiner race in 1999 were invited to this cohort study. During 2012, cross-sectional data on AF, stroke, co-morbid conditions, medication use, history of exercise, socioeconomic status and other possible confounding factors were collected by questionnaires. AF diagnoses were confirmed during a review of medical records in individuals with self-reported AF, and if no evidence for relevant co-morbid conditions was found, AF was classified as lone.
Results: In total, 2081 male veteran skiers aged 53–74 years were included in this analysis (mean age 62.8 years). The prevalence of self-reported AF was 13%. The prevalence of stroke was 11% in skiers with confirmed AF (n=112), compared to 4% in skiers without AF ($p<0.01$). After adjustment for age, body mass index, socioeconomic status, concomitant heart disease, hypertension, diabetes mellitus, lipid-lowering treatment, smoking and exercise, AF was associated with an adjusted odds ratio (aOR) for stroke of 2.21 (95% confidence interval (CI) 1.00–4.93). Also among skiers with lone AF (n=70), the prevalence of stroke was 11% and lone AF was associated with an aOR for stroke of 2.89 (CI 1.15–7.25). Out of 71 veteran skiers with AF and at least one additional risk factor (corresponding to a CHA2DS2-VASc Score ≥1), 70% used oral anticoagulation (OAC) treatment, while 13% were treated with acetylsalisylic acid.
Conclusions: This study demonstrates a high prevalence of stroke among veteran endurance athletes with AF. AF was associated with a two to three-fold increased risk of stroke, also in skiers without co-morbid conditions. Our results challenge the favourable prognosis suggested for lone AF and support that veteran athletes with AF should be treated with OAC in line with general guidelines.
Acknowledgement/Funding: This work was supported by Diakonhjemmet Hospital, the Kavli Research Center for Geriatrics and Dementia, the Norwegian Institute of Public Health and

P5602 | BEDSIDE
Progression from paroxysmal to sustained atrial fibrillation as an increased risk of stroke or systemic embolism: The Fushimi AF Registry

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Background: Atrial fibrillation (AF) increases the risks of thromboembolism and death, and the prevalence of AF is increasing significantly (reportedly, 0.6% of total population in Japan). Progression from paroxysmal to sustained types (persistent or permanent) of AF is sometimes seen, but outcomes of such patients were unknown. We investigated the association between progression of AF and clinical events in AF patients.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients living in Fushimi-ku, Kyoto, which is a typical urban district of Japan with a population of 283,000. At present, we have enrolled 4,174 Japanese AF patients from March 2011 to November 2014. We studied 1,625 paroxysmal AF patients at baseline whose follow-up data were available.
Results: During the median follow-up of 777 days, progression from paroxysmal to sustained AF occurred in 164 patients (10.1%). Patients with AF progression did not show significant differences in the number of male (59.2% vs. 57.6%; p=0.70), mean age (72.7 vs. 72.3 years of age; p=0.69), mean BMI (23.4 vs. 22.8 kg/m^2; p=0.07), systolic blood pressure (124.6 vs. 125.7 mmHg; p=0.51), pulse rate (75.1 vs. 76.2 bpm; p=0.43) and CHADS2 score (1.91 vs. 1.81; p=0.34). Past history and comorbidities were comparable between patients with and without AF progression. Patients with AF progression were more frequently prescribed oral anticoagulants (OAC) (56.1% vs. 37.4%; $p<0.01$). Prescription of anti-arrhythmic drugs were comparable between patients with and without AF progression (31.1% vs. 33.1%; p=0.61). However, catheter ablation were less performed in patients with AF progression (4.3% vs. 9.0%; p=0.04). Stroke or systemic embolism occurred in 11 patients (6.7%) with AF progression, and in 47 (3.2%) without AF progression, with a multivariate hazard ratio adjusted by age and OAC prescription, history of stroke or transient ischemic attack, heart failure, hypertension, diabetes and catheter ablation, of 2.13 (95% confidence interval, 1.02 to 4.11; p=0.04).
Conclusion: We identified that progression of AF was associated with an increased risk of stroke or systemic embolism in Japanese AF patients.
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P5603 | BEDSIDE
Insertable cardiac monitors for detection of atrial fibrillation in patients with embolic stroke of undetermined source (ESUS) selected by risk factors

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Background: Clinically silent paroxysmal atrial fibrillation (AF) was recently detected in 12.4% of patients with embolic stroke or transitory ischemic attack (TIA) of undetermined source (ESUS) who have undergone insertion of an implantable cardiac monitor (ICM), after 12 months of monitoring. However, the large majority of these patients still undergo implantation of the ICM without clinical benefit. Our aim was to assess (1) if a risk factor-based pre-selection of ICM candidates would enhance the rate of AF detection within 12 months and (2) to determine which risk factors have significant predictive value for AF detection.
Methods: A cohort of 75 patients with ESUS were prospectively enrolled at the Stroke Unit of a university in Germany, if at least one risk factor was present: a CHA2DS2-VASc score ≥4, atrial runs in Holter monitoring, left atrial (LA)-size >45 mm, left atrial appendage (LAA)-flow ≤0.2 m/s, or spontaneous echo contrast in the LAA as assessed by transesophageal echocardiography. Study endpoint was the detection of ≥1 episodes of AF (lasting ≥2 minutes according to the software algorithm of the ICM).
Results: At the date of ICM insertion, one patient presented with AF. Therefore, 74/75 patients underwent implantation of the ICM. After a follow-up period of 6 months, we detected paroxysmal AF in 19 of the 75 patients (25.3%). After 12 months, AF detection rate was 30.6% (23/75 patients). Episodes of AF were mostly asymptomatic (91.3%). In multivariable analysis, LA-size >45 mm and presence of atrial runs were independent predictors of paroxysmal AF with hazard ratios of 5.1 (95% confidence interval 2.1–12.0, $p<0.0001$) and 2.6 (1.1–6.2), p=0.027), respectively.
Conclusions: Using a risk-factor based approach of preselection of ICM-candidates after ESUS, detection rate of AF can be enhanced to 31% within one year. LA dilation and atrial runs independently predict AF.
Acknowledgement/Funding: AKF research grant (intramural research-funding program of University of Tuebingen, Germany)

P5604 | BEDSIDE
Under reporting of intracranial haemorrhage associated with antiplatelet and anticoagulant use to the health products regulatory authority versus referrals to a national neurosurgery centre

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Intracranial Haemorrhage (ICH) is a much-feared side effect of antiplatelet and anticoagulant agents; it is of particular prominence with the advent of the novel antiplatelet and anticoagulant agents. Postmarket reports of bleeding highlighted the fact that newly marketed products, by virtue of their novelty alone, may elicit adverse-event reports at high rates; reporting rates decreasing over time (the Weber effect). Hence established medications, such as Warfarin and Aspirin, would be far less likely to elicit adverse-event reports than would newer medications with similar risks.
The hypothesis of this study was to compare the number of referrals of ICH associated with antiplatelet and anticoagulant use to our National Neurosurgical Centre Hospital with the number of ICH reported to the Health Products Regulatory Authority (HPRA) as an adverse event of these medications.
Our National Neurosurgical Centre has an estimated referral population of 4 million. All consecutive referrals from July 2013 to January 2014 were reviewed. Data

collected included baseline demographics, antiplatelet/anticoagulation usage and indication for same, and CT brain findings of the ICH. The HPRA were contacted and supplied their adverse event reports for the same period.
There were 977 consecutive patients with an ICH referred in this period. Of these 328 (33.6%), with a mean age of 77yrs, female 42.6%, were on an antiplatelet and/or an anticoagulant agent; ASA alone (n=166, 50.6%), Warfarin alone (106, 32.3%), Clopidogrel alone (11, 3.3%), Rivaroxaban alone (4, 1.2%), Dabigatran alone (4, 1.2%), ASA/dipyridamole alone (3, 0.9%). Thirty one (9.4%) patients were on two agents, 19 on ASA & Clopidogrel, 7 on ASA & Warfarin, 2 on Clopidogrel and Warfarin, 2 on Rivaroxaban and ASA, and 1 patient on ASA and Prasugrel. Three patients were on 3 agents, 2 on ASA, Clopidogrel and Warfarin, one on ASA, Clopidogrel and Rivaroxaban. We excluded 22 patients who had an ICH following thrombolysis or recent heparin therapy. The HPRA received 4 reports of ICH associated with antiplatelets or anticoagulants; 2 associated with Warfarin, 1 with Rivaroxaban and 1 with Rivaroxaban and Warfarin.
These results highlight the lack of adverse reporting with novel and established medications alike. It emphasizes the importance of reporting to national authorities so their statistics can be a true reflection of the number of adverse events, especially when the adverse outcomes can be catastrophic, like ICH.

P5605 | BEDSIDE
Spontaneous echo contrast is associated with increased risk for cardioembolic events a metaanalysis

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Background: Spontaneous echo contrast (SEC) is a swirling smoke-like image seen inside the heart chambers or in the aorta on 2-dimensional echocardiogram. It is theorized to be due to reduced blood flow or stasis, and is considered a prethrombotic lesion. Its association with cardio-embolic (CE) events, however, is not yet established.
Research question: Is there an association between spontaneous echo contrast (SEC) and cardio-embolic (CE) events among adult patients?
Objectives: We aim to determine the association of spontaneous echo contrast (SEC) with cardio-embolic (CE) events (stroke and peripheral embolism).
Inclusion criteria: Studies were (i) were observational studies; (ii) whose populations were of adults >/= 19 years old with documented SEC either in the cardiac chambers and/or the aorta; (iii) reported data on CE events, especially stroke; (iv) and controlled for confounding variables by doing logistic regression and/or multivariate analysis.
Methods: We conducted a systematic search of studies using MEDLINE, EMBASE, ScienceDirect, and Cochrane Central Register of Controlled Trials databases in all languages and examined reference lists of studies. We identified 14 studies that met inclusion criteria, and obtained full articles of all of them. Each study was assessed for quality using the Newcastle-Ottawa Quality Assessment Scale. The outcome of interest was assessed using Mantel-Haenzel analysis of random effects to compute for risk ratios, carried out using Review Manager (RevMan) 5.0.18 (The Nordic Cochrane Centre, The Cochrane Collaboration).
Results: Pooled analysis from the 14 studies enrolling 4,659 patients showed that the presence of SEC was associated with increased CE events (27.9% vs 26.4%) (RR 3.50, 95% CI 2.01, 5.93; P<0.00001; I2=89%). There was no evidence of publication bias by funnel-plot method. To control for heterogeneity, we did subgroup and sensitivity analysis, and this revealed that intracardiac SEC, particularly left atrial or left ventricular SEC, was primarily responsible for this association (22.8% vs 5.8%) (RR 4.69, 95% CI 3.42, 6.43; P<0.00001; I2=0%), compared to extracardiac SEC, represented by aortic SEC (26.8% vs 16.7%) (RR 1.70, 95% CI 1.05, 2.77; P=0.03; I2=53%).
Conclusion: The presence of SEC is associated with significantly increased risk for cardio-embolic events among adult patients. This supports the need to be aggressive in the management of patients among SEC particularly in reducing CE event risk. Clinical trials are warranted.

P5606 | BEDSIDE
Discontinuation of oral anticoagulation agents in patients with atrial fibrillation and concomitant risks of stroke and bleeding using therapy approach guided by insertable cardiac monitors

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Introduction: In patients (pts) with atrial fibrillation (AF) who are at high risk for bleeding, long-term usage of oral anticoagulants (OACs) used for stroke prevention may not be safe.
Purpose: To investigate whether insertable cardiac monitor (ICM)-guided assessment of AF burden and optimization of oral antiarrhythmic agents (OAAs) to maintain normal sinus rhythm (NSR) may allow safe-withdrawal of OACs.
Methods: In pts at dual risk of stroke and bleeding, we inserted ICM [Medtronic Reveal], after cardioversion, treatment with OAA (Ic, III) and OAC (warfarin, NOACs). Upon regular follow-up we categorized the pts into 3 groups;(1) Group A (NSR/low AF burden, <1%), (2) Group B (intermediate AF burden, 1–2%), and (3) Group C (high AF burden >2%) (Figure 1). We allowed discontinuation of OACs only if NSR/low AF burden for 3 months was maintained.
Results: 83 pts (median age 74 years; 53% male) were followed over 15.3 months (mean, range 6–46). Group A, B and C had 45 (54%), 29 (35%) and 9 (11%) pts with similar demographics and CHADS2 scores: 2.09±0.63, 2.03±0.8 and 2.1±0.33, CHA2DS2-VASc scores:3.09±0.97, 2.76±1.1, and 2.92±0.73, and HAS-BLED scores: 3.13±1.03, 3.24±0.80 and 3.1±0.71 (p>0.05) respectively. With OAAs 25 (86%) pts in Group B maintained NSR/low AF burden. Overall, 68 (82%) pts (43 in Group A, 25 in Group B) had NSR/low AF burden. 60 (88%) pts (40 in Group A, 20 in Group B) discontinued OACs without any untoward outcomes. 5 (6%) pts, all on OAC, suffered severe bleeding compared to none who discontinued OAC (p<0.00003). 6 (7%) pts died from unrelated causes including respiratory failure, cancer and sepsis.

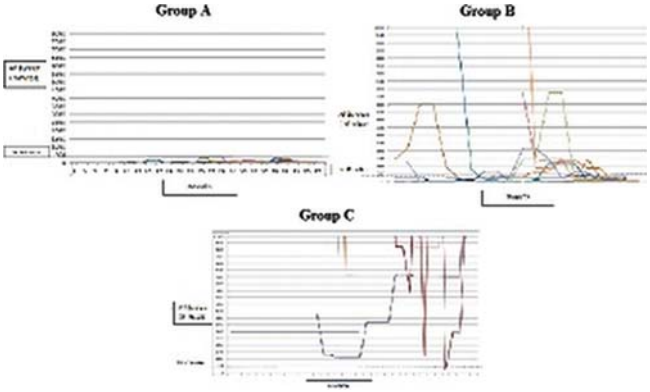

Figure 1

Conclusions: In pts with AF who are at high risk of bleeding, a strategy of ICM-guided rhythm control with OAA and assessment of AF burden may allow safe discontinuation of OAC.

P5607 | BEDSIDE
The role of functional characteristics in symptomatic carotid artery prediction in ischemic stroke

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Background: Recent studies with positron emission tomography have shown that in patients with recent acute ischemic stroke and bilateral carotid artery disease, ipsilateral carotids exhibit higher inflammatory activation. Microwave Radiometry (MWR) indirectly evaluates the inflammatory status of internal tissues, while the absence of radiation allows repetitive measurements. The aim of the present study was to investigate the role of local inflammation in the prediction of the culprit carotid arteries in patients with recent ischemic stroke.
Methods: Consecutive patients with recent acute ischemic stroke due to large artery atherosclerosis were included in the study. Subjects with history of atrial fibrillation were excluded. Patients with bilateral carotid plaques underwent both MWR and carotid ultrasound evaluation within 24 hours from symptoms onset. During ultrasound study, maximum plaque thickness (MPT) was determined in each carotid artery. Temperature difference (ΔT) by MWR was assigned as maximal temperature along the carotid artery minus minimum. Culprit were defined the carotid arteries ipsilateral to cerebral ischemia. Patients with lacunar infarcts or transient ischemic attacks were excluded. The following models for culprit carotid artery prediction were considered and were compared with the use of Harrel's c-statistic: traditional risk factors (TRF – sex, age, smoking, dyslipidemia, arterial hypertension, diabetes mellitus and family history) plus MPT, b)TRF plus ΔT and c) TRF plus MPT plus ΔT.
Results: One hundred carotid arteries from fifty patients were finally evaluated. Culprit carotid plaques had higher ΔT compared to nonculprit (0.93±0.58 versus 0.58±0.35°C, respectively, p<0.001). Regarding the predictive capacity of the various models for the culprit carotid artery identification, the models TRF plus MPT and TRF plus ΔT showed similar c-statistic values (0.691, 95% CI 0.588–0.794, p<0.001 vs 0.747, 95% CI 0.644–0.850, p<0.001, respectively, pdiff.=0.36). On the contrary the model TRF plus MPT plus ΔT showed the highest c-statistic value (0.768, 95% CI 0.666–0.870, p<0.001, pdiff=0.05).
Conclusions: The evaluation with MWR of functional carotid artery characteristics could significantly contribute to culprit carotid artery identification in patients with recent ischemic stroke due to large artery atherosclerosis.

P5608 | BEDSIDE
Pre-event CHA2DS2-VASc score and severity of acute stroke in patients with atrial fibrillation: findings from the RAF study

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Background: Current guidelines recommend CHA2DS2-VASc score to assess the risk of stroke in patients with atrial fibrillation (AF). The association between pre-event CHA2DS2-VASc score and the severity of acute stroke has never been defined.
Aim: We investigated the association between CHA2DS2-VASc score and the severity of acute stroke in a prospective multicentre study which enrolled consecutive patients with acute stroke and AF (RAF study).
Methods: Severity of stroke was evaluated on admission by the National Institute of Health Stroke Scale (NIHSS) score, that was considered both as a continuous and dichotomized variable (severe stroke=NIHSS>10). Correlations between severity of stroke and pre-event CHA2DS2-VASc was evaluated using multiple logistic regression after adjustment for other risk factors.
Results: Of the consecutive patients enrolled in the study, 598 patients had an admission NIHSS score greater than 10 and 399 patients lower than 10. The median NIHSS scores for CHA2DS2-VASc score of 0–8/9 were: 5.18, 8.30, 8.31, 8.86, 9.12, 9.67, 9.70, 10.30, 12.09, respectively. A linear correlation was found between severity of stroke and CHA2DS2-VASc score (r2 0.010, p=0.001). On multivariate analysis, CHA2DS2-VASc score correlated with the severity of stroke (OR 1.084, p=0.041, for each point increase).
Conclusions: In patients with AF, CHA2DS2-VASc score is a predictor of severity of stroke in addition to be a predictor of risk of stroke. This observation increases the value of the assessment of CHA2DS2-VASc score when considering the use of anticoagulant treatment.
Acknowledgement/Funding: No financial support

P5609 | BEDSIDE
Carotid atherosclerosis and the risk for ischemic stroke in patients with atrial fibrillation on oral anticoagulant treatment

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Background: Ischemic heart disease, peripheral artery disease and aortic plaque are risk factors for ischemic stroke in patients with atrial fibrillation (AF) according to the CHA2DS2-vasc score. Whether carotid atherosclerosis is a risk factor for ischemic stroke in these patients is undefined.
Methods: Ambulatory patients with AF on oral anticoagulant treatment were included in a multicenter, prospective study. All patients underwent carotid ultrasonography for the assessment of internal carotid stenosis defined according to the criteria of the Consensus Panel Gray-Scale (Internal Carotid Artery Peak Sistolic Velocity higher than 125 cm/sec or non detectable or Internal to Common Carotid Artery Peak Sistolic Velocity ratio over 2). The presence/absence of atherosclerotic plaques was also reported. Ischemic stroke was the primary study outcome; stroke plus systemic embolism and all-cause death were secondary study outcomes.
Results: Overall, 587 patients were included in the study (mean age 74.5±9, range 43–92; mean CHADS2 2.0±1, range 0–6; mean CHA2DS2-vasc 3.4±2, range 0–8). Forty-four patients were found to have carotid stenosis (7.5%; 18 in the right and 31 in the left internal carotid artery), of whom 5 had internal carotid artery occlusion. 238 patients had at least one plaque at carotid ultrasonography (40.5%).
Over a median follow-up of 24.3 months (range 0 to 62), 23 patients had an ischemic stroke or transient ischemic attack (1.5% per patient-year, 95% CI 0.8 to 2.1) and 54 died (3.6% per patient-year, 95% CI 2.7 to 4.5). A not significant increase in the risk for ischemic stroke (HR 1.29 95% CI 0.30 to 5.51), ischemic stroke or systemic embolism (HR 2.09, 95% CI 0.73 to 6.00) or death (HR 1.57 95% CI 0.67 to 3.68) was observed in patients with carotid stenosis as compared to patients without it at Cox Regression analysis.
Conclusions: In this study in patients with AF, carotid stenosis as detected by ultrasonography was associated with a not significant increase in the risk for stroke while on anticoagulant treatment. Further evidence is needed to assess the incremental prognostic value of carotid stenosis over that of accepted risk factors for stroke in patients with AF.

P5610 | BEDSIDE
Association of polymorphisms of TOMM40 and SLC22A4 with ischemic stroke

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Purpose: Recent meta-analyses of genome-wide association studies (GWASs) have identified various genes and loci that confer susceptibility to coronary artery disease (CAD) or myocardial infarction (MI) in Caucasian populations. Among these genes and loci, some of the genetic variants that were originally detected to affect a risk of CAD were also related to ischemic stroke, suggesting a shared genetic architecture. Although CAD and ischemic stroke have been suggested to share genetic factors in Caucasian populations, the genes that confer susceptibility to both conditions in Japanese individuals have not been identified definitively. The purpose of the present study was to examine the possible association of ischemic stroke in Japanese individuals with 29 polymorphisms previously identified as susceptibility loci for CAD or MI by the meta-analyses of GWASs in Caucasian populations.
Methods: The study population comprised 3187 Japanese individuals, including 894 subjects with ischemic stroke (atherothrombotic cerebral infarction) and 2293 controls. Subjects with cardiogenic embolic infarction, lacunar infarction alone, transient ischemic attack, moyamoya disease, cerebral venous sinus thrombosis, or traumatic cerebrovascular diseases were excluded from the study. The control individuals had no history of CAD, aortic aneurysm, or peripheral artery disease; of ischemic or hemorrhagic stroke or other cerebrovascular diseases. The genotypes for 29 polymorphisms were determined by the multiplex bead-based Luminex assay.
Results: Comparisons of allele frequencies by the chi-square test between subjects with ischemic stroke and controls revealed that rs9319428 (G→A) of the fms-related tyrosine kinase 1 gene (FLT1, P=0.0475), rs2075650 (G→A) of the translocase of outer mitochondrial membrane 40 homolog gene (TOMM40, P=0.0095), and rs273909 (T→C) of the solute carrier family 22 (organic cation transporter), member 4 gene (SLC22A4, P=0.0069) were significantly ($P<0.05$) associated with the prevalence of ischemic stroke. Multivariable logistic regression analysis with adjustment for age, gender, body mass index, and the prevalence of smoking, hypertension, diabetes mellitus, and dyslipidemia revealed that rs2075650 of TOMM40 (P=0.0443; odds ratio, 0.50; recessive model) and rs273909 of SLC22A4 (P=0.0123; odds ratio, 0.45; dominant model) were significantly associated with ischemic stroke, with the minor G and C alleles, respectively, being protective against this condition.
Conclusions: TOMM40 and SLC22A4 may thus be susceptibility loci for ischemic stroke in Japanese individuals.

P5611 | BEDSIDE
Frequent atrial ectopic activity and risk of recurrent cryptogenic ischemic stroke and transient ischemic attack

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Background: Frequent atrial ectopic activity (FAEA) was recognized as a risk factor for paroxysmal atrial fibrillation, first ischemic stroke and death. Its occurrence in patients with cryptogenic cerebral ischemic events (CCIE) is poorly studied and its role as a risk factor for stroke/TIA recurrence in these patients is unknown.
Methods: We retrospectively identified patients who had undergone Holter monitoring in our hospital between 2005 and 2012, who had ischemic stroke or TIA of undetermined etiology (CCIE) according to TOAST classification. Demographic, clinical and imaging data were collected and patients were classified according to ASCO phenotype. We defined FAEA as occurrence of >10 atrial ectopic beats (AEB) per hour. Recurrence of ischemic stroke or TIA during hospital follow-up was recorded.
Results: 184 patients with CCIE were identified and followed for a median of 28 months (IQR 12.4–55.0) –52.2% male, median age 56 years. Ischemic stroke was the index event in 73.9% and TIA in 26.1%. Recurrence rate was 3.1 per 100 patients/ year in patients without FAEA (n=152), and 17.6 per 100 patients/year in patients with FAEA (n=32) ($p<0.001$). Patients with and without recurrences differed significantly regarding age, arterial hypertension and presence of FAEA. Univariate analysis revealed increased risk of recurrence in patients >65 years (HR=3.98, p=0.002) and presence of FAEA (HR=4.52, p=0.001). Risk of recurrence was higher, albeit non significant, in patients with FAEA (HR=2.49, p=0.087) in multivariate analysis adjusted for age, arterial hypertension and anticoagulation.
Conclusion: This study suggests that FAEA is associated with an increased risk of recurrent cryptogenic ischemic stroke or TIA. Although this association is weakened in multivariate analysis, we argue that there is a trend for increased recurrence in patients with FAEA. Atrial ectopic activity prospective studies in this group of patients may have a significant impact in clinical practice.

P5612 | BEDSIDE
Does the left atrial appendage morphology correlate with stroke risk in patients with sinus rhythm?

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Objectives: Ischemic strokes without a well-defined etiology are labeled as cryptogenic, and account for 30–40% of strokes in the registries. The left atrial appendage (LAA) is the most typical origin for intracardiac thrombus formation when associated with atrial fibrillation. We examined whether LAA morphology detected with transesophageal echocardiography (TEE) constitutes a risk factor of thrombus formation and cryptogenic stroke in patients without atrial fibrillation.
Aim: To correlate LAA morphology detected by TEE with the incidence of stroke/transient ischemic attack (TIA) in patients without atrial fibrillation.
Methods: 110 consecutive pts (65 F, 45 M) with a mean age of 31.2±17.2 (16–52) years with the history of cryptogenic cerebrovascular event (TIA/stroke) and normal sinus rhythm, who underwent TEEs, were analyzed. The patients with PFO were excluded.
The diagnosis of stroke was based on the occurrence of a new and abrupt focal neurological deficit, with neurological signs and symptoms persisting for >24 hours, subsequently confirmed by computed tomography and/or MRI.
A group of 110 healthy volunteers, (65 F, 45 M), mean age of 32.2±9.15 (range 16–52), matched for age and gender served as controls.
All patients underwent TEE according to guidelines using commercially available instruments. Four different morphologies were used to categorize LAA according to the literature: Cactus, Chicken Wing, Windsock, and Cauliflower.
Results: LAA morphologies distribution differed significantly in stroke group as compared to the controls. In stroke patients this was: Cauliflower (66 [60%]), Cactus (22 [20%]), Chicken Wing (12 [10.9%]), Windsock (10 [9.1%]), and in the control group: Cauliflower (6 [5.5%]), Cactus (30 [27.3%]), Chicken Wing (40 [36.4%]) and Windsock (34 [30.8%]), (p=0.0001). In a multivariable logistic model, Cauliflower morphology was found to be 74% more likely to have a stroke/TIA history (odd ratio: 0.27, 95% confidence interval: 0.05 to 0.93, p=0.021). In a separate multivariate model, we entered Cauliflower as the reference group and assessed the likelihood of stroke in other groups in relation to reference. Compared with Cauliflower, Cactus was 2.08 times (p=0.043), Windsock was 6.5 times (p=0.021), and Chicken Wing was 4.0 times (p=0.024) less likely to have a stroke/TIA.
Conclusions: Patients with Cauliflower LAA morphology are more likely to have an embolic event even in case of sinus rhythm. If confirmed, these results could have a relevant impact on the anticoagulation management of patients with cryptogenic stroke/TIA.

P5613 | BEDSIDE
Predictors of stroke after aortic valve replacement with or without concurrent coronary artery bypass grafting

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Background: Stroke is arguably the most important and devastating non-mortality complication after cardiac surgery, and also an important outcome to compare between aortic valve replacement (AVR) and transcatheter aortic valve implantation.
Purpose: We analysed for the predictors of stroke after AVR with or without concurrent coronary artery bypass grafting (CABG).
Methods: All patients undergoing AVR +/– CABG at our City Hospital during 2005–2012 were included, and univariate multivariate analyses were conducted to identify predictors for post-operative stroke, defined as in-hospital new neurological deficits lasting more than 24 hours after surgery.
Results: There were 620 isolated AVR and 450 AVR+CABG patients studied. Rates of stroke was significantly higher for AVR+CABG 3.3% (15) compared to AVR alone 1.3% (8), P=0.031. Independent predictors of stroke (odds ratio and 95% confidence interval) for isolated AVR included age (1.02, 1.00–1.04), syncope (6.07, 1.03–35.8), critical pre-operative state (6.07, 2.08–25.6) and history of stroke (7.23, 1.20–43.6), while the only independent predictor identified for AVR+CABG was diabetes on insulin (6.19, 1.63–23.5). Receiver-operative characteristics analysis found the original EuroSCORE having the highest C-statistic for detecting stroke after isolated AVR 0.845 (0.783–0.907), while the Society of Thoracic Surgeon's Score had the highest though moderate C-statistic after AVR+CABG 0.642 (0.508–0.776).
Conclusion: Although rates of stroke are low at our centre, performing CABG concurrent on top of AVR was associated with significantly higher risk. We have identified a number of conventional cardiovascular risk factors that independently predict stroke in aortic valve surgery which should be taken into consideration when deciding for modality of aortic valve intervention.

P5614 | BEDSIDE
Neuroprotective effect of sitagliptin after ischemic stroke in type 2 diabetic patients: a nationwide cohort study

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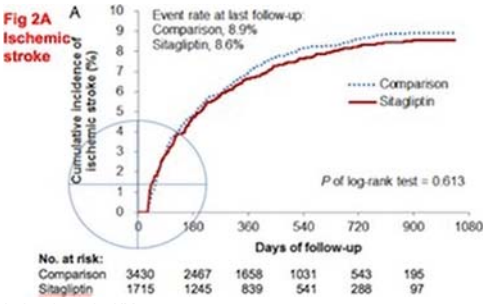
Objectives: The aim of this study was to assess the efficacy and safety of sitagliptin in type 2 diabetic patients with ischemic stroke.
Background: The cardiovascular safety and efficacy of sitagliptin, a dipeptidyl peptidase 4 inhibitor, in type 2 diabetic patients with ischemic stroke remains uncertain.
Methods: We analyzed data from the Taiwan National Health Insurance Research Database (NHIRD) between March 1st, 2009 and December 31st, 2011. Ischemic stroke patients were identified from individuals with type 2 diabetes. Subjects using sitagliptin were compared with those not using sitagliptin for cardiovascular safety and efficacy evaluation. The primary outcomes were a composite of ischemic stroke, myocardial infarction (MI) or cardiovascular death.
Results: A total of 5,145 type 2 diabetic patients with ischemic stroke met our inclusion criteria and were followed for up to 2.83 years (mean, 1.17 years). Overall, 1,715 patients (33.3%) were exposed to sitagliptin therapy and 3,430 patients (66.7%) who did not use sitagliptin were in the comparison group. The events of primary composite outcomes occurred in 190 patients in the sitagliptin group (11.1%) and in 370 patients in the comparison group (10.8%) (HR, 1.02; 95% CI, 0.85–1.21). Patients treated with sitagliptin had similar risk of ischemic stroke, hemorrhagic stroke or all-cause mortality with HR of 0.95 (95% CI, 0.78–1.16, P=0.612), 1.07 (95% CI, 0.55–2.11, P=0.834), and 1.00 (95% CI, 0.82–1.22, P=0.989) respectively, compared with non-sitagliptin group.



Ischemic stroke KM curve

Conclusions: The use of sitagliptin in type 2 diabetic patients with recent ischemic stroke was not associated with increased or decreased risks of adverse cardiovascular outcomes.

P5615 | BEDSIDE
Silent neuronal ischemias after elective percutaneous coronary intervention

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Introduction: Increased plasma levels of neuron specific enolase (NSE) is related to damage of neurons and neuroendocrine cells. We aimed to investigate elevation of NSE after elective percutaneous coronary intervention (PCI) on the prediction of silent neuronal ischemias (SNIs).
Methods and results: Patients scheduled for elective PCI (n=80) and age and sex-matched controls (n=80) with normal coronary arteries were assessed. NSE levels were studied before and 12 hour after the procedure. Patients with high baseline levels of NSE (16 patients in normal coronary artery group and 11 patients in elective PCI group) (n=27) were excluded. Elevation of greater than 0,12μg/l was considered as SNI.
Thirty-five of the 133 study patients had SNI after the procedure. NSE elevation was significantly more prevalant among patients with PCI than that of controls. Elevation of NSE was observed in 39,1% of elective PCI patients (n=27) and 12,5% of the control group (n=8) (p<0,001).
The incidence of SNI was higher in active smokers and patients who had history of myocardial infarction (MI) (%31 versus %15, p=0,03 for active smokers and %25 versus %10, p=0,02 for history of MI, respectively) (See table). However, multivariate analysis failed to identify any independent predictor of NSE elevation after elective PCI.

Clinical and angiographic characteristics of silent neuronal ischemia (+) and (–) patients in PCI group

Variables	SNI(+), n=27	SNI(–), n=42	P value
Left anterior descending artery PCI, n (%)	16 (59,3%)	18 (42,9%)	0,18
Circumflex artery PCI, n (%)	8 (29,6%)	20 (47,6%)	0,13
Right coronary artery PCI, n (%)	12 (44,4%)	15 (35,7%)	0,46
Safen greft PCI, n (%)	0	2 (28,6%)	0,46
Active smokers, n (%)	11 (31,4%)	15 (15,3%)	0,03
History of myocardial infarction, n (%)	9 (25,7%)	10 (10,2%)	0,02
History of coronary artery by-pass graft, n (%)	2 (5,7%)	5 (5,1%)	0,89

PCI, percutaneous coronary intervention; SNI, silent neuronal ischemia.

Conclusion: For patients undergoing elective PCI, NSE levels after procedure increases. Invasive coronary procedures have risk of SNIs, even in patients with normal coronary arteries. Increased recognition of SNIs may facilitate therapies aimed at preventing their occurrence and decrease the risk of adverse neurological outcomes.

CAROTID DISEASE

P5616 | BEDSIDE
Carotid artery stenting prior to the cardiac surgery - a hybrid treatment strategy in the extended TARGET-CAS study population

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Purpose: To evaluate safety and feasibility of a less-invasive hybrid strategy for patients with severe carotid and cardiac disease - carotid artery stenting (CAS) immediately followed by an open heart surgery.
Methods: In the population of 1245 patients with severe/symptomatic internal carotid artery (ICA) stenosis enrolled in the TARGET-CAS (Carotid Artery Stenting With Patient- and Lesion-Tailored Selection of the Neuroprotection System and Stent Type) study in 2009–2014; 42 subjects (3.4%; age 70.5±7.1y; 74% male) required urgent cardiac surgery. Those with CCS class III/unstable angina/NSTEMI (n=40) and multivessel coronary artery disease or left main stenosis underwent coronary artery bypass grafting (CABG) immediately after CAS. The others (n=2) with severe aortic stenosis and recent pulmonary oedema or NYHA class III symptoms had hybrid CAS and aortic valve replacement. Symptomatic ICA stenosis (stroke/transient ischaemic attack within 6 preceding months) was present in 15 (36%) patients. Mean angiographic ICA stenosis rate was 85±11% (range 60–99%). The selection of neuroprotection devices (NPD) and stent type was done according to the TARGET-CAS study algorithm. Proximal NPD was used in 19 (45%) cases and closed cell stent was implanted in 39 (93%) patients (with high risk or symptomatic ICA lesions). Each patient was assessed by an independent neurologist pre- and post-CAS, before transfer to the cardiac surgery operating room. Operation risk according to euroSCORE was 2.6±1,1% (range 1,15–6,58%). CAS was performed on acetylsalicylic acid and unfractioned heparin only. Clopidogrel (loading dose of 300 mg) was administered in the 6th – 10th postoperative hour, after surgical bleedings were excluded and continued at daily dose of 75 mg for at least a month. Most procedures (27, 64%) were done on normothermic cardiopulmonary bypass; 6 (14%) patients had off-pump CABG.
Results: No neurological complications (stroke, transient ischemic attack) in-hospital or on 30-day observation were noted. Three (7.1%) major complications in the early postoperative period occurred: one myocardial infarct (successfully treated by percutaneous angioplasty of right coronary artery) and two deaths as a result of multi-organ failure.
Conclusion: Our findings indicate that the treatment strategy by CAS simultaneous with cardiac surgery is an effective method to prevent perioperative stroke. All major complications were surgical. This hybrid method might be a promising alternative to the conventional, combined surgical carotid endarterectomy and open heart surgery.

P5617 | BEDSIDE
Long-term outcome of patients after carotid artery stenting depending on patient age

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Background: There is still a leak of real world and long-term data regarding carotid artery stenting (CAS).
Purpose: We sought to determine the influence of patient age on the long-term stroke rate after CAS from an all-comer single center registry.
Methods: Between 1999 and 2014 all consecutive patients who underwent CAS at our center were included. An independent neurologist performed a detailed in-hospital neurological assessment including NIHSS documentation pre- and post-procedurally in every patient. A 30-day telephone interview and yearly structured questionnaires was conducted in all patients. Follow-up of up to 12 years following the procedure is available. In case of adverse events patient documents were requested and carefully analyzed.
Results: Of 952 consecutive patients who underwent CAS 510 (54%) were >70 years of age. Patients aged >70 years were more often female (40% vs. 33%; p=0.02) and were more often symptomatic (31% vs. 23%; p<0.01). Additionally, they suffered more frequently from arterial hypertension (93% vs. 89%; p=0.02), from coronary heart disease (67% vs. 60%; p=0.04), from renal insufficiency (29% vs. 14%; p<0.001), from heart failure (12% vs. 6%; p<0.001) and from atrial fibrillation (17% vs. 10%; p<0.01).
Technical success was achieved in 98% (937/952) of the cases without any difference between both groups (98% vs. 98% p=0.62). After a mean follow-up of 4.8±3.3 years (4523 patients years) the composite total of overall death and any stroke rate was 39% (201/510) in patient aged >70 years and 22% (99/442) in those aged <70 years (p<0.001), respectively. The rate of any stroke was similar between both groups (7% vs. 5%; p=0.18). In the subgroup of patients with a symptomatic carotid artery stenosis (n=259) those aged >70 years had a higher stroke rate when compared to those aged <70 years (11% vs. 5%; hazard ratio 2.68; 95% confidence interval 0.99 – 7.24; p=0.05). This difference was mainly driven by an increased 30-day stroke rate among the older symptomatic patients (7% vs. 2%; p=0.07).
Conclusion: Despite a higher risk profile for cerebrovascular events older patients (age >70) did not show a statistically significant difference in the rate of any stroke during a follow-up of up to 12 years in the overall cohort. In case of symptomatic carotid artery stenosis older patients seem to be at an increased risk for stroke in the acute phase after CAS. These findings underline the results of the CREST trial and the meta-analysis of the Cochrane Stroke Group in a real world setting and a far longer follow-up.

P5618 | BEDSIDE
The clinical relevance of myocardial injury after carotid endarterectomy

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Purpose: Myocardial infarction (MI) is a frequent complication of carotid endarterectomy (CEA), yet the majority of events are silent. Routine monitoring of postoperative cardiac troponin was implemented in our center to facilitate timely recognition of silent myocardial injury and improve subsequent diagnostic and treatment strategies. We aimed to evaluate the incidence of myocardial injury after CEA and its association with adverse cardiovascular events.
Methods: This analysis included patients ≥60 years old who underwent CEA between January 1st 2011 and December 31th 2012, whose Troponin-I levels were monitored on the first three postoperative days and were included in an observational longitudinal cohort study that assessed adverse cardiovascular events. Myocardial injury was defined as a troponin concentration >60 nanogram per liter. Endpoints were myocardial infarction, stroke, coronary revascularization and cardiovascular death during follow-up.
Results: 240 consecutive patients were included in the analysis. Indications for CEA were stroke (30%), transient ischemic attack (39%), ocular symptoms (21%) and asymptomatic (10%). Postoperative myocardial injury occurred in 35 patients (15%) and was associated with age, preoperative renal insufficiency, postoperative anemia, contralateral carotid occlusion and >100% increase in postoperative transcranial doppler velocities. After a median follow-up of 1.8 years (IQR 1.0–2.6), MI occurred in 24% vs 1.6% (RR 15.0, 95% CI 4.2–54), stroke in 5.9% vs 4.2% (RR 1.4, 95% CI 0.34–6.3), coronary intervention in 2.9% vs 2.6% (RR 1.1, 95% CI 0.14–9.3) and cardiovascular death in 5.9% vs 0.5% (RR 11.2, 95% CI 1.0–121) in patients with vs without postoperative myocardial injury, respectively. All MIs in patients with myocardial injury occurred within 30 days after surgery vs none in patients without.
Conclusion: Myocardial injury after CEA occurred in 15% of patients and was associated with multiple patient- and procedure-specific factors. After a median follow-up time of 1.8 years, the incidence of MI was significantly higher in patients with myocardial injury, which was attributable to silent NSTEMIs that occurred in the early postoperative phase. Also, a higher incidence of cardiovascular death was observed in patients with myocardial injury.

P5619 | BEDSIDE
Patients with carotid artery stenosis and recent cerebral ischemic event are less likely to have a well-developed cerebral collateral pathways, which should prompt early carotid intervention

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Background: Cerebral collateral pathways are of utmost importance in the occurrence of the first cerebral ischemic event (CIE), as well as CIE recurrence in patients with internal carotid artery stenosis (CAS).
Purpose: To assess collateral pathways in the cerebral arteries associated with severe internal carotid artery stenosis (ICAS) in patients who suffered from cerebral ischemic event (CIE) within 1 month, 3 months, distant (over 3 months), and no history of CIE.
Methods: Study group included 316 subjects in mean age 65.8±8.9y, 224 (71%)

men, who were referred to carotid artery stenting, including 54 subjects who had CIE during last 1 month, 33 with CIE between 1 and 3 months, 149 with distant CIE (over 3 months) and 80 patients who had no history of CIE.
Transcranial color-coded Doppler ultrasound (TCCD) was performed prior to carotid artery stenting in the test groups. The prevalence of collateral pathways via the anterior communicating artery (ACoA) and posterior communicating arteries (PCoAs) was evaluated.
Results: Any cerebral collateral pathway (through the ACoA or PCoA) was identified in 39 (72%) out of 54 subjects with CIE below 1 month, 18 (54%) with CIE between 1 and 3 months, 131 (88%) with distant CIE and 72 (90%) with asymptomatic ICAS.
The ACoA was found in 53%, 36%, 80% and 86% of subjects with CIE below 1 month, between 1 and 3 months, over 3 months and asymptomatic, respectively. While PCoA was found in 46%, 39%, 50% and 35% of cases in respective groups. Functioning collateral pathways were more often encountered in asymptomatic subjects as compared to subjects with CIE below 1 month (p=0.007) and between 1 and 3 months (<0.001).
Similarly, collateral pathways were more prevalent in subjects with distant CIE as compared to patients with CIE below 1 month (0.007) and between 1 and 3 months (<0.001), respectively.
Interestingly, there was no statistical difference in the frequency of collateral cerebral circulation between asymptomatic and distant symptomatic patients (90% vs 88%; p=0.636).
Analyses revealed that subjects with recent (below 3 months) CIE were less likely to develop cerebral collateral flow (57 out of 87 subjects, 66%), as compared to subjects with CIE more distant than 3 months (p<0.001) and asymptomatic ICAS (<0.001).
Conclusions: There is lower prevalence of collateral flow in patients with recently symptomatic ICAS. Thus, when timing for carotid artery stenting, the assessment of collateral flow status should be strongly recommended, prompting early carotid intervention.

P5620 | BENCH
Hypertension and age-specific burden of carotid atherosclerosis in China: results from 25,000 individuals in the China Kadoorie biobank study

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Background: Stroke rates are extremely high in China due, in part, to the burden of untreated hypertension. Measurements of carotid intima-media thickness (cIMT) and carotid plaques allow sensitive assessment of the underlying burden of the atherosclerosis.
Methods: We analysed cross-sectional data on 25,000 randomly selected individuals in the 2nd re-survey in 2013–14 of the China Kadoorie Biobank study that had screening of their extra-cranial carotid arteries performed using automated B-mode ultrasound. Measurements of cIMT were recorded as the mean of 3 measurements over a 1-cm region in the far wall of the common carotid artery at end-diastole on each side. The presence of plaque (focal IMT >1.5 mm), number of plaques and size of maximum plaque were combined in a plaque score.
Results: The mean values of the left and right carotid arteries were highly correlated for both CIMT (r=0.60) and plaque scores (r=0.62) and each measure was strongly correlated with the other (r=0.55). Figure shows that the mean cIMT (left panel) and plaque score (right panel) increased linearly with age. Mean cIMT levels were 0.59 cm, 0.74 cm and 0.85 cm and the proportions with plaque were 4%, 39% and 49%, in those with mean age of 45, 65 and 85 years, respectively. At each age group, the mean cIMT and the mean plaque scores were also positively related to the severity of hypertension. Individuals with SBP>160 mmHg or SBP>140–159 mmHg compared with those with SBP<120 mmHg had age-equivalent differences of 11 and 7 years for cIMT and 11 and 6 years for carotid plaque scores, respectively.

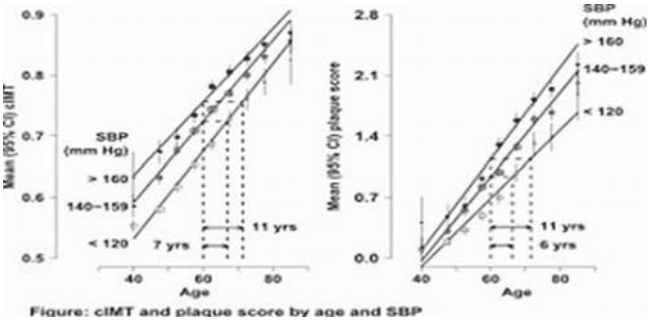

Figure: cIMT and plaque score by age and SBP

Conclusions: The high prevalence of untreated hypertension results in a high burden of atherosclerosis, suggesting that the high rates of stroke are likely to persist, or even rise further, in China over the next decade.

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P5621 | BEDSIDE
Ultrasound assessment of carotid plaque echogenicity response to statin therapy: a systematic review and meta-analysis

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Aim: To evaluate in a systematic review and meta-analysis model the effect of statin therapy on carotid plaque echogenicity assessed by ultrasound.
Methods: We have systematically searched electronic databases (PubMed, MEDLINE, EMBASE and Cochrane Center Register) up to December 2014 for studies evaluating the effect of statins on plaque echogenicity. Two researchers independently determined the eligibility of studies evaluating the effect of statin therapy on carotid plaque echogenicity, that used ultrasound and grey scale median (GSM) or integrated back scatter (IBS).
Results: Eight studies were included, in a qualitative analysis, out of 576 studies identified after electronic search. Four of the eight studies including 246 patients carotid artery data were meta-analyzed for a mean follow up of 4.3 months. A consistent increase in the echogenicity of carotid artery plaques, after statin therapy, was reported (Means standard difference =1.36, p=0.001, I2 =87.5), particularly in patients receiving high statins dose. Increased plaque echogenicity was also associated with LDL-C decrease but not CRP. Although HDL-C had an increasing trend after statin therapy the net effect was not significant (p=0.056).
Conclusions: Statin therapy is associated with a favorable increase of carotid plaque echogenicity, even after one month of treatment, and the effect was more profound using higher doses of statins. This effect seems to be related mostly to the decrease of LDL-C.

P5622 | BENCH
Fibrin clot properties are linked to the symptomatic vs. asymptomatic status of atherosclerotic carotid artery stenosis

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Background: Risk stratification in patients with carotid artery stenosis is a major challenge in contemporary vascular medicine. Although symptomatic lesion transformation is statistically rare, the consequences at patient level are devastating as 80% major strokes occur without a warning sign. In addition, only some episodes of plaque rupture or erosion lead to symptoms; others may provide a mechanism of asymptomatic plaque growth. The role of hemostatic system in modulating adverse clinical events of carotid atherosclerosis has not been elucidated.
Aim: We tested the hypothesis that clot properties might differ by symptomatic vs. asymptomatic status of carotid artery stenosis.
Methods: Fibrin clot properties including (i) the lag phase of the turbidity curve (lag, s; indicative of time required for protofibril formation), (ii) permeability coefficient (Ks; indicative of pore size), (iii) maximum absorbancy at 405nm (Abs; reflecting average fibrin fiber thickness), (iv) maximum D-dimer level increase in the clot lysis assay (D-D max, mg/L), and (v) lysis half-time (t1/2, min) were evaluated in 200 consecutive subjects (age 47–84y, mean age 66y, 109 symptomatic – 71 recently and 38 previously, 63% men) with significant carotid artery stenosis (peak systolic velocity 2.6 (1.5–6.9); end-diastolic velocity 0.8 (0.4–2.5)m/s).
Results: The groups were not different by stenosis severity, lipid profile (except HDL cholesterol that was lower in symptomatics; 1.12 v 1.21 mmol/L, p=0.017), smoking status and diabetes, renal function, hsCRP or IL-6, medical treatment and incidence of significant atherosclerotic involvement in other vascular beds (coronary, peripheral).
Symptomatic subjects showed enhanced clot formation (median lag 39.8 v 41.2, p=0.01), denser and less permeable clots (Ks 6.4 v 7.1; p=0.0001; Abs 0.94 v 0.86; p=0.006), and reduced susceptibility to fibrynolysis (D-Dmax 4.58 v 4.07; p=0.0003, t1/2 10.1 v 9.3; p<0.0001). The between-group differences remained significant after adjustment for fibrinogen level (p=0.00015). In symptomatics, the different clot characteristics showed no relation to whether ipsilateral cerebral ischaemia symptoms occurred recently or in the past, consistent with a chronic rather than acute effect of the hemostatic system properties.
Conclusions: We show, for the first time, that the symptomatic status of atherosclerotic carotid stenosis is associated with enhanced clot formation and reduced susceptibility to fibrynolysis. Apart from contribution to knowledge, this finding may be of relevence to risk prediction algorithms in patients with carotid atherosclerosis.

P5623 | BEDSIDE
Progression of atherosclerotic carotid plaque in hypertensive patients: the Campania-Salute Network

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Background: Carotid atherosclerotic plaques (CAP) progression affects prognosis in hypertensive patients. Experimental and clinical studies have shown that various antihypertensive agents exert anti-atherosclerotic action that is partly independent of the blood pressure-lowering effect. There is little information on the possible CAP progression during anti-hypertensive treatment.
Purpose: We evaluated the factors associated with CAP progression in a large hypertensive registry.
Methods: We assessed CAP progression in 2261 hypertensive patients with baseline intima-media thickness (IMT)>1.5 mm, defining clear-cut presence of CAP (age 59±10 years, 59% male) with ≥1 year follow-up. Assessment of changes in IMT was done at the time of the last available control visit. Annual IMT increase was expressed as absolute change in thickness normalized by the duration of follow-up ([change in thickness/follow-up time in years]. CAP progression was defined as an annual IMT increase ≥0.1 mm. Mean systolic and diastolic blood pressure (BP) were computed as the average values of all control visits during follow-up. Medications were considered in the model of logistic analysis when prescribed in more than 50% of the control visits during follow-up, as previously reported.
Results: At a median follow-up period of 50 (interquartile range: 12–201) months, CAP progression occurred in 554 patients (24%). Among all demographic clinical and laboratory characteristics, patients with CAP progression at the time of the last available visit exhibited older age (60.5±8.6 years) than patients without CAP progression (58.0±9.5 years; p<0.0001) and higher mean systolic BP during the follow up (139.20±12.3 vs 137.91±12.2 mmHg; p=0.03). Classes of antihypertensive medications (diuretics, ACE-inhibitors/angiotensin receptor blockers, CA++-channel blockers, beta-blockers), cholesterol lowering agent and antiplatelet agents were prescribed with similar frequency in both groups.
Conclusions: In a registry of treated hypertensive patients, the risk of CAP progression is associated with older age and less effective systolic BP control during follow-up, and is independent of the type of prescribed medications. These results suggest that only more aggressive and effective antihypertensive therapy but not specific antihypertensive medications could prevent CAP progression.

P5624 | BEDSIDE
Investigating the mechanism of action of statins in carotid plaque stability in patients undergoing endarterectomy

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Background: Oxidative stress and macrophage infiltration are associated with atherosclerotic plaque formation and instability, through endothelial dysfunction and reduced NO production. Statins are known to provide additional benefits in atherosclerosis besides lipid lowering, including the endothelial function improvement potentially by enhancement of eNOS expression and activity, but the underlying mechanisms remain unclear. We sought to elucidate the underlying signaling cascade for atherosclerotic plaque stability provided by statins.
Methods: We collected carotid atherosclerotic plaques specimens from 62 patients having undergone endarterectomy for internal carotid artery stenosis. Patients were divided into four groups: symptomatic unstable patients not receiving statins (u/nost group, n=22), symptomatic unstable patients on statin (u/st group, n=11), asymptomatic stable patients not receiving statins (s/nost group, n=9) and asymptomatic stable on statin (s/st group, n=20). Samples were examined by histopathology for plaque morphology (stable vs unstable) by immunoblotting and immunohistochemistry for p-eNOS/eNOS, p-Akt/t-Akt, iNOS and NOX-4 determination and for determination of oxidative stress biomarkers, malondialdehyde (MDA) and nitrotyrosine (NT).
Results: Stable plaques were found in 66% of patients on statins versus 33% of those not receiving statins (p=0.02). Immunohistochemistry revealed that iNOS was mainly expressed in macrophages and vascular smooth muscle cells and its expression was attenuated only in s/st group. NOX-4 expression was higher only in macrophages and reduced in both groups treated with statins. Western Blot analysis confirmed the decreased iNOS expression in the s/st group, while along with the increased p-eNOS expression in the same group. P-Akt/t-Akt ratio was significantly increased in s/nost and s/st groups and NOX-4 expression was increased in u/nost and u/st groups. MDA and NT were not different among groups.
Conclusion: Akt phosphorylation and NOX-4 expression were associated with atherosclerotic plaque stability independently of statin therapy, while p-eNOS/iNOS expression was favorable only in patients with stable plaques on statins. Oxidative stress biomarkers level did not differ among groups. p-eNOS activation with parallel decreased iNOS expression seems to be a potential mechanism for atherosclerotic plaque stabilization by statin therapy.

P5625 | BEDSIDE
Carotid artery stenting is safe and effective in patients with restenosis after carotid endarterectomy: data from a real-world single center

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Background: To investigate the periprocedural complication rate in patients with restenosis after carotid endarterectomy undergoing carotid artery stenting in a large single center series.
Methods: In our all-comer single-center registry, 68/951 (7,2%) patients underwent carotid artery stenting due to ipsilateral restenosis after prior endarterectomy. A board certified neurologist examined each patient before and after the procedure.
Results: Technical success was achieved in 97% (no stent implantation in 2 pts.). 26,5% (18/68) of the patients had a prior symptomatic carotid artery stenosis. During the 30-day FU (including procedural complications) 1 patient suffered a major stroke 5 hours after an unsuccessful attempt to position the embolic protection device and stent (total stroke rate 1,5%). This patient died during the 30-day period due to progressive neurological symptoms. Another patient died during coronary artery bypass graft surgery after previous successful treatment of the carotid restenosis (total death rate 2,9%). 1 further patient suffered a TIA during the procedure (total TIA rate 1,5%). A further restenosis after stenting occurred in 2 patients (total restenosis rate 2,9%) and could be treated successfully by balloon dilatation.
Conclusion: Carotid artery stenting in patients with a restenosis after endarterectomy can be performed safely. The rate of complications during the periprocedural period is low and comparable to patients without prior CEA.

P5626 | BEDSIDE
A prospective, multicenter study on the safety and efficacy of a novel mesh covered stent in patients with carotid artery stenosis

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Background: Carotid artery stenting (CAS) is associated with a stroke risk mainly due to dislodgement of debris from the target lesion during the procedure. The CGuard ™() is a novel thin strut nitinol stent combined with a PET-mesh covering designed to trap friable atheromatous debris to prevent embolic events from the target lesion.
Aim of the study: To evaluate the safety and efficacy of the CGuard™ system in the treatment of Carotid artery lesions in consecutive patients suitable for CAS.
Methods and results: 30 consecutive eligible patients (71.6 years, 63% male) were enrolled in 4 centers in Germany and Poland. The primary endpoint was 30 day MACE (death, stroke or myocardial infarction). Secondary endpoints included device success, procedural complications, and incidence, number and volume of new lesions assessed by DW-MRI at 48 hours post-procedure, and at 30 days. Among the risk factors, 23% were diabetics and 27% had a prior MI. Ten patients (33.3%) had a symptomatic carotid artery stenosis. Distal filter protection devices were used in 29 patients, proximal balloon protection in one. Predilatation was done in 70.9% of the cases and postdilatation in 77.4%.
The CGuard™ System was delivered and deployed in all cases, device success was 100%, the 30 day MACE was 0.0%. The flow in the external carotid artery after stenting was unimpeded in any case. The incidence of patients with new ischemic lesions at 48 hours was 46.1%, the average lesion volume 0.06 cm^3, which is a 50% reduction in the incidence and 10-fold reduction in lesion volume compared to studies also using filter protection for CAS (PROFI, JACC, April 2012, ICSS Lancet, March 2010).
Conclusions: The use of the CGuard™ system in patients undergoing CAS is feasible and safe and suggest that the MicroNetTM covered stent offers clinical benefits for patients undergoing CAS.

P5627 | BEDSIDE
Carotid arteries ipsilateral to cerebral ischemia exhibit higher temperatures in patients with ischemic stroke

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Background: Inflammation is a well recognized factor, which contributes to atherosclerosis progression and destabilization. New methods evaluating with safety, effectiveness and low cost atherosclerotic inflammation are under rigorous scientific research. Microwave radiometry (MWR) evaluates in vivo noninvasively the temperatures of internal tissues and combines the above mentioned characteristics. The aim of the present study was to evaluate the ability of Microwave Radiometry to recognize the symptomatic carotid artery, ipsilaterally to cerebral ischemia, in patients with recent ischemic stroke.

Methods: Consecutive patients with recent acute anterior circulation ischemic stroke due to large artery atherosclerosis were included in the study. Patients with history of paroxysmal or permanent atrial fibrillation were excluded. Carotid arteries of patients were evaluated within 24 hours from symptoms onset by: 1) carotid ultrasound and 2) microwave radiometry (MWR). During ultrasound study, maximum thickness of carotid plaques (maxPT) was evaluated. Only patients with bilateral carotid plaques were included in the study. During MWR measurements, temperature difference (ΔT) was defined as the maximal temperature recorded along the carotid artery minus minimum. The ipsilateral to the cerebral infarct carotid arteries, assumed to be causint the symptoms, were defined as culprit.
Results: In total 100 carotid arteries of 50 patients were analyzed. Culprit carotid arteries had higher maxPT compared to nonculprit carotid arteries (3.76±2.03 versus 2.53±1.09mm, $p<0.001$). Culprit carotid arteries had also higher temperature differences, compared to nonculprit in both vessel and patient based analysis (0.93±0.58 versus 0.58±0.35℃, $p<0.001$ and 0.98±0.59 versus 0.52±0.26℃, $p<0.001$, respectively). In multivariate logistic regression analysis, ΔT was independently associated with the culprit carotid artery, causing the symptoms, when adjusted to sex, age, vascular risk factors and maxPT (OR: 5.94, 95% CI: 1.56–22.63, p=0.01). By ROC curve analysis the optimal cutoff point of ΔT for predicting the symptomatic carotid artery was ≥0.60℃ with a sensitivity of 72% and a specificity of 60% (AUC=0.726, 95% CI: 0.626–0.827, $p<0.001$)
Conclusions: Microwave radiometry can recognize the culprit and noculprit carotid arteries in patients with recent ischemic stroke. The identification of high temperatures in asymptomatic patients with intermediate but bilateral carotid artery stenosis could better guide intensive medical treatment or intervention.

CORONARY SURGERY

P5628 | BEDSIDE
Sex specific trends in 4-year survival in 94 328 patients who underwent a first isolated coronary artery bypass graft procedure 1987-2006

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Purpose: The aim of the present study was to examine trends in age-and sex-specific 4-year survival after a first isolated coronary artery bypass grafting (CABG).
Methods: We used the National Inpatient register to identify 94,328 (74,113 men and 20,215 women) who survived the first 30 days after CABG during 1987–2006. The cohort was divided into two age groups (18–54 years, ≥55 years) and stratified into four periods (1987–1991; 1992–1996; 1997–2001, 2002–2006) with a 4-year follow-up for each five year period.
Results: A continuously decreasing trend in mortality risk was observed with a HR of (0.63, 95% CI, 0.46–0.88) in men <55 years and (HR 0.69, 95% CI, 0.63–0.76) in men aged ≥55 years in the last period (2002–2006). Among women aged <55 there was a non-significant difference in HR during the periods (HR: 1.02, 95% CI, 0.52–2.03) in 2002–2006. However, women aged ≥55 displayed a favorable decreasing trend from the first to the last period (HR: 0.62, 95% CI, 0.52–0.75)
Conclusions: During the 20 year study period there was an overall favourable trend in survival after CAGB in both men and women, except for women below 55 years of age.

P5629 | BEDSIDE
Current off-pump coronary artery bypass grafting with multiple skeletonized arterial conduits can improve clinical outcome for diabetic patients

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Background: Diabetes mellitus is a strong risk factor for worsened clinical outcome in CABG surgery. In Japan, off-pump CABG has achieved widespread application in last decade, with up to 60% of CABG cases performed via the off-pump technique. Following the development of off-pump CABG, the current trend in revascularization strategy is toward in-situ all-arterial grafting. We were interested in whether application of the current off-pump technique using multiple skeletonized arterial conduits could improve outcome for diabetic patients.
Methods: From January 2002 to December 2013, a total of 1,064 patients underwent isolated off-pump CABG. Of these 1,064 patients, 551 had diabetes (DM) and 513 did not (nDM). We compared the clinical results between the two groups using the propensity score matching technique. In the present series, over 80% of patients underwent total arterial revascularization and 74% received bilateral IMA grafting. Such a high rate of arterial reconstruction is worthy of special mention.
Results: 419 cases from each group were successfully matched in a 1:1 manner. All procedures were performed via the off-pump technique without conversion to on-pump. Eight patients in the DM group (1.9%) and four in the nDM group (1.0%) died in hospital after surgery. Multivariate analysis revealed the following independent risk factors for hospital death: peripheral vascular disease (OR 4.6, p=0.02), heart failure (OR 3.3 p=0.02), urgency (OR 5.2, p=0.001) and body mass index (OR 1.3, p=0.001); and the following risk factors for deep sterna infection: advanced age (OR 1.07, p=0.44), DM (OR 5.1, p=0.04), peripheral vascular disease (OR 8.2, p=0.007), prior cerebrovascular accident (OR 4.6, p=0.04), heart failure (OR 4.2, p=0.03), and low ejection fraction (OR 4.4, p=0.02). Follow-up was completed in 96.8% (1030/1064) of the patients to a maximum of 13 years. The rate of 12-year freedom from all causes of death was 61.5% in the DM and 73.7% in the nDM group (p=0.50). The corresponding rates for major adverse cardiac event were 71.5% and 85.4% (p=0.66). Multivariate Cox regression analysis revealed chronic kidney disease, older age, previous myocardial infarction, low ejection fraction, and peripheral vascular disease as statistically significant predictors of late death. Diabetes mellitus was not associated with any long-term outcome.
Conclusions: Off-pump CABG using multiple skeletonized arterial conduits can improve the clinical outcome of DM patients to a level equal to that of non-DM patients.

P5630 | BEDSIDE
Effect of warfarin use in patients with new-onset atrial tachyarrhythmia after isolated coronary artery bypass graft

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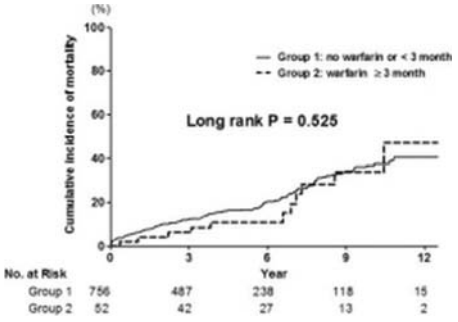
Background: New-onset atrial fibrillation (AF) has been shown to afftect late mortality after isolated coronary artery bypass graft surgery (CABG). Little is known about need for long-term warfarin therapy in patients with newly diagnosed post-CABG AF.
Methods: We evaluated long-term survival data in 4,368 patients who underwent isolated CABG from 2000 through 2011. All-cause mortality data were obtained from Korea National Registry of Vital Statistics. A Multivariable Cox proportional hazards regression model was constructed to determine the independent impact of new-onset AF after isolated CABG (POAF) on long-term survival after adjusting for several covariates.
Results: After excluding 133 patients with prior AF or atrial flutter, 4,235 consecutive patients with isolated CABG was enrolled. New-onset POAF was identified in 756 patients (17.9%) and 479 patients (63.3%) received a cardioversion or amiodarone infusion for restoration of POAF. POAF independently predicted long-term mortality (hazard ratio [HR]: 1.27; 95% confidence interval [CI]: 1.02 to 1.59) with a median follow-up duration of 6.0 years (interquartile range, 3.4–8.9 years). However, treatment with warfarin for >3 months in POAF patients did not significantly reduce long-term mortality compared with POAF patients receiving no warfarin or warfarin for <3 month (Figure).



Conclusion: Symptomatic POAF is significantly associated with poorer long-term survival. However, long-term treatment of warfarin after POAF does not provide survival benefit compared with no or short-term treatment of warfarin.

P5631 | BEDSIDE
Coronary artery bypass graft surgery in acute coronary syndrome: when to operate?

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Introduction: The optimal timing of coronary artery bypass graft (CABG) surgery in acute coronary syndrome (ACS) remains controversial. Early surgical revascularization may minimize necrosis and reduce the risk of re-infarction, but has been associated with a higher morbidity and mortality.
Purpose: This study aims to determine the impact of early and late CABG surgery in post-operatory outcomes and long-term survival, in patients after ACS.
Methods: Retrospective analysis of data of 128 patients admitted for ACS who underwent CABG, from January 2013 to November 2014. Post-operative and long-term adverse outcomes were compared between patient categories, based on ACS-to-CABG time: group A (0–6 days, n=31); group B (7–13 days, n=74); group C (≥14 days, n=23).
Results: There were no significant differences between groups in patient's age, co-morbidities, type of ACS and coronary artery disease anatomy. As the admission-to-CABG interval increased, there was a progressive increase in peak

of cardiac troponin (p=0.03). Post-operatory major organic dysfunctions (cardiac, respiratory and renal) were similar between groups. Group B presented a longer post-operatory hospital stay (median 5 days, IQR 4–7, p<0.05). Extracorporeal circulation during surgery was significantly associated with a decrease in post-operatory complications (OR 0.32, 95% confidence interval (CI) 0.13–0.74, p<0.01).
With a mean follow-up of 11.0±6.8 months, overall mortality was 3.1%. After multivariate logistic regression analysis (adjusted for age and cardiovascular risk factors), left main disease was a determinant of increased post-operatory complications, acute myocardial infarction (AMI) and long-term mortality (OR 2.84, 95% CI 1.12–7.23, p=0.03). Time from admission to CABG was not a risk factor for post-operatory complications, AMI or long-term mortality (group A: OR 0.76, 95% CI 0.29–2.02, p=0.58; group B: OR 1.63, 95% CI 0.70–3.75, p=0.25; group C: OR 0.65, 95% CI 0.24–1.77, p=0.40).
Conclusion: In this group of patients after ACS, critical left main disease, but not time from admission to CABG, was a predictor of short and long-term adverse outcomes.
Our findings emphasize the importance of early surgery in patients with left main disease, whereas in those with larger infarct extension (higher troponin values), delaying surgery may reduce the risk of post-operatory adverse events.
Ultimately, the optimal surgical timing remains an individualized decision.

P5632 | BEDSIDE
Role of HDL-C in patients undergoing coronary artery bypass grafting

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Background: Previous studies showed that high-density lipoprotein cholesterol (HDL-C) functionality may be impaired under certain conditions, affecting their beneficial effects. We previously reported about the lack of the protective role of HDL-C among patients who underwent coronary artery bypass grafting (CABG).
Purpose: To further investigate the protective role of HDL-C in the settings of CABG patients.
Methods: A consecutive series of 2016 patients undergoing isolated first-time elective CABG at one institution between 2004 and 2011 was studied. According to the ATPIII criteria, pre-operative HDL-C values were used to identify patients with high (Group A) vs. low (Group B) HDL-C. To eliminate biased estimates, a propensity score model was built and two cohorts of 1:1 optimally matched patients were obtained. Cumulative survival and major adverse cardiovascular events (MACE) were analyzed by means of Kaplan–Meier method, and Cox proportional-hazards regression models were used to identify independent predictors of MACE and death.
Results: Propensity matching identified two cohorts of 711 patients each. At a median follow-up time of 34 months, mortality was 60/711 (8.4%) in Group A, and 49/711 (6.9%) in Group B (p=0.26). Three-year survival free from MACE was 58.3±4.1% for Group A vs. 68.6±3.5% for Group B (Chi-squared 17.6, p=0.02). Regression analysis showed that pre-operative HDL-C levels were associated with increased MACE occurrence during follow-up (HR 1.76, p=0.04).
Conclusion: Higher HDL-C levels are not associated with reduced risk of vascular events in patients with coronary artery disease undergoing CABG. Present findings may encourage efforts to improve HDL-C functionality rather than arbitrary increasing their levels.

P5633 | BENCH
Should bilateral internal thoracic artery grafting be used in patients with left main disease?

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Objectives: Left main (LM) disease is a severe form of coronary artery disease. Coronary artery bypass grafting (CABG) is the standard of care for patients diagnosed with complex lesions of the left main (LM). Improved survival of patients treated with internal thoracic artery (ITA) grafts used to bypass the left anterior descending (LAD) artery is believed to be related to their better long-term patency compared to saphenous vein grafts (SVGs). Survival is further improved when two ITAs are used.
The purpose of our analysis is to compare outcomes of bilateral ITA's (BITA) grafting to that of single ITA and other conduits such as saphenous veins (SVG) and radial artery (RA) in patients with presented with LM disease.
Methods: Seven hundreds and fourty seven patients with LM who underwent BITA grafting between 1996 and 2008 were compared with 352 LM patients who underwent coronary artery bypass grafting (CABG) with only one ITA and SVG or RA.
Results: Patients undergoing SITA were older, more often female (40.9% vs.27.4% in the SITA vs. BITA groups, respectively), more likely to have chronic obstructive lung disease, (20.5% vs.12.6%),Diabetes,(50% vs. 32%) renal insufficiency,(18.2% vs. 6.6%) peripheral vascular disease (32.1% vs.21.2%) acute MI (28.4% vs. 19.1%), emergency operation (40.9% vs.27.4%). p<0.001 for all risk factors, and EF<30% (10.8% vs. 7.1%, P=0.034)
Euroscore of SITA patients was significantly higher (8.97 + 3.73 vs. 6.23 + 4.51 P=0.01). Operative mortality (3.5% vs. 3.9% in BITA and SITA) and sternal wound infections (2.4% vs. 3.1%) were not significantly different between groups.
Mean follow-up was 11.5±2 years. Ten-year survival (Kaplan-Meier) of the SITA group was significantly lower than that of the BITA group (50.0+2.8% vs. 69.1+1.7%, P<0.001, Log Rank test). However, assignment to the BITA group was not associated with better COX-adjusted survival (HR 0.958, 95% CI: 0.822–1.118, P=0.588)
Conclusions: This large cohort study does not support routine use of BITA in all patients presented with LM disease. Similar long term survival can be achieved with SITA. Larger studies of subsets of LM patients that had better Kaplan- Meier survival are required.

P5634 | BEDSIDE
Do diabetic patients benefit from bilateral internal mammary artery grafting?

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Introduction: Bilateral internal mammary artery (BIMA) grafting has been associated with increased long term survival when compared to single internal mammary artery (SIMA), but its benefit on diabetic patients remains controversial.
Purpose: To compare long-term survival following BIMA versus SIMA grafting between diabetic and non-diabetic patients.
Methods: We retrospectively reviewed all the patients who underwent isolated CABG and received two or more grafts with at least one IMA graft between 2004 and 2013. Kaplan-Meier analysis was used to compare long-term survival between BIMA and SIMA in both groups (diabetic vs. non-diabetic). Propensity score matching with 2:1 and 1:1 pairing was used to adjust for treatment selection bias.
Results: 1259 out of 3045 eligible patients were diabetic (19% insulin-dependent) and mean follow-up was 4 years. In unadjusted analysis, BIMA was less common in diabetic patients (29.7% vs. 37.6% for diabetic vs. non-diabetic patients). Although diabetic patients had a higher Euroscore II (median 1.78 vs. 1.38 for diabetics vs. non-diabetics), hospital mortality was similar (1.1% vs. 1.0% for diabetics vs. non-diabetics). Sternal wound infection was more prevalent in diabetic patients (0.9% vs. 0.2% for diabetics vs. non-diabetics). BIMA was associated with better long-term survival than SIMA in both groups (cumulative survival of 87% vs. 70% in diabetic patients and 89% vs. 79% in non-diabetic patients, respectively). After propensity score matching, BIMA was associated with increased long-term survival in the non-diabetic cohort (n=1042, HR: 0.570 CI95%: 0.342–0.950), but there was no statistically significant difference in the diabetic cohort (n=850, HR: 0.774 CI95% 0.447–1.339). In-hospital mortality and sternal wound infection were low in matching cohorts irrespectively of the number of IMA grafts.
Conclusions: BIMA grafting was associated with better long-term survival in non-diabetic patients who underwent CABG, without increasing hospital mortality or sternal wound infection regardless of diabetes status. BIMA grafting appears to be safe for diabetic patients, despite the apparent lack of significant survival advantage.

P5635 | BEDSIDE
BIMA versus SIMA in coronary artery bypass grafting surgery long-term survival: retrospective cohort with propensity matched analysis

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Background: It remains controversial whether long-term outcomes and post-operative complications favour bilateral internal mammary artery (BIMA) grafting vs. single internal mammary artery (SIMA) grafting in coronary artery bypass grafting surgery (CABG).
Purpose: Our main aim was to compare long-term survival following BIMA versus SIMA grafting in our tertiary care centre.
Methods: Retrospective cohort including consecutive patients from 2004 to 2013 who underwent isolated CABG and received two or more bypasses with at least one IMA graft. Data were obtained from the Department of Cardiothoracic Surgery database. Mean follow-up was 4 years, maximum of 10. Kaplan-Meier analysis was used to compare long-term survival between BIMA and SIMA. Propensity score matching with 2:1 pairing was also employed to adjust for treatment selection bias. Secondary end-points were hospital mortality and sternal wound infection.
Results: BIMA was performed in 1050 (34%) out of 3080 eligible procedures. BIMA was more likely to be used for patients who were younger (age 58.5±9.6 vs. 66.5±8.8), men (86.1% vs. 77.2%), more frequently active smokers (27.1% vs. 14.9%) and dyslipidemic (77.3% vs. 71.4%). On the other hand, BIMA was less frequently used for patients with diabetes (35.7% vs. 44.3%), hypertension (68.7% vs. 74.8%) and severe renal impairment (CC<50mL/min: 5.6% vs. 17.0%). Hospital mortality was 1.1%. All-cause mortality at the end of follow-up was 11.1%. BIMA was associated with longer survival on unadjusted analysis

with a cumulative survival of 88.3% vs. 75.5% for patients undergoing BIMA versus SIMA grafting, respectively (Log-Rank test p<0.001). After propensity score matching (n=2133, 41% BIMA), BIMA was associated with increased long-term survival (HR: 0.590, 95% CI: 0.412–0.845, p=0.004), without increasing hospital mortality or the risk of sternal wound infection.
Conclusions: BIMA improved long-term survival in patients undergoing CABG in our tertiary care centre. Our findings lent further support to the revision of coronary revascularisation guidelines in order to encourage BIMA over SIMA grafting.

P5636 | BEDSIDE
An event driven myocardial infarction definition using troponins after coronary artery bypass surgery in the coronary trial

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Background: The Third Universal definition for myocardial infarction (MI) after coronary artery bypass (CABG) surgery is arbitrarily based on cardiac biomarker threshold >10 times the 99th percentile of the upper limit of normal (ULN). Given the ubiquitous release of troponins during CABG surgery and the sensitivity of troponins for cardiomyocyte injury, the prognostic value of this threshold is debated after CABG.
Methods: The CORONARY Trial was a large randomized controlled trial that compared on-pump versus off-pump CABG. Using data from CORONARY, we aimed to establish the peak troponin thresholds during the first 3 postoperative days associated with an increase at least 2-fold in 30-day mortality. In order to combine different troponin assays, we analysed the troponins in multiples of their respective ULN. We used a modification of the Mazumdar method to identify the lowest troponin threshold that had an independent hazard ratio (HR) greater than 2 for 30-day mortality after adjustment for EuroSCORE and on-pump versus off-pump surgery.
Results: Peak troponin results were available for 1528 patients who underwent on-pump (n=760) or off-pump CABG (n=768) in the CORONARY trial. Peak troponins were >10xULN in 46% (705/1538) of patients. The median peak troponin results were 8.7xULN (interquartile range 27.83). The sensitivity of a peak troponin >10xULN for 30-day mortality was 65% (95% CI 46–80). The associated specificity was 54% (95% CI 52–57). With the Mazumdar method, the first threshold we evaluated was 180xULN because 177xULN corresponded to the 95th percentile. This threshold was associated with an adjusted HR for 30-day mortality of 7.6 (95% CI 3.4–17.1) when compared to <130xULN. The next independent threshold was 130xULN with an adjusted HR for 30-day mortality of 7.8 (95% CI 2.3–26.1) when compared to <130xULN. The next threshold that we tested (70xULN) did not meet our criteria for significance.
Discussion and conclusion: In light of the very high incidence of troponin elevations >10xULN after CABG surgery, the current MI definition biomarker criterion is neither sensitive nor specific. Our results suggest that a clinically relevant troponin threshold is much higher. However, our sample size did not allow a finer exploration of thresholds between 70xULN and 130xULN. The VISION (Vascular events In Surgery patIents cOhort evaluatioN) Cardiac Surgery Study, a 15,000-patient cohort that is currently recruiting will allow derivation of a more precise estimate for the optimal event driven MI definition after cardiac surgery.

P5637 | BEDSIDE
Usefulness of the logistic clinical syntax score in prediction saphaneous vein graft failure in patients undergoing coronary artery bypass grafting

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Background: We investigated the association between the preoperative logistic clinical syntax score (log CSS), saphenous vein graft (SVG) patency, and major adverse cardiac and cerebrovascular events (MACCE) after coronary artery bypass surgery (CABG).
Methods: Of 1875 patients undergoing isolated CABG between 2009 and 2011, 267 patients, who later underwent coronary angiography, were included in the study. The primary endpoint was at least one graft occlusion on the follow-up coronary angiogram. The secondary endpoint was a composite of MACCE.
Results: Both SYNTAX score and log CSS were significantly higher in the patients with graft failure than in those without (31.6±5.5 vs. 27.0±5.2, P<0.001 for SYNTAX score and 12.28±2.76 vs. 4.56±2.15, P<0.001 for log CSS, respectively) In multivariate analysis, log CSS was found as a strong predictor of SVG failure (OR: 0.66, 95% CI: 0.46–0.94, P=0.02; and OR: 2.21, 95% CI: 1.02–4.75, P=0.04, respectively).If the level of score 8 was used as a cutoff value, higher levels of log CSS could predict the presence of SVG failure with 95.0% sensitivity and 95.7% specificity.
Regarding the relation between MACCE and log CSS, log CSS was also higher in the patients with MACCE compared to those without (11.7±2.9 vs. 6.1±3.9, P<0.001). The AUC was significantly higher for log CSS compared with the SYNTAX score (0.862 and 0.683, respectively; P=0.001). In the ROC analysis, in predicting MACCE, log CSS >9.5 had a 84.4% sensitivity and 81.1% specificity.
Conclusion: The addition of clinical parameters to the anatomical SYNTAX score, termed as "log CSS", augmented the accuracy and reliability of the prediction of SVG failure and MACCE in patients undergoing CABG.
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P5638 | BEDSIDE
Does metformin exhibit liver protective properties in diabetic patients undergoing CABG?

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Background: Metformin is an oral antidiabetic drug belonging to biguanide class. It is considered as the first line of treatment in diabetics especially for those who are obese. Recent studies have demonstrated some cardioprotective properties of metformin in patients with acute coronary ischemia. Other end organ effects are yet to be validated.
Methods: At a single center, a total of 200 consecutive diabetic patients underwent on-pump isolated CABG from July 2013 to July 2014. All patients on metformin prior to surgery continued taking the drug until the day of surgery and -unless contraindicated- metformin was restarted the next day after surgery. All clinical parameters including cardiac, kidney and liver function test were serially collected until discharge.
Results: At the time of CABG, 68 patients were taking metformin (34%) and 132 patients were taking other antidiabetic agents (66%) respectively. Both groups were comparable in the following: age in years (58.3±9.1 vs. 57.5±10.0; p=0.544), body mass index kg/M2 (28.4±5.6 vs. 27.7±4.4; p=0.388), pre-operative left ventricular ejection fraction of <40% (17.6% vs. 15.2%; p=0.546), and viral hepatitis (1.5% vs. 0.8%; p=0.631). Prior to surgery, the metformin users had a slightly higher glycosylated hemoglobin HbA1C% (8.8±1.6 vs. 7.8±1.9; p=0.001) but a significantly lower serum creatinine umol/l (85.0±21.6 vs. 95.20±23.9; p=0.006). During surgery both groups respectively had similar cardiopulmonary bypass times in minutes (60.9±45.1 vs. 64.4±42.3; p=0.604) and similar ICU stay in hours (41.3±36.1 vs. 40.0±45.0; p=0.955). The peak postoperative cardiac enzymes CKMB U/l (74.3±104.8 vs. 80.8±62.8; p=0.647) and peak Troponin I ug/l (2.3±3.2 vs. 3.1±4.1; p=0.209) were similar in the two groups. The postoperative median serum creatinine umol/l was significantly higher in the non-metformin users (90.1±22.7 vs. 107.8±61.7; p=0.004). The median transaminase liver enzymes ALT U/l (47.6±17.9 vs. 66.2±77.9; p=0.010) and AST U/l (38.1±26.0 vs. 51.9±50.9; p=0.012) were significantly higher in the non-metformin users. All clinical endpoints including: death, myocardial infarction, stroke, renal failure, and atrial fibrillation were similar.
Conclusion: The patients who are taking metformin prior to CABG and who continue its use after surgery seem to have a reduced surge in the transaminase enzymes. This novel finding may suggest that metformin may exhibit some liver protective properties. Further experimental studies are warranted to verify this finding.

P5639 | BEDSIDE
The anemia conundrum in cardiac surgery: does it enhance risk assessment?

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Objective: Preoperative anemia is a well-known predictor of morbidity and mortality after cardiac surgery procedures. Nevertheless, the European System for Cardiac Operative Risk Evaluation (EuroSCORE), even in its most recent version, ignores this feature. This study explored whether adding anemia to conventional scoring could enhance risk assessment.
Methods: Data on 1765 consecutive patients (age: 67.6±10.3; female: 33.1%; anemic: 33.8%; preoperative creatinine clearance: 75.6±21.2mL/min; mean euroSCORE: 5.8±2.9; urgent/emergent: 12.9%; redo: 6.2%; isolated CABG: 40.1%; isolated valve procedures: 30.4%; combined: 11.2%; aortic: 13%), who underwent on-pump procedures in a single centre from 2011 to 2013, were retrieved from Puglia Adult Cardiac Surgery Registry. Logistic regression analysis of mortality predictors was performed forcing anemia and additive euroSCORE into the model. The c-statistic of a predictive model encompassing both anemia and euroSCORE was calculated and confronted to that inherent to isolated euroSCORE.
Results: Overall observed mortality rate was 2.6%; the medium risk group (EuroSCORE 3–5) had 544 patients with 1.8% observed mortality (1% vs 3.7% in non anemic vs anemic patients; p=0.044), the high risk group (EuroSCORE 6 plus) had 874 patients with 3.9% observed mortality (2.7% vs 5.5% in non anemic vs anemic patients; p=0.027). Both anemia (β=2.13; 95% CI: 1.14–3.98; p=0.018) and EuroSCORE (β=1.34; 95% CI: 1.21–1.48; p<0.0001) proved predictors of mortality. The area under the ROC curve of the model encompassing both anemia and Euroscore was 0.773, 95% CI: 0.71–0.83, while c-statistic of the isolated Euroscore was 0.736; 95% CI: 0.663–0.809.
Conclusions: Preoperative risk stratification is enhanced when taking into account preoperative anemia.

P5640 | BEDSIDE
Validation of STS and EuroSCORE 2 for risk prediction in off-pump coronary artery bypass graft surgery (CABG)

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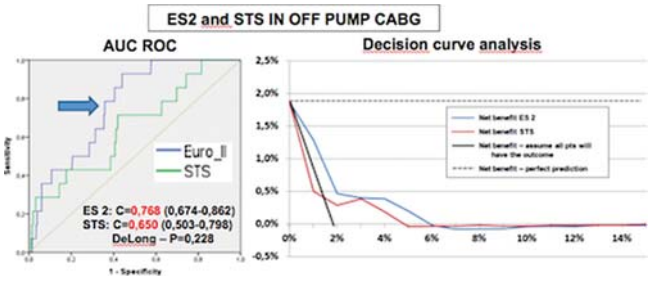
Introduction: Risk prediction in CABG with risk scores is still evolving.
Purpose: To evaluate predictive value of STS/ES2 in off (OPCAB) and on-pump (ONCAB) CABG.
Methods: All CABG pts (Jan2010-Dec2014) included. Predictive ability (STS/ES2) was evaluated for performance (O/E mortality ratio), calibration (calibr. plots, Hosmer-Lemeshow H-L), discrimination (ROC), Net Reclassification Improvement (NRI) and decision analysis (net clinical benefit).
Results: 1754pts, 63y, 69%male. OPCAB 749pts (48%). Mean ES2 (1.81%), STS (1.33%). Overall mortality: 4,2%. OPCAB had lower mortality (1.9% x 5,9%,p=0.008) and MACCE (8.1% x 12,7%, p=0.002). ES2 (OR=1.37) and STS (OR=1.29) were independent predictors of in-hospital mortality (p<0.001). Both tended to underestimate risk in overall cohort (O/E>1.8) and ONCAB (O/E >2.4). In OPCAB, STS also underestimates risk (O/E=1.8), but ES2 is well calibrated (O/E 1.13). Calibration plots showed adequate calibration for both (H-L p=0.38 and p=0.46) in the ONCAB group. Accuracy of ES II and STS was similar, overall (AUC 0,741 and 0,721, p=0,237). In ONCAB, accuracy of ES2 was better than STS ((AUC=0,768 vs 0,650, DeLong:p<0,0228). ES2 improved NRI vs STS (NRIev:+34,7%, NRInonev: –23,4%, NRItotal:+11,3%; p<0,001). In OPCAB, ES2 NRI was even better (NRIev:+50%, NRInonev:- 22,2%, NRItotal:+27,8%; p<0,001). At clinically relevant threshold probabilities there is a Net Benefit of using ES2 (for each 1000pts, 4 more outcomes correctly predicted without increasing false positive).



ROC curve/Decision Analysis

Conclusion: ES2 and STS have good calibration and discrimination in CABG. In OPCAB pts, ES2 have better calibration and discrimination improves risk reclassification and has a relevant Net Benefit (clinical impact); therefore, ES2 is the risk model of choice in OPCAB.

P5641 | BEDSIDE
Female gender is an independent predictor of survival in coronary artery bypass surgery: a single centre experience

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Introduction: The impact of gender on coronary artery bypass graft (CABG) outcomes remains controversial.
Purpose: In this study, evaluates the impact of sex as an independent factor for early and late mortality following isolated CABG surgery.
Methods: We retrospectively analysed a cohort of 3396 patients who underwent isolated CABG between January 2004 and December 2013. Clinical data, hospital mortality, morbidity from clinical records and late mortality were compared between male and female patients. Survival analysis was performed using Kaplan-Meier curves, multivariable adjustment with Cox regression and a propensity score analysis.
Results: Females (20%) were older (66.56±9.5 vs 62.95±10.1 p<0.001 for female and male, respectively) and had more obesity (32.2% vs 21.7% p<0.001), hypertension (84,5% vs 69,4% p<0.001), diabetes (53.0% vs 37.3% p<0.001), NYHA III-IV (11.8% vs. 6.5% p<0.001), renal impairment (25.9% vs 11.9% p<0.001), previous myocardial infarction (50.0% vs 46.1% p<0.001), angina pectoris (71.7% vs 67.7% p<0.001) and critical pre-operative state (6,2% vs 4.4% p=0,046). On the other hand, they had a lower prevalence of smoking (2.9% vs 23.0% p<0.001) and peripheral artery disease (PAD 13.3% vs 18.2% p=0.002). Bilateral internal mammary arteries (BIMA) were used less commonly in females (21.2% vs 33.5% p<0.001). Despite presenting a similar number of diseased coronary vessels, female received a lower number of grafts (2.54±0.88 vs 2.70±0.88 p<0.001). After propensity score matching (675 per group), female gender was an independent predictor of better long-term survival (HR 0.682 95% CI 0.510–0.912). Moreover, women had a lower risk of hospital mortality (OR 0.384 95% CI 0.157–0.935) and a lower incidence of post-operative low cardiac output syndrome (OR 0.756 95% CI 0.601–0.952). Female gender, BIMA CABG (HR 0.584 95% CI 0.371–0.917) was also associated with better long-term survival. On the other hand, age (HR 1.036 95% CI 1.022–1.049), PAD (HR 1.687 95% CI 1.352–2.104), NYHA III-IV (HR 1.802 95% CI 1.196–2.715), critical preoperative state (HR 1.516 95% CI 1.050–2.187), left ventricular ejection <44% (HR 1.443 95% CI 1.122–1.855), previous cerebrovascular disease (HR 1.392 95% CI 1.039–1.866), severe renal impairment (HR 2.097 95% CI 1.613–2.727) and no mammary artery graft (HR 1.925 95% CI 1.241–2.986) were independently associated with worse long-term survival.
Conclusions: In this patient population, women undergoing CABG showed lower hospital and long-term mortality, even if they had more risk factors and received a lower number of grafts and less frequently BIMA.
Acknowledgement/Funding: FCT

P5642 | BEDSIDE
Impact of gender on long-term outcomes following surgical versus interventional revascularization

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Background: Coronary artery bypass grafting (CABG) has historically had a higher mortality in women than men. Data regarding the impact of gender on outcomes for percutaneous coronary interventions (PCI) have been heterogeneous. Since patient selection for randomized clinical trials comparing CABG with PCI may not reflect clinical practice, we investigated the impact of gender on outcomes of CABG vs. PCI in a prospective community-based registry of all coronary revascularization (CR) patients.
Methods: All patients undergoing isolated CR in a network of 8 community hospitals were enrolled. Follow-up was obtained after 5 or more years (63.5±27.9 months; median, 79.7) by patient and/or physician contact and query of the Social Security Death Index. ST-elevation myocardial infarction and salvage patients were excluded. Propensity-score matching was used to account for differences between groups.
Results: There were 2,162 men (673 CABG, 1489 PCI) and 991 women (294 CABG, 697 PCI). The incidence of major adverse cardiac events (MACE) for CABG versus PCI was 26.5% vs. 41.8% (p<0.001) for men, but 35.7% vs. 41.9% for women (p=0.07). Using propensity score-matching to account for differences between CABG and PCI populations, MACE for men remained significantly different (25.8% vs. 41.8%, p<0.001), while female patients showed no difference between CABG and PCI (39.1% vs. 42.6%; p=0.496). Overall MACE for men was lower than that for women (33.4% vs. 40.5%; p=0.016) and appeared to be related to improved outcomes following CABG in men compared with women. However, when matched groups were used to account for differences in risk factors between male and female patients, MACE was comparable between men and women for both CABG (male vs. female, 25.1% vs. 30.6%, p=0.167) and PCI (37.1% vs. 39.3%, p=0412).
Conclusions: In an unselected cohort of patients undergoing CR in a contemporary community hospital setting, comparable male patients appear to benefit from improved long-term survival and reduced MACE with CABG vs. PCI. However, female patients appear to have equivalent outcomes with either procedure. Further analysis suggests that it is the difference in risk factors between the sexes, rather than gender itself, that accounts for this difference, emphasizing the critical importance of accounting for gender differences in evaluating outcomes following CR.
Acknowledgement/Funding: Cardiopulmonary Research Science & Technology Institute; Florida Heart Research Institute

P5643 | BEDSIDE
Reduced benefit of delayed coronary artery bypass graft surgery after acute coronary syndromes

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Background: In patients with acute coronary syndromes (ACS), early myocardial revascularization is increasingly used, but the optimal timing remains uncertain, especially in patients eligible for coronary artery bypass graft surgery (CABG). Many patients submitted to coronary angiography and with a suitable coronary anatomy, do not proceed to CABG during the initial hospitalization and are discharged with a planned surgical procedure.
Objective: To evaluate the benefit of this unselected delayed CABG (cases = planned CABG at discharge), in comparison with the patients referred for CABG during the initial hospitalization (controls).
Methods: We studied 408 consecutive patients admitted for non-ST-segment elevation acute coronary syndromes (NSTEACS) with obstructive coronary disease referred for CABG since 2009. Our study population included 55 cases and 353

controls. Patients with cardiogenic shock or mechanical complications were excluded. The study endpoint was the incidence of death at 1 year.
Results: CABG was performed in 89% of cases with a median time delay of 105 days and in 99% controls (2 patients died before surgery) with a median time delay of 7 days after admission (p=0.026). The cumulative incidence of death at 1 year was 21.8% in cases and 11.5% in controls (p=0.033). Cox proportional hazard models identified delayed CABG (HR 1.96; 95% CI 1.03–3.73), left ventricular ejection fraction <50% (HR 2.58; 1.46–4.56) and GRACE score ≥158 (HR 2.12; 1.20–3.74) as independent predictors of mortality at 1 year.
Conclusions: In our population, a post-discharge surgical coronary revascularization practice was associated with increased mortality at 1 year.

P5644 | BEDSIDE
Sleep apnea is associated with new-onset atrial fibrillation after coronary artery bypass grafting: Results from SABOT study

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Background: Previous studies using questionnaire as a surrogate for sleep apnea have produced conflicting findings on the relationship between sleep apnea and occurrence of post-coronary artery bypass grafting (CABG) AF.
Methods: We prospectively recruited 171 patients listed for an elective CABG for an overnight sleep study. Sleep apnea was defined as Apnea-Hypopnea Index ≥5. Primary endpoint is new-onset AF during in-hospital stay.
Results: Among the 160 patients who completed the study, those in the sleep apnea group (n=128, 80%) had larger left atrial diameter (40.4±5.4 versus 38.4±6.0 mm, p=0.03) and left ventricular end diastolic dimension (52.6±7.9 versus 49.2±6.8 mm, p=0.03) than those in the non-sleep apnea group. Patients in the sleep apnea group had a higher body mass index and waist circumference. The incidence of post-CABG AF (adjudicated independently) was higher for the sleep apnea than non-sleep apnea groups (24.8% versus 9.7%, p=0.07). The AF occurred on an average of 75±92 and 45±39 hours after the CABG in the sleep apnea and non-sleep apnea groups, respectively (p=0.60). There was one in-hospital death and two acute renal failure requiring dialysis after CABG in the sleep apnea group. None of the patients developed in-hospital stroke. Length of hospital stay was similar between the two groups (8.3±3.9 versus 7.8±3.6 days, p=0.4). Multiple logistic regression analysis showed the sleep apnea was an independent predictor of post-CABG AF (OR 4.8, 95% CI 1.1–18.1, p=0.004).

Multiple logistic regression of sleep apnea and post-CABG AF

Post-CABG AF	Adjusted odds ratio	Robust 95% CI	p-value
Sleep apnoea			
No (AHI <5)	Reference	Reference	Reference
Yes (AHI ≥5)	4.38	1.06–18.07	0.04
Mitral E/A	1.47	0.66–3.28	0.35
Age (years)	1.05	0.99–1.12	0.12
Hyperlipidemia			
Without	Reference	Reference	Reference
With	4.15	1.24–13.89	0.02
Left atrial diameter (mm)	1.18	1.05–1.32	<0.01
Left ventricular diastolic dimension (mm)	1.01	0.95–1.08	0.73
Chronic renal failure			
Without	Reference	Reference	Reference
With	6.28	1.87–21.06	<0.01

CI, confidence interval.

Conclusion: The incidence of post-CABG AF for patients in the sleep apnea group was nearly five times as high as that for patients in the non-sleep apnea group, probably related to atrial and ventricular remodeling.
Acknowledgement/Funding: National Medical Research Council, Singapore Ministry of Health

P5645 | SPOTLIGHT
Hospital-acquired pneumonia increases risk of mediastinitis after cardiac surgery

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Background: Mediastinitis after heart surgery prolongs in-hospital stay, and increases morbidity by 50% and mortality by 14 to 47%. In Mexico, its incidence has been reported to be 0.34%, and worldwide, 0.6%-4%. Postoperative pneumonia has not been reported as an established risk factor for mediastinits, however it is linked with a high mortality rate.
Materials and methods: We retrospectivily reviewed patients who underwent cardiac surgery (n=3398) from May 2009 to May 2014, diagnosed with mediastinitis according to clinical 2014 CDC criteria were selected and compared with a control group. Healtchare-associated pneumonia was identified in patients with and without mediastinitis and its relationship analysed with multivariate chi square test, and was also performed for other epidemiologic characteristics. The statistical analysis was made using the Stata software.
Results: Forty-nine patients fulfilled the CDC criteria for mediastinitis. Mean age was 53.6±16.2. Both groups were well balanced. Staphylococcus epidermidis was the leading microorganism at the surgical wound. There was a prevalence of 18.8% for in-hospital pneumonia, 42.5% were related to mediastinitis, finding the same germ in 45% of the cases. The presence of Pneumonia confers an OR=6.3 (CI: 2.7–14.34) P<0.01, for developping mediastinits, obesity confered an OR of 2.5 (CI: 1.2–5.4) p<0.01 and diabetes confers an OR of 2.6 (CI: 1.2–5.6) p0.005 Of note mediastinitis was not related to the need of blood or plasma transfusion, OR 0.99 p=0.37. Mortality in patients with mediastinitis was 28.5%.
Conclusions: Mediastinitis after open heart surgery is an overwhelming complication. Among different risk factors pneumonia, obesity and diabetes stand out. Future research should focus in evaluating temporal relationship with pneumonia and mediastinitis and implementing measures to prevent this dreadful complication.

P5646 | BEDSIDE
Comparison of quality of life among patients with multivessel coronary artery disease treated with CABG or hybrid coronary revascularization

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Background: Even though CABG is still a gold standard for treatment of patients with multivessel coronary artery disease (MVCAD), hybrid coronary revascularization (HCR) a strategy consist of minimally invasive direct coronary artery bypass (MIDCAB) LIMA-LAD grafting using endoscopic LIMA harvesting and catheterbased techniques with implantation of DESs in non-LAD vessels, is a new, accepted method of revascularization in this group of patients. There is a lack of data comparing those two methods in terms of quality of life.
Aim: The aim of this study was to assess the quality of life (QoL) in patients with multivessel coronary artery disease according to the method of revascularization: standard coronary artery bypass grafting (CABG) or hybrid coronary revascularization (HCR) with the use of the generic SF-36 questionnaire.
Methods: From a total of 200 patients with MVCAD enrolled to the POLMIDES study (Prospective randomized pilOt study evaluating the safety and efficacy of hybrid revascularization in MultI-vessel coronary artery DisEaSe) randomly assigned to undergo CABG or HCR (in a 1:1 ratio) we analyzed 159 patients (75 from HCR and 84 from CABG group) who completed correctly SF-36 questionnaire before revascularization procedures and during follow-up visit at 12 months. The differences between second and first score in both HCR and CABG groups were assessed.
Results: Most of the baseline clinical characteristics were similar in HCR and CABG groups. In both groups significant improvement in QoL was seen at follow-up visit. Patients from HCR group had both at baseline (51.3 vs. 59.2; p=0.006) and at 12-month follow-up (65.6 vs. 73.7; p=0.0034) significantly better scores than patients from CABG group. The differences between scores at 12-month follow-up and at baseline were not statistically significant between the groups. Additionally significant clinical improvement had been noted in Social Functioning (SF) and Role Emotional (RE) in patients with preserved left ventricle ejection fraction on admission (p=0.0058 and p=0.039, respectively) and in General Health (GH) and Bodily Pain (BP) in older patients (p=0.018 and p=0.026, respectively).
Conclusion: Both methods of revascularization in multivessel coronary artery disease (CABG surgery and Hybrid Coronary Revascularization) are associated with the improvement in quality of life at 1 year after the procedures. We did not find any clear evidence on the advantage of one method over the other in terms of the quality of life.

P5647 | BEDSIDE
Aorto-coronary bypass graft outcomes predicted by the distal vessel quality score: optimization of revascularization strategy

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Introduction: Coronary artery bypass graft (CABG) is recommended by the guideliness in several scenarios. However, it is not uncommon the early occlusion of the grafts. Some clinical factors have been describe as predictors of this early dysfuntion but the impact of the grafted distal vessel on outcomes is poorly understood.
Aims: We aimed to create an easily applicable score to depict the quality of the distal vessel and evaluate its impact on the outcomes of aorto-coronary grafts.
Methods: We created a score to assess visibility, diameter, and size of the vessel-dependent myocardial territory as angiographically evaluated for each vessel. Each variable was quantified from 0 (worst) to 3 (best). The final Distal Vessel Quality (DVQ) score was the result of the cumulative score for all distal vessels

that were grafted divided by the numer of vessels. Two independent cardiologist blindt to the outcomes calculated the DVQ score with low interobserver variability.
Results: We evaluated a total of 116 consecutive patients who underwent single CABG, with a mean follow-up of 6.5±0.3 yrs (available for all patients, all with >6 yrs of follow-up). Mean age was 66.2±9.9 yrs, 82.1% were males and risk factors included hypertension in 46.2%, diabetes in 30.8%, and dislipidemia in 48.7%. Each patient received a mean of 2.8 bypass grafts, up to a total of 337 grafts, specially to left anterior descending artery (34.1%) and obtuse marginal artery (29.1%). A total of 235 (69.7%) venous and 102 (30.3%) grafts were implanted. In the follow-up 14.5% of the patients were admitted due to NTEACS (1.7%), unstable angina (9.4%), and stable angina (3.4%). Occlusion of 32 grafts was angiographically demonstrated at a median time from surgery of 1.2 (IQR: 0.5–2.5) yrs, specially affecting those sutured to the obtuse marginal artery (40.3%). Occlusion was more frequent in women (18 vs. 9%, p=0.036), venous grafts (12.3 vs. 2.9%, p=0.007), and patients with lower single vessel (5.78±1.01 vs. 6.47±1.36, p=0.006) and mean (5.86±1.03 vs. 6.32±0.79, p=0.019) DVQ score. Multivariate analysis demonstrate that the use of arterial grafts (OR=0.217, 95% CI [0.064–0.737], p=0.014) and higher values of mean DVQ score (OR=0.555, 95% CI [0.370–0.832], p=0.004) were related to longer patency duration of the grafts.
Conclusions: The DVQ score is a new simple tool to accurately predict good outcomes of coronary artery bypass grafts. Therefore, lower values of this score ought to preclude from grafting specific vessels. Percutaneous or hybrid strategies could be used to optimize outcomes. External validation of the DVQ score is warranted.

P5648 | BEDSIDE
Sleep apnoea screening in patients scheduled for coronary artery bypass surgery

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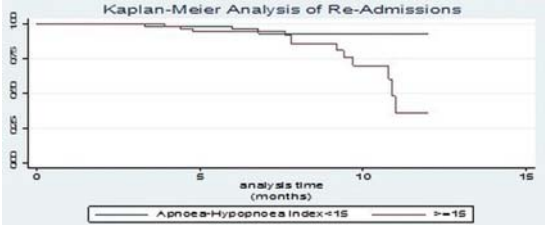
Objectives: Although it has been recognised as a cardiovascular risk factor, data on sleep apnoea screening before coronary artery bypass grafting (CABG) are scarce. This study sought to determine the prevalence, predictors and effects of sleep apnoea on re-admission in patients undergoing CABG.
Methods: We prospectively recruited 152 patients to undergo an overnight sleep study before CABG. Sleep apnoea was defined as an apnoea-hypopnoea index of ≥15. Data on unscheduled re-admission due to cardiovascular events were adjudicated.
Results: Among the 138 patients who completed the sleep study, sleep apnoea was diagnosed in 69 (50%). The patients who had sleep apnoea had a lower LVEF (p=0.029), a larger left atrial diameter (p=0.014) and a larger left ventricular end-systolic dimension (p=0.019) than those who did not. Angiographic SYNTAX and Gensini scores were similar in patients with and without sleep apnoea. The generalised structural equation model revealed that hypertension, a high body mass index and chronic renal failure were independent predictors of sleep apnoea (p<0.05). After an average follow-up of 6±3 months, 12 patients with sleep apnoea (17.3%) and three patients without sleep apnoea (4.3%) were involved in unscheduled re-admission due to cardiovascular events. Patients with sleep apnoea were five times more likely to have an unscheduled re-admission due to cardiovascular events (adjusted odds ratio: 4.63, 95% CI: 1.24–17.31, p=0.023) than those without sleep apnoea. As depicted in the Kaplan-Meier curves, patients with sleep apnoea had a poorer prognosis in terms of time to re-admissions (log-rank test, p=0.01) (Figure).



Kaplan-Meier analysis of re-admissions of patients with sleep apnoea

Conclusions: Sleep apnoea was prevalent and predictive of unscheduled re-admissions in patients scheduled for CABG.

P5649 | BEDSIDE
The forgotten variable of shear stress in saphenous venous graft disease: whole blood viscosity

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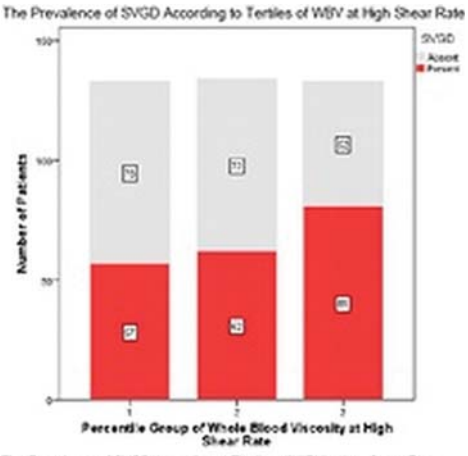
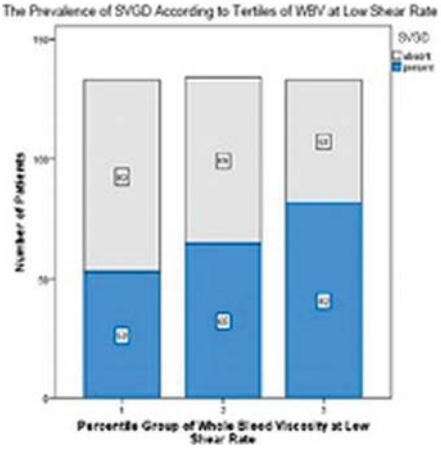
Introduction: Starting with the process of grafting saphenous venous conduits into arterial environment, the endothelial shear stres (ESS) constitutes a crucial trigger in the pathophysiology of saphenous venous graft disease (SVGD. To date, the blood viscosity as the major component of ESS has been disregarded in this process. Whole blood viscosity (WBV) can be calculated from the hematocrit and total protein levels for both low (LSR) (0.5 sec^{-1}) and high shear rate (HSR) (208 sec^{-1}) with a confirmed formula. Our aim is to evaluate the association of WBV with SVGD.
Methods: 200 patients with SVGD and 200 patients without SVGD as the control group were included. Patients were divided into tertiles according to the WBV levels both for LSR and HSR
Results: In patients with SVGD, both WBV at HSR (17.6±1.6 vs. 17.0±1.5 p<0.001) and at LSR (73.5±14.9 vs. 65.3±12.7 p<0.001) was higher than control group. The prevalence of SVGD was greatest in the highest WBV tertile groups for both shear rate. In multivariate analysis, WBV at HSR (HR: 1.044, 95% CI: 1.028–1.061 p<0.001) and at LSR (HR: 1.261, 95% CI: 1.105–1.439 p=0.001) were revealed as independent predictors of SVGD. In ROC analysis for predicting SVGD a cut of value 17.1 of WBV at HSR (AUC:0.595, p=0.001) has a 55% sensivity and a 50.5% specificity and a cut of value 67.9 of WBV at LSR (AUC:0.652, p<0.001) has a 67.9% sensivity and a 60.5% specificity.





Discussion: The well-known but neglected determinant of endothelial shear stress, WBV, especially at LSR was an independent predictor of SVGD. With bedside extrapolation of WBV with this simple calculation, may contribute to the evaluation of patients more comprehensively.

P5650 | BEDSIDE
Feasibility of platelet function point-of-care test in ticagrelor or clopidogrel-treated patients undergoing coronary artery bypass graft surgery

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Background: Dual antiplatelet therapy (DAPT) is the gold standard treatment in acute coronary syndromes (ACS). Patients (Pts.) with ACS on DAPT undergoing coronary artery bypass grafting (CABG) should expect a washout period of 5-day for clopidogrel (C) and ticagrelor (T). Some guidelines support the use of platelet function tests (PFT) for timing CABG.
Purpose: Evaluate the utility of PFT in Pts on DAPT undergoing on-pump CABG.
Methods: We included prospectively Pts with ACS on DAPT undergoing CABG. Platelet aggregation assessed with VerifyNow P2Y12 assay (California). Result reported in Platelet Reaction Units (PRU) and % of platelet inhibition (% Inh), calculated as [(Baseline-PRU)/Baseline] x 100. In all Pts. %Inh was measured

daily after deciding CABG (basal); When ≤15% Inh was reached, CABG was scheduled. Primary end point: intraoperative and 24 hrs bleeding after CABG. Secondary endpoint: 24 hrs blood consumption and reinterventions. Excessive bleeding: >200 mL/h (or 100 mL/h) in the first 4 hrs.
Results: We studied 11 Pts, 5 T and 6 C. Pharmacodynamic showed in fig. T greatest %Inh and faster reversibility. T Pts. were operated in 3.6±0.5 days vs C 3.8±1.17 days, p=0.069, in both groups CABG performed in less than recommended 5-day, p=0.00001. Surgical bleeding: T 325±253 ml vs C 433±261 ml, p=NS. 24 hrs bleeding: T 470.7±110 ml vs C 560.8±245.5 ml, p=NS. No differences in packed red blood cells consumption or plateletpheresis. No one Pts met excessive bleeding criterion and 0% of reinterventions.

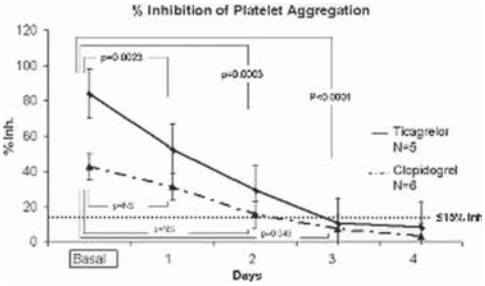

Figure 1

Conclusions: In our study, PFT guiding CABG allowed 25% reduction in waiting time than recommended in the current guidelines without increase in bleeding or blood transfusion requirements. Security and benefit of this stategy must be confirmed in large scale trails.

COMORBIDITIES

P5651 | BEDSIDE
Additive positive effect of the reversion of depression and physical capacity improvement on the sympathovagal balance in the course of home-based telerehabilitation in heart failure patients

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Autonomic nervous system (ANS) dysfunction appears in the course of both heart failure (CHF) and depression. Comprehensive cardiac rehabilitation (CCR) apart from improving physical capacity, can reduce depressive symptoms and leads to the restoration of ANS function among CHF patients.
Purpose: To evaluate the influence of the reversion of depression (measured by BDI score) and the physical capacity improvement (measured by peak oxygen consumption [pVO2; ml/kg/min]) on the sympathovagal balance (measured by low/high frequency ratio [LF/HF]) after CCR in CHF patients.
Methods: The study group comprised 111 CHF patients (NYHAII-III;EF≤40%). Patients were randomized (2:1) to 8-week CCR based on Nordic walking training (five times weekly) at 40–70% of maximal heart rate, training group (TG) n=77, or to control group (CG) n=34. The effectiveness of CCR was assessed by changes - delta (Δ) in LF/HF, BDI score and pVO2, as a result of comparing these parameters from the beginning and the end of the program.
Results: Eventually, 46 patients in TG and 23 patients in CG were eligible for simultaneous ANS and psychological status analysis. Only in TG the LF/HF decreased 2.06±1.14 vs 1.19±0.80,($p<0.0001$) and pVO2 increased 16.83±3.72 vs 19.14±4.20 ml/kg/min,($p<0.0001$). Favorable results in CG were not observed. The differences between TG and CG were significant: ΔpVO2 ($p<0.0001$);ΔLF/HF (p=0.0001). Depressive symptoms (BDI score) were substantially reduced in both groups (TG, p=0.0006; CG, p=0.0490). Nevertheless, the greatest improvement of sympathovagal balance was observed in patients whose depression was reversed thanks to the CCR in comparison to other patients from TG and the entire CG (Kruskal-Wallis test; p=0.0003).
Conclusion: Positive effect of the sympatho-parasympathetic balance obtained during the home CCR based on Nordic walking training results from the additive effects of the reversion of depression and physical capacity improvement in CHF patients.
Acknowledgement/Funding: The study was supported by the National Science Centre, Poland - grant number NN404 107936.

P5652 | BEDSIDE
Value of renal vascular Doppler sonography in management of cardiorenal syndrome type 1

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Introduction: Recent studies have demonstrated the relief of the congestion has demonstrated to improve renal functions in decompensated heart failure.
Purpose: The current trial was set up to investigate the changes of renal venous impedance and renal arteriolar resistivity indices with diuretic therapy, in patients with congestive renal failure.
Methods: A total of 64 patients who presented with acute cardiorenal syndrome type 1 were enrolled. Daily measurements of renal arterial resistivity indices, renal venous impedance indices and serum creatinine levels were obtained.
Results: Thirty of the patients had improvement of serum creatinine levels along with diuretic therapy. Table shows the comparison of the renal Doppler parameters on admission and at time of creatinine nadir stratified according to those who had improvement of creatinine with diuresis and those who did not. Multivariable regression model revealed that only high arterial resistivity index which was obtained on admission might be a predictor of the creatinine drop along with diuretic therapy among patients with congestive renal failure (OR: 6.25, 95% CI 1.84–14.3, p=0.003).

Table 1. Renal arterial and venous Doppler parameters on admission and at time of creatinine nadir

Parameter	Improvement of creatinine with diuresis (n=30)	No improvement of creatinine with diuresis (n=34)	P
On admission			
Creatinine, mg/dl±SD	1.68±0.45	1.59±0.36	0.28
Median VII, (min–max)	0.86 (0.34–1)	0.66 (0.3–1)	<0.001
Pulsatile venous waveform, n (%)	19 (63)	8 (24)	0.002
Non-pulsatile venous waveform, (%)	11 (37)	26 (76)	0.002
Median arterial RI, (min–max)	0.78 (0.6–1)	0.65 (0.54–0.78)	<0.001
Time of creatinine nadir			
Creatinine, mg/dl±SD	1.29±.43	1.51±0.29	0.04
Median VII, (min–max)	0.60 (0.4–1)	0.44 (0.32–1)	0.005
Pulsatile venous waveform, (%)	4 (13)	2 (6)	0.31
Non-pulsatile venous waveform, (%)	26 (87)	32 (94)	0.31
Median arterial RI, (min–max)	0.65 (0.45–0.87)	0.7 (0.48–0.78)	0.61

Conclusions: High renal arteriolar resistivity index may indicate the patients with congestive renal failure who benefit diuretic therapy in regard to improvement of kidney functions.

P5653 | BEDSIDE
The reverse remodeling of left atrium in patients after renal transplantation - the value of left atrium volume index

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Background: Cardiovascular diseases compose a kind of continuum initiated by cardiovascular risk factors in consequence leading to the development of atherosclerosis, infarct and secondary heart failure. Research concerning reverse process, which can be present due to disappearing of causative factors is not numerous and but rather incomplete. The main aim of study is the assessment of left atrium (LA) reverse remodeling in patients with end-stage renal disease (ESRD) after renal transplantation (RT).
Materials and methods: Study group consisted of 42 patients after RT from non-related renal transplant donors; age 43,3±12,6 years, including 19 women 49,9±10,9 years old and 23 men 41,5±12,91 years old. The study protocol has been consisted of 5 stages: 1 week after RT, 3 months after RT, 6 months after RT, 1 year after RT, 3 years after RT. The echocardiographic examination was performed and following measurements were done: LAmax, LAmin, LAwaveP. LAshortmax, LAshortmin, LAshortwaveP, LAlongmax, LAlongmin, LAlongwaveP, LAcircmax, LAareamax, On the base of obtained parameters according to adequate formulas the following indices were calculated: left atrium volume (LAV), LAV index (LAVI) and hemodynamic indices of LA (LAEF, LAAE, LAPE, LAIE, LAFS).
Results: The exact analysis of parameters concerning LA showed constant and progressive reduction either planimetric and volumetric LA dimensions. The LAVI value measured after RT was – 34,63±10,34 ml/m^2, 3 months after RT – 32,24±9,59 ml/m^2, 6 months after RT – 31,36±9,20 ml/m^2, 1 year after RT – 28,29±8,32 ml/m^2, 3 years after RT – 27,57±8,40 ml/m^2. The progressive decrease of LA size was the most marked during early stages of observation after RT and subsequently the slow down of this process was observed in the end of observation. Simultaneously with continuous decreasing of LA size its contractility was improved which was expressed by progressive and statistically significant increasing of indices such as: LAEF, LAFS, LAAE, and LAIE.
Conclusions: Disappearance of causative factors of unfavourable changes in cardio-vascular system allows to initiate the reparative processes leading to at least partial restitution of LA structure and function, which is called reverse remodelling. Reduction of LAVI coexisting with improvement of LA hemodynamic indices are the hallmarks of left atrium reverse remodeling due to uremic atrial cardiomyopathy in patients after RT.

P5654 | BEDSIDE

Cardiac involvement in hemoglobin SC disease compared to homozygous sickle-cell anemia

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Background: Hemoglobin SC (HbSC) disease and homozygous sickle-cell anemia (SCA) are the most frequent genotypes (accounting for respectively 25% and 70%) of sickle-cell disease. Although the SCA cardiac involvement was well studied, the cardiac remodeling associated to HbSC has never been specifically investigated.
The aim of the study was to describe the HbSC cardiac remodeling versus SCA.
Methods: Using a case-control design, 61 HbSC (mean age 31.3±10.0 years, 36 women) patients underwent a comprehensive echocardiography and were compared to 61 SCA patients in stable conditions.
LV end diastolic volume index and LV ejection fraction were measured by Simpson method. LV mass index, left atrial volume index, septal E/e' ratio, peak tricuspid regurgitation velocity (TRV) and cardiac index were also measured as recommended. All the parameters were the average of three measures.
Results: Both LV morphological and diastolic functional parameters differed dramatically between the two groups of patients (table, mean ± SD). Moreover, the pulmonary artery systolic pressure as estimated by TRV was lower in HbSC patients.

	SCA patients (n=61)	HbSC patients (n=61)	p value
Heart rate (beats/min)	70±11	72±10	0.26
LV mass index (g/m^2)	103±26	77±16	<0.0001
LV end diastolic volume index (ml/m^2)	92±19	64±15	<0.0001
Cardiac index (L/min/m^2)	4.2±1.0	3.1±0.6	<0.0001
LV ejection fraction (%)	60±5	61±6	0.88
Septal E/e' ratio	10.9±2.4	7.2±2.1	<0.0001
Left atrial volume index (ml/m^2)	51.1±11.9	33.8±7.5	<0.0001
Tricuspid regurgitation velocity (m/s)	2.57±0.26	2.26±0.23	<0.0001
Tricuspid regurgitation velocity >2.5m/s, n (%)	34 (56)	4 (7)	<0.0001

Conclusions: Cardiac remodeling is very different in HbSC compared to SCA. Clinical interpretation of echocardiography data should be adjusted to each variant of the disease. Moreover, this study is further evidence that the both genotypes of sickle-cell disease have different organ involvements and should not be pooled in clinical studies.

P5655 | BEDSIDE

Lack of association between central chemosensitivity and disease severity in optimally treated patients with mild heart failure

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Background: Previous studies reporting the association between augmented central chemosensitivity and exercise intolerance and worse clinical status in chronic heart failure (CHF) involved predominantly patients with moderate-severe disease. We investigated whether this relationship is still present in CHF patients with mild symptoms, receiving optimal management.
Methods: The study is based on data collected in the SICA-HF (Studies Investigating Co-morbidities Aggravating Heart Failure) prospective, multinational, observational study. In the subset of 169 CHF patients in NYHA class I-II (age: 57±10 y, LVEF: 34±7%, all receiving ACE-I/ARB and beta-blocker) in addition to standard clinical assessment, echocardiography and cardiopulmonary exercise testing, central chemosensitivity was evaluated using the rebreathing method (hypercapnic ventilatory response [HCVR], L/min/mmHg).
Results: The HCVR in the entire CHF population was elevated with the mean value: 0.70±0.49 L/min/mmHg ($p<0.001$ vs. reference value in our laboratory). CHF patients were divided according to HCVR tertiles: 1st tertile (HCVR <0.49 L/min/mmHg, N=56), 2nd tertile (HCVR: 0.49–0.83 L/min/mmHg, N=57), 3rd tertile (HCVR >0.83 L/min/mmHg, N=56). There was no difference between the 1st, 2nd and 3rd tertiles in all investigated clinical/laboratory indices (see table below).
Conclusion: In contrast to previous reports, our study demonstrates lack of association between central chemosensitivity and severity of the disease and magnitude of exercise intolerance in patients with mild CHF.
Acknowledgement/Funding: Supported by the 7th FP (grant agreement: 241558) of the EC, and the Russian Ministry of Science and Education (state contract: 02.527.11.0007)

	1st HCVR tertile (N=56)	2nd HCVR tertile (N=57)	3rd HCVR tertile (N=56)
Age (years)	57±10	58±11	60±11
NYHA class I/II (%)	17/83	15/85	11/89
Heart rate (beats/min)	71±9	70±11	68±10
Systolic blood pressure (mmHg)	115±20	114±15	113±14
LVEF (%)	32±7	31±7	31±7
NT-proBNP (pg/dL)	1079 (437; 2310)	786 (402; 2413)	835 (430; 1862)
eGFR (mL/min/1.73m^2)	91±21	85±22	88±22
Sodium (mmol/L)	141±2	141±2	138±2
Peak VO2 (mL/kg/min)	18.5±5.7	18.9±5.4	19.0±4.7
VE/VCO2 slope	34±9	35±7	37±12

P5656 | BEDSIDE

Pulmonary hypertension due to left heart disease: comparison between transpulmonary pressure gradient and diastolic pulmonary vascular pressure gradient

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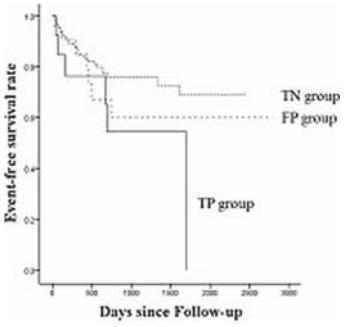
Background: As compared to transpulmonary pressure gradient (TPPG), diastolic pulmonary vascular pressure gradient (DPG) may be more sensitive and specific indicator for pulmonary hypertension (PH) due to left heart disease (LHD) with significant pulmonary vascular disease (PVD). The aim of this study was to investigate the incidence and clinical features of PH-LHD with PVD classified by DPG and TPPG.
Methods: We analyzed 410 patients admitted for symptomatic heart failure (NYHA≥2) and underwent right heart catheterization (RHC) at compensated stage between 2007 and 2012. Patients with PH-LHD was divided into 3 groups according to the value of DPG and TPPG (True negative (TN) group: DPG<7mmHg and TPPG≤12mmHg; False positive (FP) group: DPG<7mmHg and TPPG>12mmHg; True positive (TP) group: DPG≥7mmHg). Multivariate Cox regression analysis was applied to investigate whether each PH-LHD predict death or heart failure (HF) readmission after adjusting for other variables.
Results: PH-LHD was observed in 164 patients (40%) in symptomatic heart failure. Thirteen patients (3%) were allocated into TP group, while 24 patients were allocated into FP group (6%). TP group was significantly associated with death or HF readmission as compared to TN group (hazard ratio: 3.27 [95% CI: 1.20 to 8.89], P=0.02), while FP group did not reach statistical significance (hazard ratio: 1.96 [95% CI: 0.82 to 4.69], P=0.13).



Kaplan-Meier curve

Conclusions: PH-LHD with PVD classified by DPG was significantly associated with poor long-term clinical outcomes, which suggests DPG as better indicator for PH-LHD with PVD than TPPG.

P5657 | BEDSIDE

Serial changes in red blood cell volume during transition of heart failure status: a reflection of cellular hydration status?

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Background: In heart failure (HF), alterations in body fluid accompany changes in both extracellular water space (ECW) and intracellular water compartment (ICW). Assessment of the changes in ICW during HF follow-up would be clinically important for understanding the HF status because as much as 40% of body mass is composed of ICW, but there are few methods for assessing ICW. Erythrocytes (RBCs) have long served as the paradigm for studying cellular water content.
Purpose: We tested the hypothesis that changes in HF status induce changes in the index of erythrocyte hydration as determined by mean red cell volume (MCV).
Methods: Data from 47 patients (32% men; 78.2±9.7 years) with mild-to-moderate HF that experienced a worsening and recovery of HF were analyzed. Under the worsening HF, each study patient had at least 2 HF-related signs. Blood tests included measurements of RBC count, hemoglobin, hematocrit, MCV, electrolytes, blood urea nitrogen (BUN), creatinine, total protein, albumin, and b-type natriuretic peptide.
Results: During worsening of HF, the incidence of an increase, no change, or decrease in MCV was 24/47 (51%), 10/47 (21%), and 13/47 (28%), respectively. Overall, mean MCV did not change (from 96.0±5.2 to 96.8±6.0 fL, NS). Among

a total of 47 worsening HF events, changes in MCV were positively correlated with the changes in body weight (r=0.31, P=0.034), serum sodium (Na) (r=0.42, P=0.0036), and chlorine (Cl) (r=0.457, P=0.0012), and negatively correlated with the changes in BUN (r=–0.389, P=0.0069) and creatinine (r=–0.494, P=0.0004). Multivariate logistic regression analysis demonstrated independent association between the increase in serum Cl concentration and the increase in MCV from stability to worsening of HF (OR: 6.02, 95% CI: 1.09–33.2, P=0.039). At recovery from worsening HF after decongestive therapy, MCV decreased to 94.9±5.6 fL (P<0.001). The incidence of an increase, no change, or decrease in MCV was 9/47 (19%), 10/47 (21%), and 28/47 (60%), respectively. No correlation was detected between the change in MCV and blood tests upon recovery, though change in MCV was positively correlated with the change in body weight (r=0.323, P=0.027).

Conclusions: We observed serial changes in MCV according to the transition of HF status, which might reflect changes in cellular hydration status. Changes in MCV were significantly associated with changes in the serum Cl, indicating a role for this solute as an important osmolyte in the regulation of MCV. Whether MCV changes in HF patients actually reflect the cellular hydration status of the whole body warrants further research.

P5658 | SPOTLIGHT
Anemia and (combined) hematinic factors deficiency in heart failure

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Anemia is frequent in Heart Failure (HF) patients. The guidelines recommend evaluation and treatment of iron deficiency (ID), but there are no recommendations regarding vitamin B12 and folates. Little is known specially in those with preserved ejection fraction (HF-PEF), with only a few studies showing that these values are low in only a minority of HF patients. However HF patients are old and with many dietary deficiencies, making them a risk population for hematinic factors (Hemfx) deficiency anemia.

Objectives: Evaluate the prevalence of Hemfx nutritional deficits and anemia caused by nutritional deficits in an HF Unit and according to EF.

Methods: Prospective study of patients admitted consecutively in a HF Unit over one year. Anemia was diagnosed according to WHO's criteria, ID was considered: ferritin <100 ng/ml (absolute ID) or 100–299 ng/ml and transferrin saturation <20% (functional ID) and vitamin B12 and folate deficiency when <200 pmol/L and <6.25 nmol/L, respectively.

Results: 202 admissions; mean age: 74,95±11,84 years, 30,2% (61) male, 57.9%HF-PEF. Prevalence of Hemfx deficiencies are presented in Table 1, as well as its association to anemia.

Table 1

	Total	Anemia	Without anemia	Mean cell volume
Absolute ID	49.2% (n=88)	72.7% (n=64)	27.3% (n=24)	87.0±7.5 fl
Relative ID	19.1% (n=34)	67.6% (n=23)	32.4% (=11)	90.2±6.8 fl
Vitamin B12 deficiency	14.5% (n=27)	81.5% (n=22)	18.5% (n=5)	88.0±12.7 fl
Folate deficiency	2.7% (n=5)	100% (n=5)	0	94.9±9.2 fl

Anemia was found in 69.7%: 40.2% absolute ID, 19.1% functional ID, 14.5% vitamin B12 deficiency and 2.7% folate deficiency. 13% had both ID and Vitamin B12 deficiency, 1.2% ID and folate deficiency.

Concerning ejection fraction, Heart failure with Reduced Ejection Fraction (HF-REF) Vs HF-PEF and ID Anemia: 18% Vs 31,4% (p=0,509). HF-REF Vs HF-PEF and Vitamin B12 Deficiency Anemia: 4% Vs 10,7% (p=0,192). HF-REF Vs HF-PEF and Folic acid Deficiency Anemia: 1,7% Vs 1,2% (p=0,302).

Conclusion: The prevalence of Hemfx deficiency with or without anemia is high In HF patients, even in this high risk population. Although HF guidelines recommend iron reposition alone, the high prevalence of combined deficiencies (iron and B12) requires systematic assessment of all these factors, otherwise triggering B12 and folate deficiency clinical scenarios in both types of HF.

P5659 | BEDSIDE
Effects of functional tricuspid regurgitation and right ventricular dysfunction on renal function in patients with heart failure and left ventricular dysfuncytion

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Aims: To assess the role of functional tricuspid regurgitation (FTR) and right ventricular (RV) function on renal dysfunction (RD) and long-term prognosis in patients with heart failure (HF).

Methods: We enrolled 413 consecutive patients (mean age 74.2±11 years) with chronic systolic HF, defined as left ventricular ejection fraction <50%, with and without FTR. FTR was assessed by multiparametric approach. Renal dysfunction was defined as estimated glomerular filtration rate <60 ml/min/1.73m^2. RV dysfunction was defined as a tricuspid annular plane systolic excursion (TAPSE) value <16mm. The association between moderate/severe FTR, RV dysfunction and RD as well as its impact on HF episodes and overall mortality was assessed.

Results: Median follow-up was 36 months. Of the enrolled patients 68.6% had no/mild FTR, 21.6% moderate, and 9.8% severe FTR. At the univariate analysis atrial fibrillation, NYHA class III/IV, age, increased pulmonary systolic pressure and moderate/severe FTR (OR: 1.5, 95% CI: 1.0–2.3, p=0.03) were associated to RD, but not the RV dysfunction (OR: 1.1, 95% CI: 0.6–2.0, p=0.7). At the multivariate analysis, neither moderate/severe FTR nor RV dysfunction were independent determinants of RD, whereas the interaction between moderate/severe FTR with RV dysfunction was an independent determinant of RD (OR: 1.2, 95% CI: 1.1–1.5, p=0.04). Kaplan–Meier analysis showed significant lower event-free survival rates in patients with moderate/severe FTR compared with absent/mild FTR (at 9 years, 43% vs. 63%; Log-rank test 10.8, p=0.001). At multivariate Cox regression analysis moderate/severe FTR (HR: 1.3, 95% CI: 1.2–2.7, p=0.02), RV dysfunction (HR: 1.29, 95% CI: 1.0–3.7, p=0.01) as well as interaction of moderate/severe FTR with RV dysfunction (HR: 1.5, 95% CI: 1.2–1.8, p=0.001) were significantly related to HF episodes. Kaplan-Meier analysis showed a lower survival in patients with moderate/severe FTR compared with absent/mild FTR (at 9 years, 22% vs. 47%; Log-rank test 8.6, p=0.003). The multivariate Cox regression analysis showed that RV dysfunction (HR: 1.3, 95% CI: 1.1–1.8, p=0.03) and the interaction of moderate/severe FTR with RV dysfunction (HR: 1.5, 95% CI: 1.1–1.7, p=0.02) but not FTR were significantly related to the outcome.

Conclusions: The combination of significant FTR and RV dysfunction, but not FTR and RV dysfunction alone, is independently associated with RD, and both factors portend worse prognosis.

P5660 | BEDSIDE
Chronic kidney disease and community-acquired acute kidney injury are associated with cardio-hepatic syndrome in patients with decompensated heart failure

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Objective: Cardiorenal syndrome is a common and serious problem with negative impact on outcomes in patients with acute decompensated heart failure (ADHF). Over the last several years prevalence and prognostic value of cardiohepatic syndrome in this population has been discussed. The aim of the study was to assess possible relationship between renal and hepatic abnormalities in patients with ADHF.

Methods: In 200 patients with ADHF (84 male, 72.9±10.7 years (M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, known chronic kidney disease (CKD) 38%, chronic anemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45±12%, EF<35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT) and aspartate transaminase (AST) were measured baseline. Transaminases (TA) were considered abnormal when levels exceeded 50 U/L (local upper normal limit (UNL)). CKD and acute kidney injury (AKI) were diagnosed based on KDIGO 2012 Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. P<0.05 was considered statistically significant.

Results: Mean baseline ALT and AST values in patients with versus without increase of TA were 95±36 vs 21±14U/l and 87±26 vs 25±11U/l respectively (p<0.001). Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/ alone AST/ both TA – in 42.3, 19.2, 38.5% respectively). Community-acquired AKI occurred in 36 (18%) patients. Patients with versus without community-acquired AKI had higher levels of ALT (38±37 vs 21±18U/l, p<0.001) and AST (41±31 vs 25±14U/l, p<0.001). Incidence of cytolysis was higher in patients with versus without community-acquired AKI (20 vs 2%, p<0.001). Incidence of AKI was higher in patients with versus without cytolysis (70 vs 17.3%, p<0.001). Combination of cytolysis with CKD or AKI was revealed in 10 (5%) patients. The independent predictors of cytolysis were AF at admission (odds ratio (OR) 11.3, 95% confidence interval (CI) 2.6–48.9), community-acquired AKI (OR 11.2, CI 4.1–30.3), CKD (OR 4.2, CI 1.6–11.0), chronic anemia (OR 2.7, CI 1.1–6.4), EF<40% (OR 2.4, CI 1.1–5.7).

Conclusions: Cardiohepatic syndrome occurred in 14.5% of patients with ADHF. Community-acquired AKI was diagnosed in 18% of patients. Different phenotypes of cardiorenohepatic interrelations were revealed in 5% of patients. CKD and AKI along with AF at admission, chronic anemia, and EF <40% were the independent predictors of TA increase.

P5661 | BEDSIDE
Sleep-disordered breathing is of high prevalence in patients with acute cardiac decompensation

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Background and purpose: Most recently, sleep-disordered breathing (SDB) was identified as a co-morbidity independently associated with poor outcome (mortality and rehospitalization) in patients with acute decompensated heart failure (ADHF). This study investigated the prevalence of SDB in patients presenting with acute cardiac decompensation in a large cohort of these patients.

Methods and results: 233 patients (age 70.8±12.2 years, 82.4% male, BMI 27.9±4.3 kg/m^2, NYHA 3.2±0.5, LVEF 31.9±13.3%, BNP 1377.3±926.8) were enrolled and underwent multichannel cardiorespiratory polygraphy (PG) within the first three days of admission to our hospital for acute cardiac decompensa-

tion. None of the patients was treated with ventilation therapy and all patients were naïve to ventilation therapy. The prevalence of SDB (apnea-hypopnea index [AHI] ≥5/h) was 59.1% (AHI ≥15/h was 51.3% and AHI ≥15/h was 32.2%). Mean AHI was 35.3±23.9/h, mean ODI (3%) was 36.2±25.4/h, mean oxygen saturation was 91.4±3.1%, lowest oxygen saturation 78.8±9.4%, mean oxygen desaturation 6.4±3.3%. Average oxygen saturation time under 90% was 28.9±30%.
Conclusions: SDB is of high prevalence in ADHF patients with 50% of these patients demonstrating moderate to severe SDB. Whether treatment of SDB in the setting of ADHF is of any benefit, is currently investigated in a randomized controlled study (CAT-HF).

P5662 | BENCH
Improvement of left ventricular function by unloading the rat hearts of diabetic cardiomyopathy

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Objectives: Ventricular assist devices may function as a bridge to recovery or heart transplantation, however, little is known about its mechanisms. To create a model of minicking VAD by unloading rats with HF (heart failure) after diabetic cardiomyopathy in rats.
Methods: Diabetes cardiomyopathy (DCM) was induced by a single intraperitoneal injection of streptozotocin. Twelve weeks after streptozotocin injection (STZ, 60 mg/kg), the rats hearts with DCM were unloaded by heterotopic cardiac transplantation (n=14). Two weeks later, the function of normal and DCM hearts with or without loading was evaluated by Langendorff perfusion model.
Results: The rate of unloading the rats with DCM successfully was 84.9%. Two weeks after transplantation, Langendorff perfusion demonstrated that both maximum dP/dt (2756.02±101.34 versus 2026.12±105.3 mm Hg/s, $P<0.05$) and minimum dP/dt (1409.65±89.1 versus 1021.09±89.1mm Hg/s, $P<0.01$) were improved in DCM-unloaded hearts compared with DCM hearts.
Conclusions: We establish a model mimicking partially the Left Venticular assist Device (LVAD).The left ventricular function of diabetic cardiomyopathy could be improved by unloading the hearts.

THERAPY

P5663 | BEDSIDE
Effects of beta-blocker therapy on hs-CRP levels in elderly patients with ischemic and non-ischemic heart failure: results from the CIBIS-ELD trail

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Background: C-reactive protein (CRP) is a biomarker that indicates systemic inflammation. In the past years, high-sensitivity CRP assays were developed in order to measure lower levels of CRP, down to 0.3mg/l (hs-CRP). Elevated hs-CRP is associated with the risk in chronic heart failure (HF) and in coronary artery disease, indicating a possible role of inflammation in the progression of both conditions. Certain data indicated an anti-inflammatory effect of beta-blockers in HF, but little is known about the effects of beta-blocker titration on hs-CRP levels in ischemic and non-ischemic HF patients. Also, little is known whether this effect differs between beta-blocker substances.
Purpose: The aim of this analysis was to explore the trajectories of hs-CRP before and after beta-blocker titration in elderly HF patients depending on the etiology (ischemic vs non-ischemic) comparing two distinct beta-blockers (bisoprolol and carvedilol).
Methods: We assessed plasma levels of hs-CRP and NT-proBNP in 520 HF patients ≥65 years (72.06±0.24 y, 38% f, LVEF 41.8±13.8%; ischemic n=243; non-ischemic n=277) from the CIBIS-ELD study. In this trial, patients were randomized to bisoprolol vs. carvedilol and doses were up-titrated to the target or maximally tolerated dose (ESC guidelines). Plasma levels of hs-CRP and NT-proBNP were assessed at baseline (BL) and at follow-up (FU), after 12 weeks.
Results: In patients with ischemic HF, hs-CRP levels decreased in the bisoprolol group (BL=0.60±0.94 mg/dl, n=166; FU=0.43±0.694 mg/dl, n=131; p=0.010), but did not change in the carvedilol group (BL=0.60±1.69 mg/dl, n=181; FU=0.57±0.982 mg/dl, n=136; p=0.731). There were no changes of hs-CRP levels in non-ischemic patients in both groups (bisoprolol: BL=0.64±1.175 mg/dl, n=197; FU=0.470±0.81 mg/dl, n=152, p=0.069; carvedilol: BL=0.45±0.78 mg/dl, n=198; FU=0.41±0.701 mg/dl, n=152, p=0.420). Plasma levels of NT-proBNP decreased in ischemic patients treated with bisoprolol, (BL=1594±2146 pg/ml, n=169; FU=1468±2110 pg/ml, n=133, p=0.04), while changes in the carvedilol group were not significant (BL=1648±1991 pg/ml, n=188; FU=1567±2119 pg/ml, n=135, p=0.556). In the non-ischemic group NT-proBNP levels did not change significantly in the carvedilol group, while there was an increase in non-ischemic patients in the bisoprolol group (BL=1427±3113 pg/ml, n=208; FU=1533±5385 pg/ml, n=166, p=0.017).
Conclusion: Titration of bisoprolol but not carvedilol was associated with a decrease of hs-CRP and NR-proBNP levels in ischemic HF patients, which suggests a superior role of bisoprolol when compared with carvedilol in this patient population.

P5664 | BEDSIDE
The effects of Baduanjin exercise on fatigue and quality of life in patients with heart failure

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Background: Fatigue was a common symptom in patients with heart failure due to reduced cardiac output which caused activity intolerance and reduced quality of life. Exercise was found to be safe and beneficial for heart failure patients, specifically regarding exercise capacity and quality of life. Baduanjin is a traditional Chinese exercise characterized by slow, simple, relaxing movements which are easy to learn. However, little is known about the effects of Baduanjin exercise on fatigue and quality of life of patients with heart failure.
Purpose: The purpose of this study was to examine the effects of a simple traditional exercise programme (Baduanjin exercise) on fatigue and quality of life of patients with heart failure.
Methods: The study used randomized control trial research design. Subjects were recruited using convenience sampling from two medical centers in northern Taiwan. Participants were randomly assigned into the intervention (n=39) or control group (n=41). Patients in the intervention group performed a 12-week Baduanjin exercise program, three times per week. A 35-min Baduanjin exercise demonstration videotape, a picture-based educational brochure, and a performance record form were provided. The control group had no any intervention. Data were collected by a structural questionnaire including demographic information, the modified Piper Fatigue Scale, Minnesota Living with Heart Failure Questionnaire at four time points: baseline, 4 weeks, 8 weeks, and 12 weeks after intervention.
Results: Subjects in the Baduanjin exercise group had significantly improved fatigue ($F=5.083$, $p<0.01$) and quality of life ($F=9.108$, $p=0.001$) from week 4 to week 12 after intervention. Those in control group showed significantly worse in fatigue ($F=3.464$, $p<0.05$) and no significant changes in quality of life ($F=0.701$, $p>0.05$). Generalized estimating equations revealed that compared to the control group, exercise group had significantly greater improvement on fatigue ($p<0.01$) and quality of life ($p<0.01$) at 4 weeks, 8 weeks, and 12 weeks. Overall adherence rate for exercise was 85%, and there were no reported adverse events.
Conclusion: These results provide support for the effects of Baduanjin exercise on fatigue and quality of life of patients with heart failure. We recommend application of this simple traditional exercise in patients with heart failure to improve their fatigue and quality of life.
Acknowledgement/Funding: Ministry of Science and Technology

P5665 | BEDSIDE
Three-year experience of the left sided radiofrequency ablation in patients with long-standing persistent atrial fibrillation and rheumatic mitral valve disease

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Background: In patients with long-standing persistent atrial fibrillation (AF) associated with rheumatic mitral valve (MV) disease, the results of left atrial ablation are controversial. The aim of this study was to evaluate the effectiveness of the left sided radiofrequency ablation (RFA) for long-standing persistent AF added to mitral valve procedures.
Methods: Between 2011 and 2015 187 patients in our Center underwent RFA. Of those, 63 patients had left atrial ablation for long-standing persistent AF added to surgery for rheumatic mitral valve disease. The saline-irrigated cooled-tip monopolar ablating device was used in all cases. Mean age was 54 years (±12.4), 40 men (63.4%). AF duration was 58 months (±15.4). Primary indications for surgery were: rheumatic mitral stenosis (75%), mitral insufficiency (25%). Mean left ventricular ejection fraction was 46,5% Clinical follow-up, 24-hour Holter, echocardiogram were done at 1, 6, 12, 24 up to 38 months post surgery.
Results: After a mean follow-up of 28 months (±9.3), 62 patients (98.4%) remained alive and 32 (50.8%) were in sinus rhythm. 27 patients did not represent signs of heart failure, and 5 (8%) were in NYHA class I. Of those who had AF, 19 (70%) patients were in NYHA class 0–I, 7 (29%) were in NYHA class II, and 4 (14%) NYHA class III. Peace-maker implantation was indicated in 2 cases (3.1%). One (1.5%) patient died because of prosthesis endocarditis.
Conclusions: The RFA is effective for treating long-standing persistent AF associated with rheumatic MV disease resulting in absence of AF in 50% of patients after 3 years post operatively.

P5666 | BEDSIDE

Improvement of symptoms and quality of life with ivabradine, in patients with heart failure and left ventricular systolic dysfunction. The OPTIMIZE QOL study

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Introduction: In chronic heart failure (CHF), symptoms reduce the level of patients' usual activities, impacting negatively on quality of life.
Purpose: To record the effect of ivabradine on symptoms, NYHA classification and quality of life, in patients with CHF (NYHA II-IV) and left ventricular systolic dysfunction (LVSD) (left ventricular ejection fraction $\leq$35%).
Methods: In this non-interventional study, 1245 patients with CHF and LVSD were prospectively studied in 102 cardiology hospital clinics/private cabinets. Data were recorded at baseline, at 1 and 4 months after inclusion. In all visits, patients' quality of life (QOL) was assessed by means of the Left Ventricular Dysfunction (LVD 36) questionnaire. The effect of treatment was assessed by the patient and by the treating physician at the 2nd and 3rd visit, using the Patient and the Physician Global Assessment questionnaire (PaGA/PhGA).
Results: During the total study duration, 81.3%, 77.9%, 84.3% and 53.6% of patients were receiving β-blockers, ACE inhibitors/ARBs, diuretics and mineralocorticoid antagonists respectively. Ivabradine administration decreased the number of patients in NYHA III&IV from 52.7% to 18.9%, while increased the number of patients in NYHA I/II from 0.0%/47.3% to 18.2%/62.9% respectively (from inclusion to study completion) ($P<0.001$). Additionally, symptoms improved markedly, since 47% fewer patients reported dyspnea, 31.8% less orthopnea, 28.5% less ankle edema, 28.5% less fatigue, 25.7% less angina and 24.2% less reduced exercise capacity. As a consequence, QOL was improved by 29 points, while 75.9% of patients presented a >10-point improvement, which is considered significant ($P<0.001$). 23%/20.7% of patients and physicians respectively reported mild improvement and 67%/69.7% reported a moderate/significant improvement after a 4-month ivabradine administration ($P<0.001$). Mean heart rate (HR) was reduced by 16.4 bpm at study completion, while this reduction was related to baseline HR level; patients with HR>80 bpm, 70–80 bpm, <70 bpm presented a mean HR reduction of 21.3 bpm, 11.7 bpm, and 4.7 bpm respectively ($P<0.001$). 98.8% of patients received Ivabradine "every day" or "quite often", while at the 1st month almost 40% of patients received 7.5 mg bid, a dosage maintained by study completion.
Conclusions: Treatment with ivabradine significantly improves symptoms, NYHA classification and QOL in patients with CHF and LVSD. The abovementioned results are confirmed by both patients' and treating physicians' assessment.
Acknowledgement/Funding: SERVIER HELLAS

P5667 | BEDSIDE

Guidelines implementation in different populations - summarizing from CIBIS ELD and CIBIS ELD 24 Months FUP studies

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Introduction and aims: Data of recent Registries are collected from the western developed countries. This study gives us the insight into the basic differences of the patients' characteristics and implementation of Guidelines for treatment of chronic heart failure (HF) in patients from Germany and South-Eastern Europe (SEE).
Results: We included 297 patients from Germany (age 74 years, 46% male, 37% with systolic HF, LVEF 51.5%, 45% on beta-blocker therapy) and 579 patients from SEE – 532 from Serbia, 30 from Slovenia and 17 from Montenegro (age 72 years, 71% male, 89% with systolic HF, LVEF 36.6%, 68% on beta blocker therapy) in CIBIS ELD study. 68.4% did not consume alcohol from SEE and 59.3% from Germany, $p<0.01$. 60.1% of patients from Germany never smoked, 31.8% were ex-smokers and 8.1% were smokers. Among patients from SEE 55.9% never smoked, 35.1% were ex smokers and 9% smoked (p=n.s.). BMI in patients from Germany was 29.4 vs. 26.9 (SEE), $p<0.05$. 13.5% from Germany suffered from depression vs. 3% of patients from SEE.
After 24 months of follow up, 17.2% of patients from Germany and 23.2% from SEE ($p<0.05$) died.
82% of patients from Germany continued to use beta blocker, 43.8% had ACE inhibitor and 27.3% had AT1 blocker and 34% loop diuretic in therapy. However 92.7% of patients from SEE continued with beta blocker, 86.8% had ACE inhibitor and 9.7% AT1 blocker and 66% had loop diuretic in therapy.
Conclusions: Roughly taken, patients from developed Germany with HF were older, more often females with diastolic HF, overweight alcohol consumers, more likely depressed and less likely smokers, compared to those from developing countries from SEE who had more often beta blockers, ACE inhibitors, loop diuretics and less likely expensive AT1 blockers in therapy. Patients from Germany and SEE have different profiles of cardiovascular characteristics, co-morbidities, and risk factors. Data suggest that use of medication is possibly better adapted to the patients' needs and economic status in different European regions. Having so different socio-economic, environmental milieu in this HF patients we must pose the question are the Guidelines for diagnosis and management for cardiovascular diseases suitable for all and how could we bring them closer to clinical practice? Should we start with the new plan for controlled, randomized studies so that we include environmental factors, as well?

P5668 | BEDSIDE

First clinical experience with ONO-4232, a healthy volunteer study of a novel lusitropic agent for acutely decompensated heart failure

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Background: ONO-4232 is a novel, first-in-class prostaglandin E receptor 4 (EP4) selective agonist with a dual lusitropic and venodilatory action, being developed for the treatment of acutely decompensated heart failure (ADHF) patients.
Methods: This first-in-human Phase 1, randomized, double-blind, placebo-controlled, single dose, sequential-group dose-escalation study was designed to evaluate the safety, tolerability, and pharmacokinetics (PK) of ONO-4232 in healthy adult volunteers of both genders. The drug was administered as a continuous IV infusion over 3 hours. Adverse events (AEs), safety labs, vital signs, 12-lead ECG, telemetry, orthostatic effects and PK data were assessed.
Results: Total of 57 subjects received ONO-4232 and 19 subjects received placebo. Ten cohorts (dose range from 0.001 to 0.27 ng/kg/min) were conducted; dose escalation was terminated at 0.27 ng/kg/min due to orthostatic effects. A total of 34 treatment-emergent adverse events (TEAEs) were reported in 23 subjects. Overall, the majority of TEAEs were mild. No serious TEAEs or deaths were reported and no subjects discontinued due to AEs. The most frequently reported TEAE was self-limited infusion site erythema. Other TEAEs were headache and orthostatic hypotension. There were trends to a dose dependent decrease in diastolic (DBP) and systolic blood pressures (SBP) associated with increase in heart rate starting at 0.04 ng/kg/min. More orthostatic events occurred in the higher dose groups. The greatest reduction in SBP was seen at the 0.27 ng/kg/min dose. There were no clinically significant changes in 12-lead ECG data or telemetry data.
The plasma concentration of ONO-4232 appeared to reach steady state approximately 2 hours after the start of infusion. Mean terminal half-life of ONO-4232 was less than 1 hour. Median Tmax for all cohorts with measurable plasma concentrations was approximately 3 hours. Plasma AUClast and Cmax increased dose proportionally across the range of 0.02 to 0.27 ng/kg/min and plasma AUCinf increased dose proportionally across the range of 0.04 to 0.27 ng/kg/min.
Conclusions: ONO-4232 was generally well tolerated in healthy volunteers up to 0.27 ng/kg/min. There was a trend to dose related changes in vital signs and infusion site erythema which were both consistent with a venodilatory effect of ONO-4232. These study results support further clinical evaluation of the lusitropic effects of ONO-4232 in ADHF patients. In healthy volunteers, ONO-4232 demonstrated predictable pharmacokinetics; pharmacokinetics in patients with HF remains to be established.
Acknowledgement/Funding: The study was funded by Ono Pharmaceutical Co., Ltd.

P5669 | BEDSIDE

Family focused approach to improve heart failure care in Lebanon quality (family) intervention: randomized controlled trial for implementing an education family session

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Introduction: Heart failure is a complex clinical condition with poor outcomes. Self-care is a vital component in maintaining wellbeing and avoiding complications of heart failure. Family involvement in care of patients with this health condition is common in a non-western culture, but is not well established and not well studied.
Aim: To evaluate the effect of involving the primary family caregiver in self-care on improving outcomes in patients with heart failure.
Methods: The FAMILY study was a Randomised controlled trial conducted in three hospitals in Lebanon. Adult patients were recruited if they had presented to one of the sites for heart failure exacerbation and were willing along with their primary family caregiver to participate. Patients with life expectancy of less than 30 days of planned heart surgery with limited functionality were excluded. A total of 256 patients were randomised into an intervention group (n=126 patients) or a usual care group (n=130 patients). Family-centred education was provided to the intervention group on self-care and symptom management. The primary endpoint was 30 day readmission, and the secondary endpoints were emergency department presentation, health related quality of life, self-care and health care utilization.
Results: Participants were mostly older adults (67 years), men (55%) and married (63%). The average ejection fraction for the sample was 36% and the majority had a NYHA class of II or III upon discharge. At 30 days, 218 (85%) cases were analysed. Readmission was significantly reduced in the intervention group as compared to the usual care group [n=10 (33%) vs. n=20 (67%), $p<0.05$]. Sim-

ilar trends were seen in mortality (n=26, 10%). Self-care scores, low at baseline, improved significantly in the maintenance and confidence scales (all $p<0.0$). Significantly more participants in the usual care group needed health care facilities than in the intervention group (n=24 (23%) vs. n=12 (11%) respectively, $p<0.05$).
Conclusion: Involving the family in self-care of heart failure is a new approach in the Lebanese context. Significant improvement is noted when this care is structured through a family-centred educational intervention.

P5670 | BEDSIDE
Audit and clinical service evaluation for acute heart failure patients dying within 48 hours of admission

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Purpose: In the United States, better outcomes for acute heart failure (AHF) are found in higher spending hospitals with more Intensive Treatment Unit (ITU) and High Dependency Unit (HDU) resources. The National Heart Failure Audit shows that in-patient mortality for AHF is lower when care is delivered in cardiology than in general medicine.
Despite lower than the National average inpatient mortality, we reviewed all cases dying within 48 hours of non-elective heart failure admission to this Trust, to assess potential for improving service delivery.
Methods: Medical records were reviewed from July 2012 to June 2014 for all patients dying within 48 hours of non-elective admission to our hospital with HF in the primary diagnosis code (n=24).
Results: For 50% (n=12) this was the first ever presentation with heart failure. Respiratory failure was documented in 88% (n=21) on arterial blood gas (63% type 1, 25% type 2), and acute renal failure in 63% (n=15). Only 21% (n=5) were cared for in a Level 2 (ITU/HDU) area (13%, n=3 in Cardiothoracic ITU, 8%, n=2 in General ITU). Only 3 patients (13%) received invasive ventilation (non-invasive ventilation in 34% - CPAP 21%, BiPAP 13%).
Most (51%) died in general medical wards (38%, n=9, acute medical unit, 13%, n=3, medical ward). Care was delivered in cardiology for 21%. The majority died without senior cardiology review (13%, n=3 received HF Consultant review, 16%, n=4, non-HF Consultant Cardiologist review).
Left bundle branch block was present in 17% (n=4).
Acute triggers for decompensation included infection in 42%, suspected acute coronary syndrome in 29% and arrhythmia in 13%. One patient received palliative care input (4%).
Conclusions: This audit of acute heart failure patients dying within 48 hours of admission demonstrates that despite multi-organ failure at presentation, most do not receive level 2 care or above and most die without senior cardiology review. Inpatient mortality is well below the national average at this Trust, indicating that the potential to improve acute heart failure management within the first 48 hours may be widespread. The data provides supportive evidence for investment in level 2 care capacity to manage these complex patients and to streamline care delivery to specialist heart failure teams.

P5671 | BEDSIDE
Chronic vagus nerve stimulation improves baroreflex sensitivity assessed by heart rate turbulence in heart failure patients

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Introduction: Autonomic regulation therapy (ART) by chronic vagus nerve stimulation (VNS) improves ventricular function in heart failure (HF) patients, but its effects on baroreflex sensitivity remain unknown.
Methods: Effects of ART on heart rate turbulence (HRT), an indicator of baroreflex sensitivity and promising marker of cardiovascular mortality risk, were studied in patients with chronic, symptomatic HF and reduced ejection fraction enrolled in the ANTHEM-HF study (NCT01823887). The brief heart rate acceleration (turbulence onset, TO) and less rapid deceleration (turbulence slope, TS) following a ventricular ectopic beat were quantified using commercial software (GE Healthcare, Milwaukee, USA) from 24-hour ambulatory ECG recordings. Measurements were made prior to implantation of the ART system Cyberonics, Inc. involving the left or right vagus nerve and after 6 months of therapy (10 Hz, 250 μsec pulse width, 18% duty cycle, maximum tolerable current amplitude after 10 weeks of titration). Effects of left- (n=12) vs right-sided (n=8) and low- (<2 mA, n=9) vs high-intensity ($\geq$2mA, n=11) stimulation were investigated.
Results: In the group of 20 patients studied, mean TS levels increased from 4.14 msec/R-R interval at baseline to 6.35 at 6 months after ART implantation (p=0.02). In patients with high-intensity stimulation (n=11), mean TS levels increased from 3.5 to 5.0 (p=0.05). In patients with left-sided stimulation (n=12), mean TS rose from 3.66 to 6.16 (p=0.02). The increase in TS with either low-intensity or right-sided ART did not achieve statistical significance. TO was unchanged by ART.
Conclusion: Chronic, high-intensity vagus nerve stimulation, particularly on the left side, in patients with symptomatic HF can improve baroreflex sensitivity, as reflected in increased HRT slope, an indicator of reduced cardiovascular mortality risk.
Acknowledgement/Funding: Cyberonics Inc., Houston USA

P5672 | BEDSIDE
The effects of temperature and air pollution on heart failure incidence and readmissions: is beta-blocker protective?

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Background: The effects of seasonal variation on heart failure (HF) incidence and readmissions are uncertain. We measured factors associated with seasonal variations (temperature and air pollution), and investigated their relationships with HF incidence and readmission.
Methods: This Tasmanian statewide data linkage included all patients with a first-ever HF admission and their subsequent readmissions during 2009–2012. Daily temperature and particulate matter $<2.5\mu$m (PM2.5) in Tasmania were also recorded. Poisson regression was used, with adjustment for time trend, public and school holidays, day of week, flu infections and relative humidity.
Results: There were 1727 HF incidences (average 1.5±1.4/day) and 3355 readmissions (average 3.1±3.1/day). Greater HF incidences and readmissions ($p<0.001$) occurred in winter than other seasons. While higher average temperature was protectively associated with HF incidences (RR=0.60 [0.53, 0.67]) and readmissions (RR=0.70 [0.64, 0.77]), PM2.5 was detrimentally associated with HF incidences (RR=1.32 [1.21, 1.44]) and weakly so with readmissions (RR=1.08 [1.01, 1.16]). The effects of temperature and PM2.5 had a four-day and one-day lagging period respectively. In multivariable analyses, while both temperature (RR=0.67 [0.57, 0.79]) and PM2.5 (RR=1.14 [1.03, 1.27]) predicted HF incidences, only temperature (RR=0.76 [0.67, 0.87]) predicted readmissions. Stratified analyses showed that exposure to PM2.5 predicted readmissions among patients not taking beta-blockers (p=0.002), but not among those taking beta-blockers (Figure 1).

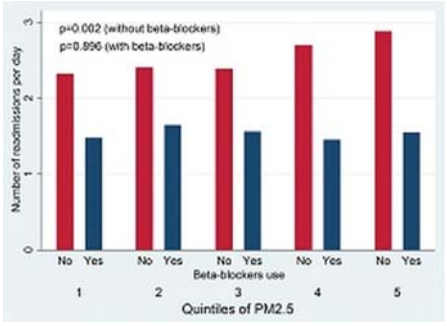

Figure 1

Conclusions: Both temperature and PM2.5 predicted HF incidences and readmissions with some lagging periods. The weak effects of PM2.5 on readmissions among this HF population may be due to protective effects of beta-blockers.

P5673 | BEDSIDE
Impact of evaluation of left ventricular dys-synchrony and scar burden upon outcome of cardiac resynchronization therapy

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Methods: Thirty patients underwent CRT implantation. Pre-implantation CMR was done to document scar burden and lateral wall involvement. Degree of dyssynchrony was assessed through LV phase analysis.
Results: Thirty patients received CRT (mean age 58.7±9.0, 24 males). CRT implantation had a favorable prognosis on cardiac functions (LVEF pre-implantation: 30±5% versus 37±7% post-implantation; P=0.017). Echocardiographic response, defined as relative decrease in LVES by $\geq$15%, was documented in 19 patients (63.3%). After adjusting for CMR scar burden, neither Histogram BW nor SD was correlated to LV remodeling. Applying ROC curve for CMR examination data for LV scar analysis showed that a cutoff value of 38.5% for global LV scar burden had a sensitivity of 72.7% and specificity of 68.4%. A cutoff value of 12% for lateral wall scar burden had a sensitivity of 81.8% and specificity of 68.4%.
Conclusions: Global and lateral scar burden of the left ventricle have unfavorable impact on CRT outcome. CMR is superior to gated SPECT in detection of scar burden and providing acceptable predictors for potential CRT non-responders. Mechanical dyssynchrony depends largely on underlying LV scar substrate.

IMAGING IN HEART FAILURE MANAGEMENT

P5674 | BENCH

The Kruppel like factor 15 rs9838915 single nucleotide polymorphism is associated with left ventricular hypertrophy and heart failure in patients with type 2 diabetes

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Background: Left ventricular hypertrophy (LVH) is common in patients with type 2 diabetes mellitus (T2DM) and a strong independent predictor of heart failure. Left ventricular (LV) mass is highly heritable. The Kruppel like factor 15 (KLF15), a transcriptional factor, is highly expressed in the heart and regulates cardiac hypertrophy.
Purpose: We investigated the association of two KLF15 single nucleotide polymorphisms (SNPs) with LVH and heart failure hospitalisation in patients with T2DM.
Methods: We recruited 347 ambulatory Caucasian patients with T2DM for a transthoracic echocardiogram. Patients with moderate/severe valvular dysfunction or valvular replacement/repair (n=28) were excluded. No patients had a previous history of heart failure. Two KLF15 SNPs (rs9838915 and rs6918698) were genotyped in 319 patients. LVH was defined as LV mass (indexed to body surface area) of >115 g/m^2 in men and >95 g/m^2 in women. Data are presented as mean ± SD and medians [25, 75th quartile] for non-parametric variables.
Results: The mean age of the cohort was 64±12 years (male = 54%) with a body mass index (BMI) of 31.7±6.1 kg/m^2 and median diabetes duration of 10 years [5, 16]. LVH was present in 35% of patients. The KLF15 SNP rs9838915 A allele was significantly associated with increased LV mass (GA + AA genotype vs. GG homozygotes: 105.8±28.3 vs. 95.9±25.5 g/m^2, p=0.001), interventricular septum thickness (1.11±0.15 vs. 1.05±0.15 cm, p = <0.0001) and posterior wall thickness (1.08±0.15 vs. 1.04±0.15 cm, p=0.003) in a co-dominant genetic model independent of age, gender, BMI and hypertension. There were no significant associations between the KLF15 SNP rs6918698 and LV mass before and after adjustment for the same covariates. Over a 6-yr period, patients with LVH and who carried the rs9838915 SNP A allele had a 4-fold increase in heart failure hospitalisations compared to those without LVH and who were GG homozygotes (hazard ratio 4.7 (95% confidence intervals, 1.3 to 16.9), p=0.018). This association was independent of age, gender, BMI, hypertension, systolic blood pressure and renal function.
Conclusion: In patients with T2DM, the KLF15 SNP rs9838915 A allele is associated with increased LV mass and heart failure hospitalisation. Our findings suggest that genetic variation in KLF15 may contribute to LVH, and studies are now required to identify the mechanisms by which SNP rs9838915 contributes to cardiac hypertrophy.

P5675 | BEDSIDE

Echocardiographic myocardial strain during left ventricular assist device support

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Purpose: The aim of this study was to determine the radial strain and radial strain rate values by Speckle Tracking Echocardiography in patients receiving continuous flow LVAD support and to examine the influence, if any, of reducing pump speed on these measurements.
Methods: We studied twenty ambulatory patients supported with continuous flow LVADs. Fourteen patients were on HVAD support and six patients on HMII. Transthoracic echocardiography was first carried out at the patient's baseline LVAD speed. Measurements were repeated after reducing the pump speed (at increments of 100 rpm over 1 minute to reach 1,800 rpm for HVAD and at increments of 1,000 rpm over 1 minute to reach 6,000 rpm for HMII). Radial strain and strain rate measurements were performed offline on digitally archived images using commercially available software (GE HC, Buckinghamshire, UK).
Results: Speckle-tracking was feasible from at least one short axis view in all 20 patients. The calculated radial strain mean value was 12.6±7.6%, median values was 9.8% (IQR 6.9%, 16.7%). The radial strain rate mean value was 1.24±0.67 s^{-1}, median values was 1.08 s^{-1} (IQR 0.79 s^{-1}, 1.7 s^{-1}). With the LVAD speeds reduced, the calculated radial strain and strain rate mean values did not significantly change. Reduction of LVAD speed was associated with a significant increase in LV size in diastole (62±13 mm vs 71±12mm, p=0.03) and a trend towards increase in systole. However, LV function assessed by LVEF (25±14 vs 27±10, p=0.50) did not change significantly.
Conclusions: This study demonstrate that strain values can be easily derived and provides added value to existing measures, such as LVEF, and may provide insight into the mechanical LV function in LVAD patients. Performing strain measurements routinely in stable LVAD patients may better evaluation of the underlying LV function and monitor for temporal changes.

P5676 | BEDSIDE

Depressive symptomatology accompanies impaired ventricular diastolic function, detected by Doppler imaging, in patients with chronic systolic heart failure

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Introduction: Short-term depressive symptoms have been associated with worsen prognosis of heart failure patients; although the involved mechanisms have not well understood. The aim of the present work is to evaluate any relationship between depressive symptoms and left ventricular systolic and diastolic function in patients with chronic heart failure.
Methods: We enrolled 202 males (mean age 63±13 years) and 39 females (mean age 65±13 years), all consecutive patients with chronic heart failure due to ischemic or dilated cardiomyopathy, under optimal medical treatment. At the echocardiographic assessment pulsed tissue Doppler imaging (TDI) of the systolic and diastolic function of mitral annulus was characterized by the systolic wave Smv, and the diastolic waves: Emv and Amv. Furthermore the ratio E/Emv was also calculated; where E is the rapid mitral filling wave, detected by pulse Doppler. Detailed information regarding their medical records, anthropometric data, physical activity, nutrition and smoking habits were recorded; while short term depressive symptom were evaluated using the Zung depressive scale (0–80).
Results: Patients in the higher tertile in Zung scale showed compared to those in the lower tertile, higher E/Emv, lower ejection fraction and lower Smv ratio (all p<0.05). Linear regression analysis, after adjustment for left ventricular ejection function, arterial hypertension, smoking, physical activity, creatinine clerance, diabetes mellitus, and hemoglobin levels, revealed that Zung levels were associated with E/Emv ratio (b=1.719, 95% CI: 0.86–2.59, p<0.001) Conclusion: This study reveals that depressive symptomatology is associated with more advanced left ventricular diastolic and systolic dysfunction, in patients with chronic heart failure.

P5677 | BEDSIDE

Scar burden and mechanical dyssynchrony assessment with SPECT-myocardial perfusion imaging as a potential tool to predict responsiveness to cardiac resynchronization therapy

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Introduction: QRS morfology and duration on the electrocardiogram (ECG), are the best predictors of response to cardiac resynchronization therapy (CRT). A considerable number of patients (pts) who meet the criteria for CRT do not improve (~30–35%) and additional criteria for best selection are needed. Assessment of scar burden and left ventricular mechanical dyssynchrony (LVMD) by phase analysis of gated SPECT myocardial perfusion imaging (MPI), may be useful tools for improving the prediction of CRT response.
Methods: We retrospectively evaluated heart failure (HF) pts with LV ejection fraction (EF) <50% who underwent SPECT-MPI. We obtained parameters of dyssynchrony by phase analysis of SPECT-MPI: histogram bandwidth (hb – a measure of the time dispersion of the onset of systolic contraction between regional LV count changes) and standard deviation (sd) for each patient. The presence of myocardial scar (persistent perfusion defect) was defined as a "summed stress score (SSS)" >3 with a "summed difference score (SDS)" <4, and the presence of ischemia was defined as a SSS >3 with an SDS >3.
Results: Ninety-four patients (74 males; mean age 63±9 years) underwent SPECT-MPI with phase analysis. Thirty-seven pts (39%) were classified as having ischemic cardiomyopathy (ICM) and 57 pts (60,6%) were classified as having non-ICM (nICM). Mean QRS duration was 139±32ms (134±35ms for ICM and 143±30ms for nICM, p=0,128), and LBBB was present in 51 pts (69%) with a higher frequency in nICM (38 vs 13 pts; p=0,003). Mean EF was 29,9±9,2%, with no significant difference between ICM VS nICM (P=0,06). Mean hb and sd values were 162±77° and 52±21° in ICM and 99±65° and 33±19° in nICM (normal values of ~38° for hb and 14° for sd; p=<0,001 and p=<0,001 respectively). In patients SSS>3 and SDS<4 (scar), increasing values of SSS are correlated with higher hb and sd values (r=0,57; p<0,001), suggesting that increasing scar burden is associated with increasing mechanical dyssynchrony. Myocardial scar, was present in both populations of pts, although, as expected, was more frequent in ICM (p=0,004).
Conclusions: Extensive myocardial scarring is a predictor for non-response to CRT. Although mean EF and mean QRS duration were not different between groups, LVMD assessed with SPECT-MPI phase analysis is significantly higher in patients with ICM compared to nICM, and this was related to a higher scar burden. These findings suggest that LVMD assessed with phase analysis of SPECT-MPI may be a surrogate marker of the extension of myocardial scarring and may be a useful predictor of CRT response, in addition to ECG parameters.

P5678 | BEDSIDE
Relationship between transmural myocardial mechanic and acute heart failure in STEMI patients treated with primary percutaneous coronary intervention

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In patients with ST segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (pPCI) post-procedural acute heart failure (HF) has important impact on prognosis. Contemporary echocardiographic techniques offer possibility to comprehensively explore left ventricular (LV) systolic function, beyond ejection fraction (EF), measuring myocardial deformation by strain and strain rate.
Aim: Aim of this echocardiographic study was to analyze relation between LV myocardial mechanics and postprocedural HF (Killip class≥2) in STEMI pts treated with pPCI.
Methods: In 35 consecutive STEMI patients treated with pPCI early echocardiography was done including conventional echo parameters as well as longitudinal (L), radial (R) and circumferential (C) peak global strain (S;%) and peak systolic strain rate (SR;1/s) on endocardial (endo), medial (mid) and epicardial (epi) level. Transmural gradients of LS (LSgrad) and CS (CSgrad) were calculated as difference between endocardial and epicardial values. Echo studies were done on VIVID 9-GE echo machine and EchoPack was used for speckle tracking analysis.
Results: 20% of all pts had HF. HF pts had significantly lower peak global LS on all three myocardial levels (LSendo: –10.53±5.47 vs –15.99±4.18, p=0.006; LSmid 9.11±4.56 vs 13.76±3.43, p=0.005; LSepi 8.09±3.97 vs 12.15±2.89, p=0.004), lower LSgrad (–2.44±1.68 vs –3.85±1.61, p=0.049) as well systolic LSr (–0.66±0.28 vs –0.93±0.23, p=0.01). CS was also impaired in pts with HF on all three myocardial levels (CSendo: –21.42±4.49 vs –13.89±6.60, p=0.001; CSmid –14.90±3.32 vs 10.08±4.89, p=0.004; CSepi: –10.64±2.67 vs –7.67±3.85, p=0.023) and CSgrad was lower in HF pts (–6.22±3.11 vs –10.78±2.69, p=0.001). Pts with HF had also impaired RS (13.23±4.43 vs 7.74±3.64, p=0.005) and as expected lower EF (34.43±14.15 vs 52.18±9.46, p=0.015) and higher WMSI (1.90±0.28 vs 1.43±0.34, p=0.002). Comparison of area under a receiver operating characteristic (ROC) curves of all investigated parameters reveals that CSgrad has the largest urea (0.879, CI 0.697–1.061, p=0.002) with –7.41 as cut off with the best combination of sensitivity (86%) and specificity (92%) to identify HF patient.
Conclusion: Although STEMI pts with HF after pPCI have severely impaired myocardial longitudinal, circumferential and radial myocardial mechanics, as well as EF, the best discriminator to identify HF from non-HF pts is transmural gradient of circumferential strain. These data suggest that preserved circumferential systolic LV function after pPCI is of crucial importance for HF appearance in STEMI pts.

P5679 | BEDSIDE
Stress cardiomyopathy - 10 years' experience at a tertiary care hospital

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Background: Stress cardiomyopathy (SC) is an entity recognized since the 1990's. Frequently mimicking the presentation of myocardial infarction (MI), it doesn't seem to be associated to coronary atherothrombosis, although its pathophysiology still isn't fully clear. We present a description of SC cases identified at our hospital in the last 10 years.
Methods: We made a descriptive analysis of retrospectively gathered data on patients (pts) presenting to our hospital and diagnosed with SC, according to the Mayo Clinic diagnostic criteria, between 2005 and 2014.
Results: We identified 58 pts (55 women and 3 men) with a mean age of 64 years (ranging from 33 to 84 years). A precipitating factor was found in 45 cases (78%), an emotional trigger being the most common, present in 31 pts (53%), and physical stress in 14 pts (24%). The most frequent symptom at presentation was chest pain (45 pts, 78%), followed by dyspnea (8 pts, 14%). The electrocardiogram (ECG) on presentation showed in equal proportions (20 pts, 35%) T wave inversion and ST-segment elevation; 6 pts (10%) presented with a normal ECG. All pts had some degree of troponin I elevation, with a mean peak level of 3,05±2,80 ng/mL. Echocardiographic evaluation revealed left ventricular systolic dysfunction in 55 cases (95%), the majority with apical hypokinesia (51 pts, 88%); 5 pts (9%) showed isolated midventricular hypokinesia and 2 pts an "inverted Takotsubo" pattern. In-hospital complications were present in 24 cases (41%). The most common were cardiogenic shock and acute pulmonary oedema, in 6 pts each (10%), 3rd degree atrioventricular block in 4 pts (7%) and left ventricle thrombus, atrial fibrillation and pericardial effusion, in 3 pts each (5%). Other identified complications were acute kidney injury and mitral regurgitation (2 pts each). One patient had in-hospital cardiac arrest, but no deaths were documented. Discharge after hospitalization took a mean of 9±7 days.
In patients with post-discharge follow-up information available (n=38, mean follow-up 28 months) only one death was recorded (non-cardiac) and one patient was admitted for recurrent SC.
Conclusion: Our hospital's 10-year experience, in line with international data, shows SC is frequently associated with severe clinical complications, but has nonetheless a very good short and long-term prognosis. We expect country-wide information, as the current national registry on SC starts being analysed.

P5680 | BENCH
Asymmetric dimethylarginine (ADMA) in the pericardial fluid may contribute to the development of cardiac hypertrophy

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Background: Pericardial fluid (PF) contains several biologically active substances, which may play a role in modulation of cardiac function and morphology. Nitric oxide (NO) has been implicated in cardiac function and remodeling, whereas asymmetric dimethylarginine (ADMA) has been shown to inhibit NO-synthase (NOS).
Purpose: To test the hypothesis that L-arginine (L-Arg) precursor of, and ADMA a false substrate of NOS are present in PF of cardiac patients and their altered levels may contribute to altered cardiac morphology.
Methods: Levels L-Arg and ADMA in plasma and PF, and echocardiographic parameters of patients undergoing coronary artery bypass graft (CABG, n=28) or valve replacement (VR, n=25) were determined.
Results: In VR patients 35.7% and in CABG 80% demonstrated LV hypertrophy. In all groups, plasma and PF L-Arg levels were higher than that of ADMA. Plasma L-Arg level was significantly ($p<0.05$) higher in CABG than VR (75.7±4.6 μmol/L vs. 58.1±4.9 μmol/L), whereas PF ADMA level was significantly higher in VR than CABG (0.9±0.0 μmol/L vs. 0.7±0.0 μmol/L). L-Arg/ADMA ratio was significantly lower in the VR than CABG (VRplasma: 76.1±6.6 vs. CABGplasma: 125.4±10.7; VRPF: 81.7±4.8 vs. CABGPF: 110.4±7.2). There was a positive correlation between plasma L-Arg and ADMA in CABG (r=0.539); and plasma and PF L-Arg in CABG (r=0.357); and plasma and PF ADMA in VR (r=0.529); and PF L-Arg and ADMA in both CABG and VR (CABG: r=0.468; VR: r=0.371). The following echocardiographic parameters were higher in VR compared to CABG: interventricular septum (14.7±0.5 mm vs. 11.9±0.4 mm); posterior wall thickness (12.6±0.3 mm vs. 11.5±0.2 mm); left ventricular (LV) mass (318.6±23.5 g vs. 234.6±12.3 g); right ventricular (RV) (33.9±0.9 cm^2 vs. 29.7±0.7 cm^2); right atrial (18.6±1.0 cm^2 vs. 15.4±0.6 cm^2); left atrial (19.8±1.0 cm^2 vs. 16.9±0.6 cm^2) areas. There was a positive correlation between plasma ADMA and RV area (r=0.453); PF ADMA and end-diastolic (r=0.434) and systolic diameter of LV (r=0.487); and negative correlation between PF ADMA and LV ejection fraction (r=–0.445) in VR.
Conclusions: We suggest that elevated levels of ADMA in the pericardial fluid of cardiac patients indicate a reduced bioavailability of NO, which can contribute to the development of cardiac dysfunction, hypertrophy, and remodeling.

P5681 | BEDSIDE
Heart failure awareness is being increased in HF patients: TREAT-HF cohorts

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Background: Heart failure is a community-wide problem.
Purpose: Herein, results of campaigns between 2013 and 2014 to increase awareness were tested.
Methods: TREAT-HF (Turkish Research Team-Heart Failure) is a network of 16 HF centers in Turkey. Herein, a direct comparison between TREAT-HF-2013 cohort (n=503) and TREAT-HF-2014 cohort (n=437, complete records by 12th Feb 2015) were presented.
Results: Mean age of whole group was 60.7±13.8 years (670 males, 270 females). Mean age was lower in the 2014 cohort than 2013 cohort (59.±14.3 vs. 62.6±12.9 years, $p<0.001$). Gender distribution was similar in both cohorts (p=0.615). There were less patients with an index diagnosis of HF more than 5 years in the 2014 cohort than in the 2013 cohort (28.9% vs 36.7%, p=0.011). Distribution of NYHA Class I-II-III-IV was different in 2014 cohort and 2013 cohort (8.3%, 41.6%, 44.7%, 5.4% vs 15.7%, 49%, 31.4%, 3.9%, $p<0.001$). Patients in the 2014 cohort more frequently stated than patients in the 2013 cohort that they were adequately informed by their physicians (78.2% vs 68.4%, p=0.001). There were more patients reaching target dose of ACEI or ARBs in the 2014 cohort than in the 2013 cohort (27.8% vs 13.4%, $p<0.001$). Patients in the 2014 cohort were more likely to keep dietary advice than patients in the 2013 cohort (66% vs 49.8%, $p<0.001$). Patients in the 2014 cohort were more likely to enjoy being informed by "physician or health programs on TV" than patients in the 2013 cohort (93.6% vs 89.7%, p=0.033) In the 2014 cohort, patients responded more frequently than 2013 cohort that "their relatives have adequate information with regard to their disease" (83.3% vs 77.6%, p=0.029). In the 2014 cohort, patients

responded more frequently than 2013 cohort that relatives of the HF patient knew what to do in case of an emergency (79.7% vs 71%, p=0.002). Patients in the 2014 cohort were less likely to rely on alternative medicine than patients in the 2013 cohort (18.5% vs 23.4%, p=0.07). Patients were asked "when they admit hospital except for regular visits", and it was noticed that patients in 2014 cohort responded more frequently as "when my dyspnea worsens" than patients in the 2013 cohort (64.7% vs 33.3%, p<0.001). Patients in the 2014 cohort visit "more than one physician after index diagnosis of HF" more frequently than patients in the 2013 cohort (88.6% vs 79.6%, p=0.001). It seems, HF patients in Turkey seek for another medical opinion quite frequently, and this number is increasing.
Conclusion: Heart failure awareness is being improved in HF patients by various campaigns in Turkey.

P5682 | BEDSIDE
Impact of sociodemographic and clinical risk factors on hospitalisation rates among ambulatory patients with heart failure and preserved ejection fraction

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Background: There are limited quantitative data on the impact of concomitant conditions on hospitalisation rates among patients with heart failure and preserved ejection fraction (HFpEF).
Methods: We evaluated 333 outpatients with HFpEF (age 72±13 years; 58% women; 49% white, 46% black; median EF 55%) over 2 years of follow up. We calculated the attributable risk conferred by sociodemographic and clinical factors for all-cause, cardiovascular (CV), and HF-related admissions using negative binomial regression models.
Results: Mortality was 10.2% at 2 years. Of 506 total admissions, 147 (29%) were HF-related, 73 (14%) due to other CV causes, and 286 (57%) non-CV. Table 1 presents factors that attained attributable risk with P<0.1 in multivariable models. Non-married status, poor renal function and functional class, and history of revascularisation were substantial contributors across admission categories, whereas low serum albumin was a key contributor to HF admissions. Over 80% of excess risk was traced to sociodemographic and clinical factors regardless of admission type, but nonmodifiable factors accounted for ≥50% of excess risk.
Conclusions: Approximately 80% of excess admissions in HFpEF patients can be attributed to identifiable factors. However, a substantial proportion of excess HF and non-HF admissions are attributable to nonmodifiable factors.

P5683 | BEDSIDE
Systemic hypertension and heart failure: insight from different left ventricular ejection fraction

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Background: Although systemic hypertension (SH) as isolated etiology of heart failure (HF) is a relatively frequent observation, the prevalence, clinical characteristics and outcome of hypertensive patients across different HF phenotypes have not been widely studied.
Purpose: To determine prevalence, characteristics and outcome of HF population with SH as isolated etiology taking into account different left ventricular ejection fraction (LVEF) phenotypes (LVEF≤40% - HFrEF, LVEF 41–49% - HFbEF, LVEF ≥50% - HFpEF).
Methods: We analyzed all consecutive out-patients with SH and HF from November 2009 to October 2013 whose LVEF had been assessed. HF patients with SH as an isolated etiology factor (HF-SH) were defined as patients with history of hypertension in absence of other triggers of cardiac disease. Patients with ischemic, valvular and congenital heart disease were excluded. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.
Results: We found that 2610 out of 14110 (28%) hypertensive patients had SH and HF. Among them, 1974 (76%) patients were excluded (29% ischemic heart disease, 22% valvular heart disease, 17% ischemic and valvular disease, 3% other acquired/congenital heart diseases). Finally, 636 patients (24% of overall HF population) (55% males, mean age 77±9 years) showed only SH as etiologic factor associated with HF. Of these, 121 (19%) were identified as HFrEF, 88 (14%) as HFbEF and 427 (67%) as HFpEF. The most significant clinical differences were observed between HFrEF and HFpEF group. Patients with HFrEF were younger, more frequently male, more symptomatic and with less frequent atrial fibrillation. Moreover, ACE-I/sartans and antialdosterone treatments were more frequent in HFrEF, while betablockers were similarly prescribed (around 50%) across HF phenotypes. The adjusted mortality for significant predictors at 1-year and mid follow-up term of 28 months (10 to 32) were not significantly different in HFpEF and HFbEF group. Conversely, patients with HFrEF showed a different and significantly higher mortality rates than those with other HF phenotypes.
Conclusions: Our results showed that in HF patients with SH as isolated etiology, HFpEF was the most frequent HF phenotype, while one-third of cases presented LV systolic dysfunction. Among different LVEF strata, HFrEF showed the worst outcome.

EPIDEMIOLOGY & MANAGEMENT IN HEART FAILURE

P5684 | BEDSIDE
Proposed diagnostic algorithm for patients with heart failure and sleep disordered breathing

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Sleep Disordered Breathing (SDB) is a highly prevalent comorbidity in heart failure (HF) patients, that weighs on HF high morbimortality. Both HF and SDB overlap of symptoms and difficulty in scheduling a laboratory for the diagnostic gold standard, the polysomnography (PSG), are responsible for the underdiagnosis of SDB in HF patients. The use of a validated type 3 home sleep testing diagnostic device, allows an early intervention and initiation of treatment, aiming towards better outcomes.
Objective: To compare the diagnostic accuracy of the portable diagnostic device as a screening test for SDB in stabilized inpatients "versus" outpatients with HF, previously validated against PSG, and to propose a diagnostic algorithm. Hospitalization period is a crucial moment for treatment optimization in HF.
Methods: Observational, prospective study of consecutive patients discharged from an HF unit of a central university hospital during one year. The diagnostic test was performed just before discharge, on stable optimized treatment and repeated while outpatient. Outpatient diagnostic test has previously shown a good correlation with PSG. Specificity (Sp), Sensibility (S), positive predictive value (PPV) and negative predictive value (NPV) for both central apneas (CA) and obstructive apneas (OA) diagnosis were obtained to validate inpatient diagnostic test in order to take advantage of the hospitalization period, a precious moment for treatment optimization.
Results: 38 patients were included, 23 women, age 71.2±10.2 years, avg BMI 27.6±5.1kg/m^2. For an apnea-hypopnea index (AHI)>15/h as cut-off, the portable diagnostic test at discharge had NPV of 0.92 and Sp of 0.88 for CA and NPV of 0.95 for Cheyne Stokes respiration. PPV for OA was 0.89.
Conclusion: Using AHI>15/h as cut-off, the portable diagnostic test applied to inpatients with stabilized HF and drug treatment revealed to be a trustworthy method for detecting SDB and, therefore, allowing early treatment, dismissing the PSG.

P5685 | BEDSIDE
Heart failure patients in Germany: mortality and morbidity in a claims database analysis

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Background: Heart failure (HF) is one of the most important causes of morbidity

Abstract P5682 – Table 1. Attributable risks

	All admissions AR (95% CI)	P	CV admissions AR (95% CI)	P	HF admissions AR (95% CI)	P
Marital status non-married	34.3% (19.0–46.7	<0.001	40.2% (19.5–55.6)	0.001	46.1% (15.8–65.5)	0.007
BUN >26 mg/dl	19.4% (5.9–31.0)	0.006	25.6% (8.6–39.4)	0.005	39.5% (18.4–55.2)	0.001
Fasting glucose >125 mg/dl	17.0% (5.5–27.2)	0.005	18.6% (1.9–32.4)	0.031		
Atrial fibrillation	16.2% (2.5–27.9)	0.022				
NYHA Class III or IV	16.0% (4.0–26.4)	0.010	21.8% (6.5–34.6)	0.007	27.5% (6.9–43.5)	0.012
Albumin <3.5 g/dl	14.3% (3.8–23.6)	0.009			47.8% (1.2–72.4)	0.046
Hx coronary revascularisation	13.2% (2.5–22.7)	0.017	15.2% (0.7–27.6)	0.041	19.4% (0.0–35.9)	0.067
Hx noncoronary intervention, cancer, RRT	17.5% (8.3–25.8)	<0.001				
Serum K^+ <4.0 meq/L			18.7% (3.7–31.3)	0.017	24.9% (3.0–41.9)	0.029
Nonmodifiable AR*	53.6% (37.4–65.5)	<0.001	49.7% (29.0–64.4)	<0.001	56.8% (29.2–73.6)	0.001
Total AR**	80.4% (71.4–86.5)	<0.001	80.0% (68.4–87.3)	<0.001	92.4% (83.5–96.5)	<0.001

*Marital status and history. **Attributable risks are not additive. AR, attributable risk; BUN, blood urea nitrogen; HF, heart failure; Hx, history of; NYHA, New York Heart Association; RRT, renal replacement therapy.

and mortality worldwide. In Germany, HF represents the most common cause for hospital admission, and it is the third highest cause of death.
Purpose: To explore the treatment of patients with HF 2 years after the initial identification.
Methods: Analyses were performed using the HRI database - a complete, longitudinal claims data set of 7 million anonymized individual patients (ca. 10% of the statutory insured population) between 2008 and 2013. An analysis subset (ca. 4.0 million anonymized and randomly selected patients) representative for the German population in terms of age and gender was used. ICD-10 codes documented in the ambulatory and hospital settings were used and the longitudinal data were analyzed. The newly identified HF patients in 2011 (index date defined as the first HF diagnosis in 2011) must not have had any HF diagnosis code in the two years prior to the index date. All patients had to have two HF diagnoses documented at different points of time in the index year and data needed to be available from 2009 to 2013 without interruption (N=3,132,337 patients for analysis).
Results: 123.925 (4%) of the patients already had an existing HF diagnosis in 2011 (55% women, 45% men). 113,868 of these patients (92%) were at least 60 years old. For 79% severity of HF was not coded. In 3%, 9%, 6%, and 3% severity was coded as NYHA I, II, III and IV, respectively.
26,368 newly identified HF cases were documented in the study population in 2011 (51% women vs. 49% men). More than 88% of newly identified patients were 60 years of age or older. In 63% of the patients () the index diagnosis was coded by an office based physician, and for 37% by a hospital-based physician. There were 48,159 hospitalizations in the 2-year period after initial identification of the patients, and HF was found to be the most common cause for hospital admission. Overall mortality rate within two years after initial identification was 23% without differences between women and men. For NYHA I, II, III and IV, two-year mortality rate was 15%, 17%, 31%, and 53%, respectively.
Conclusion: The results underline the relevant HF disease burden in Germany. It has to be considered that the ICD-10 codes used as the basis for the analysis do not allow differentiation between HF with preserved and reduced ejection fraction – each of them usually represents about 50% according to literature. The overall mortality rate of 23% in the newly identified patients in the following 2 years highlights the medical need given in this indication.

P5686 | BEDSIDE
Acute heart failure management at a secondary hospital in Spain: current situation and opportunities for improvement based on the best available evidence

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Introduction: Acute heart failure (AHF) accounts for 101,000 hospital admissions per year in Spain, being the 2nd most frequent DRGs in patients over 75. The British National Institute for Clinical Excellence (NICE) has recently reviewed its management based on current evidence in CG187.
Objectives: Understand current management of AHF at a secondary hospital with a referral population of 210,000 and identify possible differences between various departments involved based on efficiency performance and quality metrics. Benchmark current versus required situation in view of available evidence.
Methods: All 600 discharge reports of patients admitted in 2013 with a CIE9 428 main diagnosis were reviewed. Costs per patient were analyzed using analytical accounting. We studied in-hospital stay, readmissions and mortality. We also applied an age-related and APR-DRG risk adjustment model according to disease severity and likelihood of death according to expected mortality. Organizational and coordination aspects between medical services and levels of care were also analyzed.
Results: Table 1 shows results by service according to different metrics. Solid coordination structures between services and liaison with Primary Care are lacked.

Table 1. Results

	Cardiology	Geriatric Medicine	Internal Medicine	P
Discharges (%)	121 (22)	221 (43)	185 (35)	
Cost per patient (€)	2698	2499	2936	ns
In-hospital stay (days)	6,1	7,5	9,8	<0,001
Readmissions (%)	6	15,1	9,8	0,07
Mortality (%)	5,8	6,2	4,5	ns

Conclusions: 1. Costs are constant across services in spite of a longer median stay in Internal Medicine.
2. A shorter in-hospital stay is observed in Cardiology, with a trend towards a lower readmissions rate.
3. Readmissions rate tends to be greater in Geriatric Medicine.
4. Healthcare organization is fragmented and requires greater co-ordination between medical services and healthcare levels.

P5687 | BEDSIDE
Clinical characteristics and profile of heart failure subjects attending a specialized cardiac clinic in south-western Nigeria

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Introduction: Heart failure is an important contributor to mortality due to non-communicable diseases. There is great dearth of cardiac specialists in Africa with very large populations. Specialized cardiac clinics is an alternate access to quality outpatient cardiac care in a region where tertiary centers are heavily populated and waiting time is considerably high. The aim of this study is to describe the clinical, demographic and other profiles of heart failure subjects presenting in a specialized cardiac care clinic in south West Nigeria over a three year period.
Materials and methods: Goshen Heart Clinic is an outpatient cardiac clinic located in Osogbo, Nigeria. We review the case records of all patients seen with clinical diagnosis of heart failure from May 2011- December 2014. Data were entered into Microsoft Excel and transferred into SPSS 16.0. Diagnosis was made using the Framingham's criteria. Subjects had basic investigations such as Electrocardiography, echocardiography, fasting lipid profile, fasting blood sugar and in relevant cases complete blood count and other supportive investigations. Analysis was done using SPSS 16.0. $P<0.05$ was taken as statistically significant.
Results: One hundred and thirty two subjects including 76 males (57.6%) and 56 (42.4%) were seen during this period. The mean age was 62.1±14.2 years (11–102 years). There was no statistically significant difference between males and females (62.8±12.6 vs. 61.1±16.2 years, p=0.490). Hypertension was present in 103 (78.0%) and diabetes mellitus in 23 (17.4% of patients recruited. The average systolic and diastolic blood pressures were 136.6±28.6 and 83.2±17.6 mmHg respectively. The aetiology of heart failure among the participants are hypertension, 90 (68.2%), dilated cardiomyopathy, 13 (9.8%) valvular heart disease, 8 (6.1%). Peripartal cardiomyopathy and Cor Pulmonale accounted for 3 (2.3%) each while ischaemic heart disease accounted for 2 (1.5%) of the aetiology of heart failure. Heart failure with preserved ejection fraction (EF >50%) and left ventricular systolic dysfunction was found in 70 (53.0%) and 62 (47.0%) of study participants.
Conclusion: There seems to be a minor difference in the profile of heart failure patients seen in a specialized cardiac facility compare to reports from Teaching Hospitals in the same environment. Hypertension is the major aetiology of heart failure among study participants. Control of risk factors, early identification remains a major way to reduce the burden of heart failure among Nigerians.

P5688 | BEDSIDE
High prevalence of asymptomatic left ventricular dysfunction despite excellent risk factor control in a diabetic cohort

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Introduction: Diabetes mellitus is an established cause of left ventricular dysfunction and a strong independent predictor of new onset heart failure. The STOP-HF Midlands project is a screening programme utilizing NT-proBNP and collaborative care to detect left ventricular dysfunction in an asymptomatic diabetic cohort.
Purpose: We sought to assess the prevalence of asymptomatic left ventricular dysfunction in this diabetic population.
Methods: 612 diabetic patients attending the STOP-HF Midlands were included in this analysis. The demographic characteristics and biomarkers of traditional risk factor control in diabetics were recorded, including NT-proBNP. Doppler-echocardiography was performed if the NT-proBNP was >250pg/mL. Left ventricular systolic dysfunction (LVSD) was defined as left ventricular ejection fraction of <50%. Left ventricular diastolic dysfunction (LVDD) was defined by left atrial volume index (LAVI)>34ml/m^2 with lateral E'<10cm/s.
Results: 152 (mean age 71.8 years; 57.9% male) of the diabetic cohort required echocardiography, with a median NT-proBNP of 419pg/mL [252: 808]. Treated hypertension was present in 50% of the group with use of renin angiotensin aldosterone (RAAS) modifying therapies in 60.9%. The blood pressure in this cohort was 128mmHg±18 (SD) over 71mmHg±11 (SD). The total cholesterol, HDL, LDL and triglyceride were 3.8mmol/L±0.9 (SD), 1.4mmol/L±1.3 (SD), 2.2mmmol/L±1.0 (SD), 1.6mmol/L±1.2 (SD) respectively. The creatinine was 95.2μmol/L±28.1 (SD) and HbA1c was 48.7mmol/mol±13.6 (SD). 5.3% of the cohort was found to have LVSD. 28.3% patients had LVDD. 31.3% had LVSD with or without LVDD of LAVI >34ml/m^2 with lateral E'<10cm/s.
Conclusion: These data demonstrate a high prevalence of significant asymptomatic left ventricular dysfunction in a community diabetic cohort despite excellent control of risk factors. Wider use of RAAS modifying therapy in this cohort might reduce the burden of this problem and slow the development to heart failure. The observations indicate that this population should be a focus of efforts to prevent heart failure.

P5689

ABSTRACT WITHDRAWN

P5690 | BEDSIDE

Nation and gender effects on quality of life changes in patients with heart failure: results from the CIBIS-ELD trial

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Purpose: Research shows that quality of life (QoL) depends on medication and clinical factors during treatment, but also on the patient's emotional and social situation and characteristics of the treatment setting. QoL is both an important treatment target and an endpoint in multinational randomization trials. So far, cultural aspects that may influence the perception of psychosocial treatment aspects have rarely been investigated. In order to probe cultural effects on QoL independent of clinical improvement due to beta-blocker up-titration, we analyzed QoL data of Serbian and German heart failure (HF) patients from the Cardiac Insufficiency Bisoprolol Study in Elderly trial (CIBIS-ELD).
Methods: CIBIS-ELD was a randomized, controlled trial in elderly HF patients (>65 y) who were assigned to up-titration with bisoprolol vs. carvedilol. The physical and psychosocial component scores on the short-form health survey (SF36) were recorded at baseline and after 3 months. Age and clinical parameters such as NYHA class at baseline, objective physical performance in the 6-min walk test, LVEF, initial medication and final dosage of study medication at follow-up (0, ⅛, ¼, ½, >½ of target dose) were also recorded. Complete data were available for 136 German (67 f) and 426 Serbian (117 f) patients.
Results: Physical and mental QoL differed between genders ($F>6.6$, $ps<0.0$): men reported better QoL. Further, we observed that overall Serbians reported better physical QoL. Concerning treatment effects, both QoL scores improved from baseline to follow up (effect sizes $d>0.17$, $ps\leq0.001$). This treatment response differed in nations for mental ($F=7.22$, $ps<0.001$) and marginally for physical QoL ($p=0.087$): Serbians showed a more pronounced response on physical and mental QoL compared to Germans (d=0.3–0.34 vs. d=0.07–0.12). Cultural differences in treatment response were strongest for traits that are supposedly less affected by beta-blocker treatment. Treatment effects associated to NYHA class were only observed on physical QoL ($F=9.38$, $p=0.002$). For patients in NYHA III-IV, treatment resulted in a lager improvement of physical QoL than for NYHA I-II. At follow-up, their physical QoL was not different from that of patients with less severe HF anymore ($p>0.10$).
Conclusion: Analyses proved that men report better QoL and Serbian patients show a stronger positive response to treatment/study participation. The nation effect might be associated with national differences in health care system or cultural aspects related to the perception of interpersonal factors, as these effects were more pronounced on the psychosocial QoL facet.

P5691 | BEDSIDE

Seasonal variation in patient backgrounds and in-hospital outcomes of Takotsubo cardiomyopathy: a retrospective cohort study

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Background: Although several previous studies reported seasonal difference in the incidence of Takotsubo cardiomyopathy (TTC), seasonal variation in patient backgrounds and in-hospital outcomes of TTC remains unclear.
Purpose: To examine whether patient backgrounds and in-hospital outcomes of TTC were different between four seasons.
Methods: Using the Diagnosis Procedure Combination inpatient database in Japan, we identified patients who were admitted to acute-care hospitals with TTC and underwent coronary angiography without any revascularization procedure between 2010 and 2013. The patients were classified into the four season groups (spring [March-May], summer [June-August], autumn [September-November], and winter [December-February]) according to their admission dates. Patient backgrounds including 16 relevant coexisting diseases at admission and in-hospital outcomes were compared between the groups.
Results: The study population consisted of 3300 patients (mean age, 73.5±11.2 years; male, 22.4%). The incidence of TTC was highest in the summer group (114 patients/month) and lowest in the spring group (87 patients/month). There was no significant difference in age between the four groups ($p=0.534$). The winter group showed a higher proportion of males than the other three groups (24.7% vs 18.8–20.8%, $p=0.026$). The summer group showed a higher proportion of psychiatric disease than the others (7.9% vs 4.6–5.8%, $p=0.020$), while the autumn group showed a lower proportion of cerebrovascular disease at admission (2.6% vs 4.3–4.7%, $p=0.058$). In-hospital mortality was highest in the winter group (6.2%), followed by the summer (5.8%), spring (4.8%), and autumn (4.6%) groups. There was no significant difference in survival between the four groups ($p=0.391$ for log rank test).
Conclusions: This study suggested that there was a significant seasonal variation in patient backgrounds and in-hospital outcomes of TTC.
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P5692 | BEDSIDE

Identification of climatic condition associated with the onset of acute heart failure syndrome

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Purpose: Although it is well recognized that weather conditions are associated with the incidence of cardiovascular disease, the influence of climatic conditions in the onset of acute heart failure (AHF) remains unknown.
Methods: The Acute Heart Failure Kyoto registry is a physician-directed multicenter registry in Japan enrolling consecutive patients hospitalized for AHF. Between April 2013 and March 2014, 194 patients were admitted for AHF in our hospital. Among 365 days, we identified 141 days transferred for AHF and investigated the association with local weather parameters obtained from Japan Meteorological Agency.
Results: On the AHF admission days, minimum temperature (11.7±8.7℃ vs. 9.6±8.4℃, $p=0.02$) and average temperature (15.7±8.8 ℃ vs. 13.9±8.4 ℃, $p=0.04$) were significantly low, while maximum temperature (20.5±9.5℃ vs. 18.8±9.2 ℃, $p=0.09$) tended to be lower. On the previous days, maximum temperature (20.8±9.5℃ vs. 18.4±9.0 ℃, $p=0.01$), minimum temperature (11.7±8.8℃ vs. 9.6±8.4 ℃, $p=0.02$) and average temperature (15.8±8.8℃ vs. 13.7±8.4℃, $p=0.02$) were significantly low. Compared with the previous days, maximum temperature was increasing (–0.26±3.15℃ vs. 0.42±3.28℃, $p=0.04$), diurnal temperature range was extended (–0.31±3.56℃ vs. 0.49±3.57℃, $p=0.03$) and minimum humidity was decreasing (1.67±14.73% v.s. –2.72±15.71%, $p=0.007$). A mean atmospheric pressure on the AHF admission days tended to be high (1012.1±7.1 hPa v.s. 1013.4±6.4 hPa, $p=0.08$). Interestingly, the maximum instantaneous wind speed tended to rise (–0.24±3.37 m/sec v.s. 0.44±3.99 m/sec, $p=0.08$) compared with the previous days. The wind direction showed a trend toward south and west based on the geographical features. There were no significant differences in sunshine duration. After adjustment for other factors, the difference from the pre-

vious day of minimum humidity [odds ratio (OR), 0.97; 95% confidence interval (CI), 0.96–0.99] and averaged maximum precipitation during previous 2 days [OR, 0.82; 95% CI, 0.67–0.97] were demonstrated as the independent risk factors for the onset of AHF syndrome. The difference from the previous day of the maximum instantaneous wind speed [OR, 1.04; 95% confidence interval (CI), 0.98–1.11] and maximum temperature on the previous day [OR, 0.98; 95% CI, 0.95–1.00] showed a trend toward predicting the admission for AHF.
Conclusions: Not only low temperature but rapid wind velocity, little rain and lower minimum humidity contributed to increase the onset of AHF syndrome.

PROGNOSTIC MARKERS IN HEART FAILURE

P5693 | BEDSIDE
Increased heart rate at hospital discharge augments 1-year rehospitalization rates, but does not affect two and three year rehospitalization rates in heart failure patients

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Purpose: Increased heart rate is a marker for adverse cardiovascular outcomes in heart failure patients. But the value of heart rate at hospital discharge in heart failure patients admitted to the hospital, is not very well known. So we tried to identify the value of heart rate in this setting on rehospitalization rates of heart failure patients.
Methods: We collected information from 210 consecutive heart failure patients hospitalised in our hospital between December 2010 and December 2011 who survived and had a hospital discharge heart rate record in their files. The heart rate values, laboratuary measurement values, demographic and echocardiographic parameters were recorded. One hundred and twenty-nine (61%) of the patients had systolic heart failure, 21 (10%) had diastolic heart failure, 31 (15%) had right heart failure and 29 (14%) had heart failure due to valve disease. The mean age of the patients was 72. One hundred and ten patients (52%) were men and 100 (48%) patients were women. The patients were divided into two groups according to their heart rate at hospital discharge: the patients in the first group had heart rate >75 beats/minute and the ones in the second group had heart rate ≤ 75 beats/minute. The follow-up period was 3 years. At the end of every year (first, second and third year), the patients were called and the rehospitalization status of the patients was learnt. One hundred and fifty-one patients, 142 and 85 patients (or their relatives) could be contacted at the end of first, second and third year follow-up period respectively.
Results: The patients in the first group who had discharge heart rate >75 beats/minute had higher ejection fraction, lower serum uric acid values and had been given inotropic treatment more commonly than the patients in the second group. According to Spearman's correlation analysis, discharge heart rate was positively correlated with ejection fraction and the use of inotropic treatment. Fifty-eight patients were rehospitalized during the first year follow-up. The rehospitalization rate in the first group was significantly higher than in the second group (43 vs. 15, p value=0.03). At the end of second year follow-up 73 patients were rehospitalized. (52 vs. 21, p value=0.07) At the end of third year, a total of 78 patients were rehospitalized due to heart falure. (54 vs. 24, p value=0.33)
Conclusions: In hospitalized heart failure patients, increased hospital discharge heart rate augments early 1-year rehospitalization rates, but its effect disappears in two and three years of follow-up period.

P5694 | BEDSIDE
Clinical profile and prognosis of the combination of diabetes mellitus and heart failure in ambulatory patients

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Background: The prevalence of concomitant diabetes mellitus (DM) and heart failure (HF) is increasing. This relation has a worse prognosis due to a different response to treatment in hospitalized patients as seen in recent clinical trials. Therefore, the impact of DM on HF outpatients remains unclear.
Purpose: To analyze the clinical profile and prognosis of DM in HF ambulatory patients.
Methods: A cohort of 2,498 outpatients with chronic HF recruited between 2007 and 2011 from 18 tertiary centers of HF Spanish Network was prospectively followed for a median of 40 months. Clinical, echocardiographic, ECG, and biochemical parameters were used in a competing risk model to determine the effect of DM on mortality.
Results: The prevalence of DM was 42.4%. DM patients were older, had more cardiovascular risk factors, previous myocardial infarction (MI) and comorbidities. After a multivariable analysis, the presence of concurrent DM and HF was independently related with aging, previous MI, cardiac risks factors, peripheral artery disease and anemia. After adjusting by a propensity score including previous significant variables, DM patients showed a higher HF mortality (sHR 1.22, CI 1.02–1.47), cardiac mortality (sHR 1.47, CI 1.30–1.66), and all-cause mortality (sHR 1.40, CI 1.24–1.59).

Characteristics of 2498 patients of study population

	Non DM patients (1440, 57.6%)	DM patients (1058, 42.4%)	p value
Male, n (%)	1005 (69.8%)	719 (68.0%)	0.328
Age, years, mean (SD)	65,1 (14.0)	69,1 (10.8)	<0.001
Hypertension, n (%)	863 (60.1%)	837 (79.2%)	<0.001
Previous MI, n (%)	454 (31.7%)	479 (45.9%)	<0.001
Anemia, n (%)	475 (33.2%)	503 (47.7%)	<0.001
eGFR <60 mil/min/1.72m^2	583 (40.5%)	544 (51.5%)	<0.001
NYHA III/IV class, n (%)	803 (55.8%)	639 (60.4%)	0.021
LVEF, %, mean (SD)	35 (14.7)	37 (14.5)	0.008
Beta-blockers, n (%)	1134 (79.0%)	855 (80.9%)	0.238
ACEI/ARB, n (%)	1221 (85.0%)	896 (84.8%)	0.858
Spironolactone/Eplerenone, n (%)	807 (56.2%)	575 (54.3%)	0.348

Conclusions: Coexistence of DM and HF in outpatients is very frequent, is associated with a higher risk profile, and has a very unfavorable long-term prognosis in spite of optimal medical treatment.

P5695 | BEDSIDE
The prevalence of sleep-disordered breathing and the predictors of the increased apnea-hypopnea index in patients with chronic heart failure

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Background: Sleep-disordered breathing (SDB) is a widely spread co-morbidity in patients with chronic heart failure (HF) that not only leads to a poor quality of life, but also a shorter life expectancy.
Methods: A total of 132 patients with chronic HF (mean age: 67±11 y, 23% female, left ventricular ejection fraction [LVEF] 37±13%, body mass index [BMI] 28.9±5.2 kg/m^2, New York Heart Association [NYHA] class 2.2±0.7) underwent polygraphy screening between 2011 and 2014. Patients were screened for SDB using the Embletta portable diagnostic system. SDB was defined as an apnea-hypopnea index $\geq$5/h. Patients with LVEF$\leq$40% were categorized as HF with reduced ejection fraction [HFrEF], LVEF$>$40% as HF with preserved ejection fraction [HFpEF].
Results: A total of 58 (44%) patients were diagnosed to have SDB and showed an increased apnea-hypopnea index. Patients with SDB (mean age: 68±10 y, 17% female, LVEF 33±12%, BMI 28.9±5.9 kg/m^2, NYHA class 2.3±0.7) showed lower LVEF compared to patients without SDB (33±12% vs. 40±13%, p$<$0.05). In patients with HFrEF (n=47, 81%) SDB was more common than in patients with HFpEF (n=11, 19%). Logistic regression analysis showed that reduced LVEF and higher creatinine level were predictive (both p$<$0.05) for increased apnea-hypopnea index.
Conclusion: In patients with chronic HF, predictors of SDB include reduced LVEF and high level of creatinine. This fact buttresses the view that patients with more advanced HF are more likely to develop SDB. Screening for SDB provides an easy tool to identify patients with this co-morbidity.

P5696 | BEDSIDE
Predictors of cytolisis in patients with acute decompensated heart failure

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Objective: The impact of acute decompensated heart failure (ADHF) on hepatic function has been described as cardio-hepatic syndrome that may reflect severity of HF. The aim of this study was to evaluate predictors of liver transaminase (TA) increase in patients with ADHF.
Methods: In 200 patients with ADHF (84 male, 72.9±10.7 years (M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, known chronic kidney disease (CKD) 38%, chronic anaemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45±12%, EF <35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT) and aspartate transaminase (AST) were measured baseline. TA were considered abnormal when levels exceeded 50 U/L (local upper normal limit (UNL)). Mann-Whitney test and multivariate logistic regression analysis were performed. P$<$0.05 was considered statistically significant.
Results: Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/ alone AST/ both TA – in 42.3, 19.2, 38.5% respectively). Mean baseline ALT and AST values in patients with versus without increase of TA were 95±36 vs 21±14 U/l and 87±26 vs 25±11 U/l respectively (p$<$0.001).
Patients with vs without increased TA had lower weight (76±15 vs 87±11kg,

p<0.05), higher baseline serum creatinine (152±44 vs 114±44 μmol/l, p<0.001), lower GRFCKD-EPI (34±11 vs 53±18ml/min/1.73m^2, p<0.001), higher heart rate (115±25 vs 92±25 per minute, p<0.001), left ventricular mass index (LVMI) (194±40 vs 174±48g/m^2, p<0.01), lower EF (40±11 vs 45±12%, p<0.05), higher rate of comorbidities – CKD (11 vs 2.8%, p<0.05), chronic anaemia (83 vs 24%, p<0.05), AF (11 vs 1%, p<0.001), higher rate of signs of congestion: echo-hydropericardium (33 vs 12%, p<0.01), radiological signs of hydrothorax (72 vs 32%, p<0.001), jugular venous distension (55 vs 21%, p<0.001).
Liver cytolisis was also associated with community-acquired acute kidney injury (AKI) (70% vs 17.3%, p<0.001) in patients with vs without increased TA.
Main independent predictors of TA increase were AF on admission (odds ratio (OR) 11.25, 95% confidence interval (CI) 2.59–48.89), community-acquired AKI (OR 11.17, CI 4.11–30.32), hydrothorax (OR 5.58, CI 2.12–14.64), jugular venous distension (OR 4.47, CI 1.86–10.75), CKD (OR 4.208, CI 1.605–11.036), echo-hydropericardium (OR 3.71, CI 1.32–10.47), chronic anaemia (OR 2.65, CI 1.102–6.368), EF<40% (OR 2.4, CI 1.006–5.725).
Conclusions: Main independent predictors of cytolisis were AF on admission, AKI, CKD, signs of congestion, chronic anaemia, EF<40%.

P5697 | BEDSIDE
Predictors of heart failure in patients with diabetes mellitus: insights from an observational study over 20 years

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Background: Diabetes mellitus (DM) may cause or worsen congestive heart failure (CHF) regardless the other known CHF predictors.
Purpose: We aimed to study the clinical presentation, predictors and outcomes of CHF among DM patients over a 20-year period.
Methods: A retrospective observational study was conducted for all CHF patients who were admitted in the heart hospital in Qatar between 1991 and 2010. Patients were divided into 2 groups: Group I (CHF plus DM) and Group II (CHF without DM). Patients' demographics, clinical presentation, predictors and in-hospital outcomes were analyzed and compared.
Results: A total of 7068 patients presenting with CHF, of them 57% were diabetics (Group I). In comparison to Group II, patients in Group I were 3 year older, more Arabs, and more likely to have prior myocardial infarction, renal impairment, dyslipidemia, hypertension, and obesity (p=0.001 for all). Whereas Group II were more likely males, Asians, smokers, and likely to be admitted directly to the intensive care unit when compared to Group I. Blood tests showed lower hemoglobin values, lower BNP levels and greater percent of positive troponin T in Group I in comparison to Group II. Left ventricular ejection fraction ≤30 was more prevalent in Group II (p=0.001). Non-ST-elevation acute coronary syndrome was more evident in group II. On multivariate analysis, predictors of CHF in diabetic patients were advanced age, female gender, Arabs, old MI, ACS at presentation and co-existed valvular insufficiency.

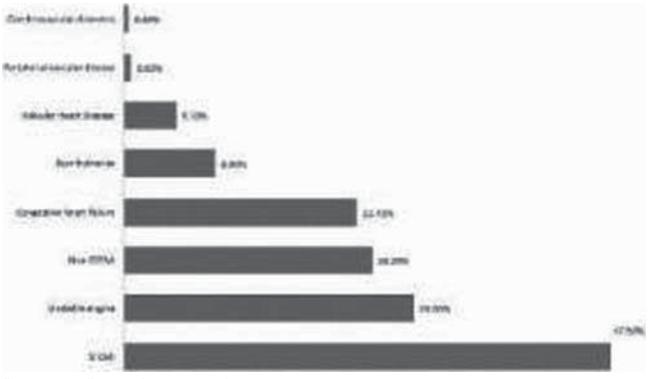

figure 1: cardiovascular presentations

Conclusions: DM is highly prevalent among CHF patients regardless of the underlying cause of CHF. Age, gender and ethnicity play important prognostic role among diabetic patients.

P5698 | BEDSIDE
Investigation of incidence, etiology, prognosis, and predictors of ischemic stroke during hospitalization for congestive heart failure

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Background: Heart failure (HF) increases the risk of ischemic stroke. Data regarding the incidence of ischemic stroke during hospitalization for HF are limited.
Methods: The study population of this retrospective cohort study consisted of patients with congestive HF, consecutively admitted to our center from October 2010 to April 2014. We excluded patients complicated with acute myocardial infarction, and those with dialysis or mechanical circulatory support. We investigated the incidence, etiology, and prognosis of ischemic stroke during hospitalization for HF. Thereafter, we divided the patients without oral anticoagulants at admission into two groups: patients with ischemic stroke and those without it, and explored the predictors of ischemic stroke.
Results: A total of 560 patients (mean age: 76.8 years, female sex: 244 patients, 272 with atrial fibrillation (AF), and 288 without AF) were enrolled. The mean ejection fraction was 47.3±16.6%. Oral anticoagulants were prescribed in 149 patients (140 with AF, 9 without AF). During the hospitalization (median length of hospitalization 18 days), symptomatic ischemic stroke (excluding catheter-related) occurred in 15 patients (2.7% of the total, 7 with AF, 8 without AF). Among 7 ischemic stroke patients with AF, 6 were caused by cardioembolism, and 1 by undetermined etiology according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. Meanwhile, 2 were caused by cardioembolism, and 6 by undetermined etiology in 8 patients without AF. Patients complicated with ischemic stroke during hospitalization for HF showed worse prognosis than those without it (hazard ratio: 3.11, 95% confidence interval: 1.21–6.52). Decongestion markers such as in-hospital weight loss and hematocrit change after admission were similar between stroke and non-stroke groups, whereas short-term increases in blood urea nitrogen (mg/dl) after admission tended to be larger in the ischemic stroke group (at day 3: 6.7±16.4 in stroke group vs. 0.8±8.0 in non-stroke group, p=0.19; and at day 7: 12.3±24.0 vs. 3.7±12.8, p=0.20, respectively). Among comorbidities, previous stroke (odds ratio: 3.33, 95% confidence interval: 1.01–11.00, p=0.04) was significantly associated with an increased risk of ischemic stroke.
Conclusions: The incidence of ischemic stroke during hospitalization for HF was high, even in patients without AF. Previous stroke was significantly associated with the incidence of ischemic stroke. Considering its frequency and poor prognosis, further studies are needed to determine predictors or risk markers of ischemic stroke.

P5699 | BEDSIDE
Left bundle branch block by Strauss criteria predicts outcome of cardiac resynchronisation therapy

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Background: QRS morphology is associated with outcomes from cardiac resynchronisation therapy (CRT). However, left bundle branch block (LBBB) has been variably defined. We hypothesized that patients with LBBB (as defined by Strauss and colleagues) are associated with better clinical outcomes with CRT, compared to LBBB-type pattern (LBBB-p).
Methods: We studied 179 advanced heart failure patients with CRT. Median follow up assessment was 311 (267–494) days. LBBB was defined as (i) a QS or rS morphology in V1–V2; (ii) a QRSd of ≥140ms (men) and ≥130 ms (women), and (iii) mid-QRS notching or slurring in ≥2 leads among I, aVL, V1, V2, V5, and V6 (n=100). Patients with QS or rS morphology in V1-V2, but QRSd less than 130ms or 140ms (women and men respectively) and/or lacked the notching/slurring in at least 2 leads were classed as LBBB-p (n=79). Right bundle branch block was excluded. Echocardiography (left ventricular end systolic volume index, LVESVi; tricuspid annular plane systolic excursion, TAPSE) and cardiac catheter assessment were undertaken. Clinical outcomes were defined as survival, free from transplantation and mechanical circulatory support.
Results: The characteristics of both groups were comparable except QRSd (Table 1). QRSd was further prolonged in both groups post-CRT. There was a significant increase in LVESVi, reduction in TAPSE and increase in right atrial pressure (RAp) in the non-LBBB group. The clinical outcome was significantly worse in the LBBB-p group (LBBB vs LBBB-p: number of patients with adverse outcome 27/100 vs 48/79, log rank p<0.001).

Table 1

	LBBB (n=100)	Non-LBBB (n=79)	p
QRSd baseline (ms)	157 (147–170)	134 (127–141)	<0.001
QRSd paced (ms)	168 (155–180)	151 (144–162)	<0.001
LVESVi baseline	104±3	106±4	0.471
LVESVi paced (ml/m^2)	107±7	115±5	0.003
TAPSE baseline (mm)	14 (12–15)	13 (11–15)	0.209
TAPSE paced (mm)	14 (12–15)	12 (10–14)	0.001
RAp baseline vs. paced (mmHg)	13±2	16±2	0.002

Conclusions: LBBB as defined by Strauss and colleagues is a stronger predictor of outcome following CRT compared to QRSd alone and should be used for the selection of patients for CRT.

P5700 | BEDSIDE

Relationship between galectin 3, myocardial function and 24 hours urinary albuminuria excretion in systolic heart failure

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Background: Galectin 3 (Gal-3) is a relatively new cardiac biomarker. It is reflecting cardiac and renal fibrosis and increased plasma concentrations are associated with a decreased glomerular filtration rate (GFR) and an increased risk of death and a re-admission in heart failure (HF). It is, however, unknown whether it is associated with myocardial function, and whether Gal-3 is associated with another cardio renal marker like 24 hrs urinary albuminuria excretion.
Purpose: This aim of this study was to evaluate the relationship of Gal-3 according to renal and myocardial function in systolic HF.
Methods: The CARDIO-REN study enrolled 149 patients referred to an outpatient HF clinic. Systolic HF was verified by echocardiography according to standard recommendation. Collected data included physical examination, blood samples and 24-hours urine sample. Baseline characteristics of the patients were median age 70 years, 26.5% female, median left ventricular ejection fraction was 33%, and 30% was in functional class III-IV.
Results: GFR was significantly lower in patients with increased plasma concentrations of Gal-3. This association remained significant in linear regression analyses (β: –0.010; 95%-CI: –0.012 to –0.008; P<0.001) adjusted for age and gender. Urinary albuminuria excretion was not associated to plasma concentrations of Gal-3 (β 0.008; 95% CI: –0.028–0.045; P=0.652). There was no significant association between Gal-3 and myocardial function estimated by LVEF, E/E' or left ventricular global longitudinal strain. However, plasma concentrations of Gal-3 was significantly associated with cardiac function estimated by NT-proBNP (β: 0.049; 95%-CI: 0.012–0.087; P=0.011) and MR-proANP (β: 5.796E-5; 95% CI: 0.000–0.000; P=0.002) in multivariate analyses adjusted for age, gender and GFR.
Conclusions: Gal-3 is associated with myocardial function estimated by natriuretic peptides and it is closely and inversely associated with GFR. However, Gal-3 is not associated with 24 hrs urinary albuminuria excretion. Therefore, Gal-3 reflects other cardio renal aspects than Albuminuria. Further studies are needed to evaluate whether plasma concentrations of Gal-3 increase before GFR declines in HF.
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P5701 | BEDSIDE

Prognostic impact of syncope in patients hospitalized with heart failure: insights from the Gulf CARE registry

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Background: The purpose of this study was to report the prevalence and the significance of history syncope up to one-year prior to hospitalization with acute heart failure (AHF).
Methods: Data were derived from a prospective, multicenter, multinational study of 5005 patients hospitalized with AHF from February 2012 to November 2012. Data were analyzed according to the presence or absence of prior history of syncope. Demographic, management, in-hospital and 1-year outcomes were compared.
Results: The prevalence of prior syncope was 4.7%. Age, gender, hypertension, dyslipidemia and sleep apnea requiring therapy were comparable between the 2 groups. Patients with syncope were more likely to be smokers and present with atrial fibrillation (16.6% vs. 12.1%, p=0.04) and have ischemic cardiomyopathy, while the prevalence of right and left bundle branch blocks were comparable between the 2 groups. Patients with syncope had higher prevalence of left ventricular hypertrophy (36% vs. 26.8%, p=0.004) when compared to non-syncope patients, while systolic and diastolic blood pressures as well as left ventricular ejection fraction and pulmonary artery systemic pressures were comparable between the 2 groups. Patients with syncope required more supportive therapy and had worse in-hospital and one-year outcome.
Conclusions: Our study identified a history of syncope in the year prior to admission with AHF to be a marker of worse outcome. Further studies are required to confirm this observation.
Acknowledgement/Funding: HMC

Table 1. Patients hospitalized with HF with and without prior history of synocpe

Variable	Prior syncope (N=229)	No prior syncope (N=4619)	P value
Non invasive ventilation	19 (8.3)	427 (9.2)	0.6
Invasive ventilation	26 (11.4)	312 (6.8)	0.008
Inotropes	73 (31)	629 (13.6)	0.001
AF requiring therapy	22 (9.6)	273 (5.9)	0.02
Ventricular arrhythmias requiring therapy	17 (7.4)	141 (3.1)	0.001
Stroke	9 (3.9)	54 (1.2)	0.001
In hospital mortality	31 (13.5)	235 (5.1)	0.001
1 year mortality	1067 (23.1)	68 (29.6)	0.03

P5702 | BEDSIDE

Aberrant brain functional connectivity in patients with heart failure

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Background: Heart failure (HF) patients show brain injury in autonomic and neuropsychologic control sites, and such damage can change resting-state functional connectivity (rs-FC, temporal correlations between neuronal activities of distinct brain regions) that may lead to alteration in overall functional organization. However, rs-FC and whole-brain organization of these interactions in HF is unknown.
Purpose: To investigate the whole-brain functional interactions and network organization of these interactions in HF and control subjects.
Methods: We acquired rs-functional MRI (3.0-Tesla scanner) data from 27 HF (age, 55.3±7.9 yrs; BMI, 27.9±5.5 kg/m^2; 20 male; LVEF, 28.0±9.2%) and 53 controls (52.7±6.2 yrs; 25.4±3.5 kg/m^2; 36 male). Data were processed using standard procedures, and group analyses were performed using ANCOVA (covariates, age and gender) and permutation tests.
Results: Decreased FC in HF (Fig. 1a, blue) were involved in the caudate, olfactory, vermis 10, and precentral gyrus, and increased FC in HF (Fig. 1b, red) were lateralized to the right hemisphere and involved in the middle frontal, superior parietal, inferior temporal, and fusiform gyri, vermis 6, and cerebellum 6. HF showed aberrant brain network organization in sites showing altered FC over controls.

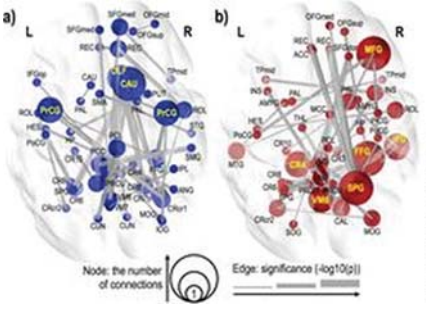

Fig. 1: Significantly decreased (a) and increased (b) FC in HF over control subjects. Node sizes and edge thicknesses represent more number of connections and significance levels, with increasing sizes and thicknesses, respectively. Bold yellow labels indicate sites with at least 3 functional connections.

Conclusions: These findings suggest that brain dysfunction in HF extends to resting conditions, and autonomic and neuropsychologic deficits in HF may stem from the altered FC and brain network organization that may contribute to higher morbidity and mortality in the condition. The outcomes likely result from the prominent structural changes in both axons and nuclear structures reported earlier in HF, and protecting neural tissue may improve FC integrity, and thus, reduce morbidity and mortality and increase quality of life.
Acknowledgement/Funding: This work was supported by National Institutes of Health R01 NR-013625 and R01 NR-014669.

HYPERTENSION HAEMODYNAMICS

P5703 | BEDSIDE

Long-term mortality in patients admitted with hypertensive crisis

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Background and introduction: Hypertensive crisis, formerly referred to as "malignant hypertension", is a severe elevation in blood pressure ≥180/110 with or without end organ involvement. Small series have reported significant morbidity and mortality despite intensive management of these patients. There is limited data on the long term outcomes of patients admitted with hypertensive crisis in the modern era of antihypertensive therapy.
Purpose: We performed a retrospective cohort analysis of consecutive adults admitted with hypertensive crisis to determine long-term mortality.
Methods: Consecutive patients with a hypertensive crisis at a university medical cxenter from 1/2000 through 12/2010 were retrospectively identified by International Classification of Diseases (ICD)-9 diagnosis codes (401.0, 405.0, 405.01, 405.09, 404.0, 403.0, 402.0) assigned during inpatient hospitalization. All avail-

able demographics and baseline clinical data were obtained from the electronic medical record. Survival was ascertained using the Social Security Death Index (SSDI) database.
Results: A total of 955 subjects were identified with hypertensive crisis; 940 (98.4%) had survival data and were included in the analysis. Mean age at presentation was 60.9±17.8 years and 56.5% were female. Comorbidities included diabetes in 35%, coronary artery disease in 34.4%, heart failure in 25%, and kidney disease in 12.8%. Mean follow-up was 5.4±3.0 years following the index hospital admission. 597 (63.5%) had a repeat hospitalization; 181 (19.2%) had 5 or more readmissions. Stroke occurred in 176 (18.7%). 223 (23.7%) subjects died during follow up. Mortality at 1, 3, 5, and 10 years were 7.7%, 14.1%, 20.2%, and 31.8% respectively. Using multivariable adjustment, age (HR 1.04, CI 1.03–1.05), a history of heart failure (HR 2.06, CI 1.55–2.75), stroke (HR 1.57, CI 1.09–2.27), and chronic kidney disease (HR 1.54, CI 1.08–2.18) were significant risk factors for long-term mortality in patients with hypertensive crisis.
Conclusions: Despite modern pharmacologic treatment, hypertensive crisis was associated with high rates of morbidity and mortality. Subjects who died during long-term follow-up were older and had a higher prevalence of stroke and chronic kidney disease. Patients with hypertensive crisis may need intensive treatment after discharge to address their risk for future cardiovascular events.

P5704 | BEDSIDE
One-point carotid wave intensity in newly diagnosed never treated hypertensive patients

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Objective: Increased left ventricular (LV) contractility is described in hypertension. In the present study we assessed the LV contractility using the traditional echocardiographic parameters and the wave intensity (WI) parameters as ventricular-arterial coupling in newly diagnosed and never treated hypertensive patients.
Methods: Participants were 145 normotensives and 145 age–and-sex match hypertensives (mean age 50±10 vs 51.9±12 years). Antropometric, office blood pressure (BP) measurements and echocardiography were performed. LV mass index, relative wall thickness, LV stress, LV ejection fraction (LVEF), midwall fractional shortening (MWFS), circumferencial end systolic stress (cESS) and the E/A ratio and E/Em as a measure of diastolic function were calculated. Wave intensity (WI) analysis was performed at the level of the common carotid artery as well non-invasive one-point measurement of pulse wave velocity (PWV), using a high definition echo-tracking system implemented in the echo-machine (Aloka).
Results: Hypertensive patients, after adjustment for weight and physical activity, had similar heart rate but significantly higher LVEF (62.9%±6.5% vs 64.6%±7.2%, p=0.016), cEES (121.9±39 vs 137.9±41.3 gr/cm^2, p=0.006), LV stress (59.5±22.2 vs 65.9±23.4 kdyn/cm^2, p=0.048), one-point PWV (5.42±1.0 vs 6.5±1.6 m/s, p<0.0001) and WI (W19,308±4,675 vs 13,646±7,368 mmHg m/s3, p=0.001; W2 2,995±1,868 vs 4,289±2,017 mmHg m/s3, p=0.001) compared with normotensive subjects. The hypertensive group was then divided in tertiles according to LVEF: systolic, diastolic BP and heart rate were similar among the 3 groups but relative wall thickness was positively related with LVEF (p=0.05) and LV internal diameter in diastole (p=0.003) negatively. MWFS (p=0.01), fractional shortening (p=0.007) significantly increased according to LVEF while the opposite was observed for cESS (p=0.004) and LV stress (p=0.003). Among the WI parameters W1 was significantly higher in the group with higher LVEF (11,934±5,836 group 1, 11,576±5,857 group 2, 17,227±8,889 mmHg m/s3 group 3 p<0.0001).
Conclusions: In patients with new onset of hypertension LV structure was similar to normal subjects but they had higher LV performance represented by LVEF and higher WI. Moreover, hypertensive patients with higher LVEF had the tendency of concentric LV remodeling, lower LV stress and higher LV performance combined with higher W1 parameter that mainly represents the inotropic capacity of the LV.

P5705 | BEDSIDE
Abnormal aortic and coronary function is associated with reduced endothelial glycocalyx thickness in hypertensives

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The integrity of endothelial glucocalyx plays a vital role in vascular permeability, inflammation and elasticity. The association between damage of endothelial glucocalyx, impaired arterial elastic properties impaired coronary microcirculation, and hypertension has not been explored.
Methods: In 120 untreated patients (age: 54±11 years) with essential hypertension and 40 controls of similar age and sex we measured a) carotid-femoral pulse wave velocity (PWVc m/sec-Complior SP ALAM) and central systolic blood pressure (cSBP -mmHg), pulse pressure (cPP-mmHg) and augmentation index (AI %-Arteriograph,TensioMed) b) LV longitudinal (GLS -%), strain, using speckle tracking echocardiography and coronary flow reserve (CFR) of the LAD after adenosine infusion using Doppler echocardiography c) perfusion boundary region (PBR- micrometers) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sideview Darkfield imaging (Microscan, Glycocheck).The PBR in microvessels is the cell-poor layer which results from the phase separation between the flowing red blood cells (RBC) and plasma.The PBR includes the most luminal part of glycocalyx that does allow cell penetration.Increased PBR is considered an accurate index of reduced endothelial glycocalyx thickness because of adeeper RBC penetration in the glycocalyx.
Results: Compared to controls, hypertensives had higher PBR (2.0±0.17 vs. 1.77±0.14), PWVc (10±2 vs. 8.5±2,), cSBP (140±21 vs. 95±20), cPP (46±17 vs. 30±5), AI (28±16 vs. 15±10) and lower CFR (2.5±0.7 vs. 3.5±1) and GLS (–17±4 vs. –22±2.5, p<0.05 for all comparisons).
Reduced endothelial glucocalyx thickness as assessed by increased PBR was related with increased clinic SBP (r=0.41), DBP (r=0.50), cSBP (r=0.50), cPP (r=0.36), AI (r=0.20) and reduced CFR (r=–0.30) (p<0.05 for all associations). These associations were more prominent for PBR measured in the microvessels ranged from 20–25 micrometers. Increased PWV and cSBP were related with reduced GLS (r=0.35, r=0.40) and CFR (r=–0.40 r=–0.35) respectively (p<0.05 for all associations) while reduced CFR was also associated with impaired GLS (r=0.36) (p<0.05 for all associations)
Conclusion: Endothelial glucocalyx is impaired in newly diagnosed untreated hypertensives and is related with abnormal aortic elastic properties and coronary microcirculatory function leading to impaired LV longitudinal deformation.

P5706 | BEDSIDE
Renal artery anatomy as a new risk factor for resistant hypertension?

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Purpose: Implementation of renal denervation into clinical practice increased the proportion of resistant hypertension patients proceeded to multidetector computer tomography (MDCT) angiography for confirmation of technical feasibility of the procedure. And the failure rates reported in different studies were really surprising thus raising a question whether we've missed association between specific features of renal arteries anatomy and resistance to antihypertensive therapy. The aim of the present study was to compare renal arteries anatomy according to MDCT angiography results in resistant hypertension patients referred to renal denervation and in control group consisting of subjects after MDCT performed for various reasons.
Material and methods: We examined 37 patients, selected for renal denervation after confirmation of true treatment resistance according to current guidelines with a mean age 51±12 years, 48.6% of patients (17) were male, 51.4% (18) female. Control group consisted of 32669 patients form the database, who routinely underwent MDCT angiography with available data on renal arteries anatomy.
MDCT was performed in two centers with 128-slides CT Somatom Definition 128 (Siemens).
Results: In resistant hypertension group additional and multiple renal arteries were detected in 20 patients (54%), fibromuscular dysplasia in 2 (5.4%) patients, early proximal division in 3 (8.1%) subjects and the rest 12 (32%) had normal anatomy of the renal arteries. Bilateral additional renal arteries were present in 5 (13.5% of the whole group, 25% of patients with additional renal arteries) patients, 9 patients (24.3% and 45%, respectively) had more than one additional renal artery. All arteries seemed intact with no hemodynamically significant stenosis.
Data from the control group database shows that additional or multiple renal arteries were present only in 8331 subject (25.5%), and only 233 (2.8%) of them bilaterally. The frequency of additional renal arteries was higher in resistant hypertension population (p=0.0001), as well as the proportion of patients with bilateral additional renal arteries (p=0.00001).
Conclusion: The resistant hypertension patients are characterized by higher incidence of additional renal arteries, both uni- and bilateral. Thus observation can indicate that renal anatomy might be of importance in resistant hypertension as an underestimated cause nowadays.

P5707 | BEDSIDE
Ankle-brachial index and brachial-ankle pulse wave velocity jointed to predict mortality in a community study

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Background: Pulse volume recordings and blood pressures at arms and ankles can be obtained automatically and simultaneously to allow fast measurements of the brachial-ankle pulse wave velocity and the ankle-brachial index. We evaluated the association between ankle-brachial index, brachial-ankle pulse and mortality in a community.
Methods: A total of 1329 residents (≥40 yrs) in Kinmen completed a health survey, including interview, physical examination, blood test, and the measure-

ments of brachial-ankle pulse wave velocity and ankle-brachial index in 10 working days. By linking with the National Death Registry, we retrieved the dates and causes of death of all participants until December 31, 2012. The median follow-up durations was 10 years. The Cox proportional hazard model was used to estimate the hazard ratios (HRs) of abnormal Ankle-brachial index (ABI <0.9 or >1.3) and high brachial-ankle pulse wave velocity (baPWV ≥ 1670 cm/sec) for total/cardiovascular mortality.
Results: A total of 115 deaths occurred and 26 cardiovascular mortality during the 10-yrs (median) fallow period. The prevalence of abnormal ABI and high baPWV were 3.09% (n=41) and 26.34% (n=350), respectively. The total mortality was 4.1 per 1000 persons for normal PWV and normal ABI, 20.6 per 1000 PYS for normal PWV and abnormal ABI, 19.6 per 1000 PYS for high PWV and normal ABI, and 48.3 per 1000 PYs for high PWV and abnormal ABI. The crude hazard ratio (HR) of 12.43 (95% confidence intervals: 6.03–25.6) for high baPWV and abnormal ABI, 4.92 (3.30–7.32) for high PWV and normal ABI, and 5.16 (1.85–14.42) for normal baPWV and abnormal ABI, compared to those with normal ABI and normal baPWV. In the multivariate model, the HRs of total mortality was 2.82 (1.12–7.11) high baPWV and abnormal ABI, was 1.87 (1.09–3.21) for high PWV and normal ABI, and was 2.67 (0.87–8.19) for normal baPWV and abnormal ABI.
Conclusion: Ankle-brachial index and brachial-ankle pulse wave velocity jointed to significantly predict total and cardiovascular mortality in a general community cohort.

P5708 | BEDSIDE
Impact of myocardial deformation on exercise tolerance in patients with arterial hypertension

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Purpose: The aim of the investigation was to assessment of the relation between exercise tolerance (ET) and myocardial deformation in patients with arterial hypertension and preserved left ventricle (LV) ejection fraction (LVEF).
Methods: We examined a cohort of 82 patients with arterial hypertension and preserved LVEF (mean age 56.3±2.5 years), who were divided depending on the severity of LV hypertrophy into 4 groups: without hypertrophy (n=28, 1st group), mild hypertrophy (n=17, 2nd group), moderate hypertrophy (n=18, 3rd group) and severe hypertrophy (n=18, 4th group). Control group consisted of 30 healthy persons. By the use of speckle tracking echocardiography we studied the parameters of myocardial deformation, which were: in absolute values of Longitudinal global systolic Strain (LGSS), Circumferential global systolic strain (CGSS), Radial global systolic strain (RGSS), rate of LGSS (LGSSR), rate of CGSS (CGSSR), rate of RGSS (RGSSR). We also assessed of LV twist, apical and basal rotation. All patients were undergoing bicycle exercise stress test (BEST) in order to assess the possibility to achieve endpoint criteria of submaximal BEST.
Results: There was no difference of LVEF among all groups. LGSS, CGSS and RGSS as well as LGSSR, CGSSR and RGSSR were significantly reduced in patients of 4th and 3rd groups ($p<0.01$ for other groups). Patients of 1st group had lower LGSS (14.3±0.1 vs 16.9±0.2%, $p<0.001$) and LGSSR (0.70±0.03 vs 0.81±0.02 c-1, $p<0.001$) than those in control group, but there was no difference of CGSS, RGSS, CGSSR and RGSSR in both groups. These data may suggest the early deterioration of longitudinal contractility in hypertensive patients even without LV hypertrophy. Patients, who achieve endpoint criteria of submaximal BEST had larger LGSS (14.5±1.2 vs 11.2±1.1%, $p<0.05$), LGSSR (0.75±0.02 vs 0.63±0.03 c-1, $p<0.01$) and lower apical rotation (4.72±0.6 vs 7.54±0.8°, $p<0.01$), and twist (9.8±0.4 vs 11.2±0.2°, $p<0.05$).
Conclusion: The reduction of LGSS and LGSSR are the early markers of impairment of the LV systolic function in patients with arterial hypertension. In hypertensive patients abnormal longitudinal mechanics and higher LV twist and apical rotation were associated with impaired exercise tolerance.

P5709 | BEDSIDE
Echocardiographic assessment of longitudinal and radial left ventricular systolic function in hypertensive patients

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Background: Few data are available on the relationship between left ventricular (LV) circumferential and longitudinal systolic function in hypertensive patients with preserved LV ejection fraction (EF). The aim of this study is to analyze LV circumferential and longitudinal systolic function and their main determinants in a group of hypertensive patients.
Methods: In 1285 hypertensive patients (547 female, mean age 57±13 yrs, 77% treated) a standard echocardiographic examination was performed, to assess LV anatomy and systolic function parameters, including EF, Midwall fractional shortening (MidFS) and MidFS adjusted for endsystolic stress (ESS_MidFS). In addition longitudinal systolic function was evaluated by the measurement of tissue Doppler peak systolic velocity of the mitral annulus (Sm). A reduced systolic function was defined in the presence of ESS_MidFS lower than 89% or Sm lower than 8cm/sec.
Results: A modest but statistically significant relationship between MidFS or ESS_MidFS and Sm (r=0,08, $p<0,001$) was observed. MidFS was independently related to age, body mass index (BMI), LV mass index, relative wall thickness (RWT) and heart rate, while the main determinants of Sm were age, heart rate, systolic blood pressure and LV mass index. According to previously defined criteria a reduction of Sm and ESS_MidFS was observed in 47% and 26% of patients, respectively.
Conclusions: Longitudinal systolic function is impaired in a high percentage of hypertensive patients with preserved EF and identifies a higher number of patients with impaired systolic function. The determinants of longitudinal and circumferential systolic function are, at least in part, different.

P5710 | BEDSIDE
Testosterone levels in hypertensive patients with vascular organ damage

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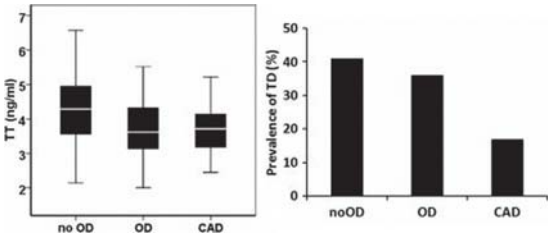
Purpose: Testosterone levels are decreased in hypertensive patients compared to normotensive subjects with similar age. Measurements of carotid IMT or aortic stiffness are reasonable for detecting vascular organ damage (OD) in patients with arterial hypertension. We investigated whether low testosterone concentration is associated with vascular OD in hypertensive patients.
Methods: 178 consecutive asymptomatic hypertensive males (40–60 y/o) were evaluated using exercise treadmill test and stress echocardiography. Men with positive one or both of the two tests were referred for coronary angiography in order to document coronary artery disease (CAD). All patients underwent carotid-femoral pulse wave velocity (PWV) and carotid IMT evaluation. Vascular OD was detected when IMT>0.9 mm (or plaque) and/or PWV>10 m/s. Total testosterone (TT) levels were measured in all participants. Testosterone deficiency (TD) was defined when TT levels were below 3.4 ng/ml.
Results: Coronary angiography revealed significant stenosis in 31 (17%) patients. The prevalence of Grade II/III hypertension was not different between CAD patients and subjects without CAD. Subjects without CAD were further divided according to presence/absence of vascular OD. Patients with vascular OD had lower TT level ($p<0.001$) and a greater prevalence of TD ($p<0.01$) compared to hypertensive subjects without OD after adjustment for age and blood pressure (figure). Interestingly, CAD patients and non CAD subjects with vascular OD had comparable TT concentration and prevalence of TD.



TT levels,TD prevalence and vascular OD

Conclusion: TT concentration is decreased in hypertensive patients with vascular OD compared to subjects without OD. The findings of this study underscore the predictive value of TD in hypertensive males with OD.

P5711 | BEDSIDE
Oscillometric mean arterial pressure-derived, not systolic pressure-derived, central blood pressure better discriminates cardiac structural abnormalities

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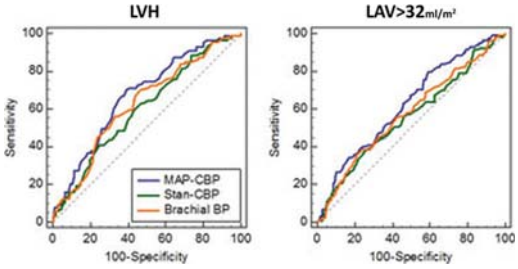
Background: Central blood pressure (CBP) independently predicts cardiovascular outcomes, but the calibration method to derive CBP noninvasively from brachial blood pressure (BP) affects its accuracy. Although standard CBP (Stan-CBP) is estimated using brachial systolic and diastolic BP, the validity of peripheral systolic BP in oscillometric method is limited. Recently, CBP derived from oscillometric mean arterial pressure (MAP) and DBP (MAP-CBP) has been validated as a better estimate of invasive CBP.
Purpose: To examine which CBP method can discriminate cardiac structural abnormalities more accurately.
Methods: 349 community-based patients with stage A heart failure (71±5 years, 174 males) had CBP by two calibration methods: MAP-CBP and Stan-CBP. LV mass index and left atrial volume by echocardiography were compared with CBPs.
Results: MAP-CBP showed higher SBP (149±20 mmHg) than Stan-CBP (128±15, $p<0.0001$). Although they were modestly correlated (rho=0.74, $p<0.001$), Bland-Altman plot demonstrated a large bias (20.5mmHg) and limits of agreements (24.4). In ROC curve analyses, systolic CBP derived by MAP-CBP significantly better discriminated LV hypertrophy (AUC 0.67) than Stan-CBP

(0.60, p=0.007) or brachial BP (0.63, p=0.26). Moreover, Stan-CBP provided no better discrimination than brachial BP (p=0.09). Continuous NRI (p<0.001) and IDI (p<0.001) corroborated superior discrimination of MAP-CBP. Similarly, MAP-CBP better distinguished LA dilatation (LAVI≥32ml/m^2) (AUC 0.63) than Stan-CBP (0.56; vs MAP-CBP, p=0.005) and brachial BP (0.58; vs MAP-CBP p=0.006); and Stan-CBP provided no better discrimination than brachial BP (p=0.09).



Conclusion: CBP is calibration-dependent. CBP derived from oscillometric MAP and DBP is a better discriminator for cardiac structural abnormalities.

P5712 | BEDSIDE
Renal resistive index in resistant hypertension: a case-control study

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Background and aim: Renal resistive index (RRI), assessed by Doppler sonography, has been classically considered as an expression of intrarenal vascular resistance. Recent studies, however, have showed that RRI is also influenced by arterial compliance, confirming its possible role as a marker of systemic vascular alterations. Our purpose was the evaluation of the renal resistive index in patients with uncontrolled hypertension with 3 or more antihypertensive drugs, including a diuretic (RH), in comparison with a group of patients with resistant drug hypertension controlled by 4 or more antihypertensive drugs (RH4) and patients with controlled hypertension by 3 antihypertensive agents (CH3). We also considered the correlation between renal resistive index and subclinical organ damage.
Design and method
We enrolled 120 patients (40 RH, 40 RH4, 40 CH3) without renal arterial stenosis and known nephropathy from our outpatient clinic for hypertension. We matched patients for age, sex and BMI. Each patients performed a 24-hour blood pressure monitoring (ABPM), office blood pressure (OBP) measurement, Glomerular Filtration Rate (according to MDRD) assessment, echocardiography and carotid echo-color-Doppler ultrasonography. We also estimated renal resistive index by Doppler sonography.
Results: OBP and ABP were higher in RH group in comparison with the RH4 and CH3 groups (OBP: 155±7/88±5 vs 130±7/79±9 vs 127±7/76±5 mmHg, p 0.001; ABP: 141±10/85±6 vs 122±8/73±6 vs 121±8/72±6 mmHg, p 0.001). Office pulse pressure was higher in RH than RH4 and CH3 groups (66±12 vs 53±10 vs 51±6 mmHg, p 0.001). Renal resistive index was similar in RH and RH4 (0.72±0.08 vs 0.70±0.07, p n.s.) but they were both higher than CH3 group (0.72±0.08 vs 0.65±0.06, p 0.004; 0.70±0.07 vs 0.65±0.06, p 0.019). We also found a significant correlation between renal resistive index and age (r=0.421, p 0.0001), Glomerular Filtration Rate (r=–0.197, p 0.036), office pulse pressure (r=0.4 p 0.0001). We did not observe significant correlation between renal resistive index and left ventricular mass index and carotid intima-media thickness.
Conclusions: Renal resistive index is higher in patients with drug-resistant hypertension. The correlation between office pulse pressure and the renal resistive index confirms that the latter depends much more on systemic haemodynamics than on renal ones. These data need to be confirmed by larger and prospective studies.

P5713 | BEDSIDE
Low systolic blood pressure is associated with increased mortality in patients with myocardial injury

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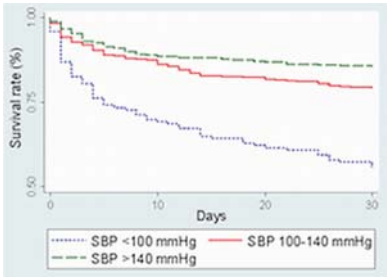
Background: Cardiac troponin (cTn) elevations are commonly found in patients with clinical conditions other than acute myocardial infarction (MI), indicating myocardial injury. Both high and low blood pressure are among the proposed mechanisms causing myocardial injury.
Purpose: To assess the prognostic implications of high and low systolic blood pressure (SBP) in hospitalized patients (pts) with myocardial injury.
Methods: We prospectively studied unselected hospitalized patients who had cTnI measured because of suspected MI. The decision limit for an MI was 30 ng/L (CV<10%). Pts with evidence of myocardial injury but otherwise not fulfilling the MI diagnosis were classified into three groups according to SBP values: Group A <100 mmHg, group B 100–140 mmHg and group C >140 mmHg. Pts were followed for 30 days with mortality as the end-point. Survival data were analyzed by using Kaplan-Meier curves and multivariate Cox regression analysis.
Results: During 2010 a total of 3762 consecutive pts were considered, 1089 of which had myocardial injury. The pts were categorized according to SBP: 143 pts (13%) had SBP <100 mmHg (group A), 389 pts (36%) had SBP 100–140 mmHg (group B) and 557 pts (51%) had SBP >140 mmHg (group C). After 30 days of follow-up 224 pts had died (21%). Mortality differed significantly between the three groups: Group A 63 pts (44%), group B 81 pts (21%) and group C 80 pts (14%), (P<0.0001, Figure). In the multivariate Cox regression analysis, the Hazard Ratio for group A pts was 3.18 (95% CI 1.33–7.58), compared with group B pts. Group C pts did not have significantly increased mortality compared with group B.



Survival analysis: Group A to C

Conclusions: In hospitalized patients with myocardial injury those with hypotension have a more than three-fold increased 30-day mortality compared with normotensive pts.
Acknowledgement/Funding: The Danish Heart Foundation. Odense University Hospital's Research Funds.

P5714 | BENCH
New diagnostic tool for masked hypertension; impaired sleep quality

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Background: The aim of this study was to evaluate a relationship between MHT and impaired sleep quality. Additionally, we evaluated the diagnostic role and prevalence of poor sleep quality among patients with newly diagnosed masked hypertension (MHT).
Methods: A total of 112 individuals, 72 patients with new diagnosed MHT and 40 normotensive healthy volunteers were included in this study. All patients underwent evaluation comprising 12-lead electrocardiography (ECG), transthoracic echocardiography, 24-hour Holter ECG, and basic laboratory tests.Additionally, all participants completed questionnaires, including the Pittsburgh Sleep Quality Index (PSQI).
Results: The total PSQI score was significantly higher in the MHT group than in the normotensive healthy volunteers (4.13±2.43 vs. 2.33±1.67, p<0.001). A PSQI score >5 was found in 45.8% (n=33) of patients in the MHT group and 15% (n=6) of patients in the normotensive group (p<0.001). Non-dipper pattern was found %17.5 in healthy volunteer group, however %59.94 (n=41) in MHT group (p<0.001). When we compared the dipping pattern of the MHT groups, there was a significant difference in PSQI score between the dipper and non-dipper groups (4.87±3.21 vs. 3.58±2.33, p<0.001).
Conclusions: This study demonstrates impaired sleep quality in subjects with MHT, particularly those with a non-dipper pattern. Additionally, this study indicates impaired sleep quality maybe helped diagnose of MHT, particularly in the non-dipper group.

DEEP DIVE INTO PERCUTANEOUS VALVULAR INTERVENTION

5784 | BEDSIDE
Percutaneous annuloplasty for mitral valve repair: multicentre trial report

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Background: The Cardioband system enables percutaneous implantation of an adjustable "surgical-like" mitral annuloplasty ring using a transseptal approach.
Purpose: The aim of this study was to evaluate the feasibility, safety and 6 month

outcome of Cardioband in patients with functional mitral regurgitation (FMR) in a multicentre study.
Methods: Between February 2013 and November 2014, 30 high-risk patients with significant FMR were enrolled at 5 sites in Europe. After a Heart Team evaluation all patients were screened by echocardiography and cardiac CT to assess feasibility. Echocardiographic data were analysed by an independent core-laboratory.
Results: The mean age of the patients was 72±7 years, 25 were male (83%). Mean Log-EuroScore and median STS score were respectively 20±13% (2.2%-51%) and 7±8% (1.0%-33.8%). At baseline 97% of patients were in NYHA class III-IV with mean left ventricular ejection fraction of 35±10% (15%-57%). Device implantation was feasible in all patients (100%). Acute procedural success (device successfully implanted with acute reduction of MR <2/4 +) was achieved in 28 patients (93%). After cinching of the device, an average of 20% reduction of the septo-lateral diameter was observed (from 36±4 mm to 29±5 mm; $p<0.01$). Thirty-day mortality was 6.7% (adjudicated as unrelated to the device). At 6 month follow-up (N=17), 81% of patients were in NYHA class I-II with significant improvement in quality of life (MLWHFQ from 38 to 18; $p<0.05$) and 88% of patients had MR≤2/4+.
Conclusions: Transseptal direct mitral annuloplasty with an adjustable "surgical-like" ring is feasible, with a good safety profile. Effective reduction in MR severity is observed in most patients related to a significant septo-lateral dimension reduction. MR reduction is stable and consistent at 6 months, with clinical benefit.
Acknowledgement/Funding: Supported by Valtech

5785 | BEDSIDE
Predictors of left ventricular reverse remodeling and outcome in heart failure patients with severe mitral regurgitation treated with the MitraClip

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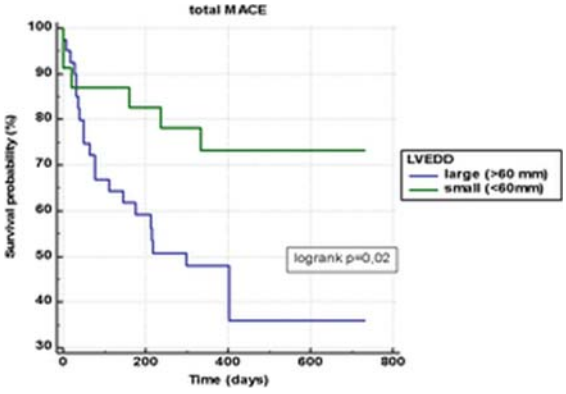
Background: Although percutaneous mitral valve repair using the MitraClip can successfully reduce the severity of mitral regurgitation (MR), clinical outcome is not consistent which might relate to a variable effect on left ventricular (LV) remodeling.
Objective: To identify predictors of LV reverse remodeling and outcome in heart failure (HF) patients (pts) with severe MR undergoing Mitraclip implantation.
Methods: Study population consisted of 88 consecutive pts with advanced HF and severe MR (age 73±10y, 80% NYHA III/IV, LV ejection fraction 36±13%, logistic EuroSCORE I 21±15). In 44 pts LV remodeling could be assessed from serial echocardiography before and 6 months after MitraClip implantation. LV reverse remodeling was defined as a >10% decrease in LV end-diastolic volume (LVEDV) as measured off-line by a core lab using biplane Simpson's method. Major adverse cardiac events (MACE) were a composite of cardiac death, need for mitral valve reintervention or hospitalisation for heart failure.
Results: MitraClip implantation reduced LVEDV from 180±67ml to 160±68ml (Δ 11±17%). Logistic regression analysis identified LV end-diastolic diameter (LVEDD) as the only independent predictor of LV reverse remodeling with an optimal cut-off value of 60mm. LV reverse remodeling was present in 33% of pts with LVEDD ≥60mm and in 78% of pts with LVEDD<60mm. During a median follow up of 366 days (range 49–731), MACE occurred in 27 pts (31%). Cox regression analysis revealed that, beyond a high logistic EuroSCORE, a LVEDD≥60mm was independently associated with MACE (RR 4.3 (95% CI 1.3–14), see figure)



LV dimension and prognosis

Conclusion: Extensive LV dilation impedes LV reverse remodeling and attenuates clinical outcome benefits after Mitraclip implantation in HF pts with severe MR.

5786 | BEDSIDE
Prevalence and impact of atrial fibrillation in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. A subanalysis of the SOURCE XT prospective multicentre registry

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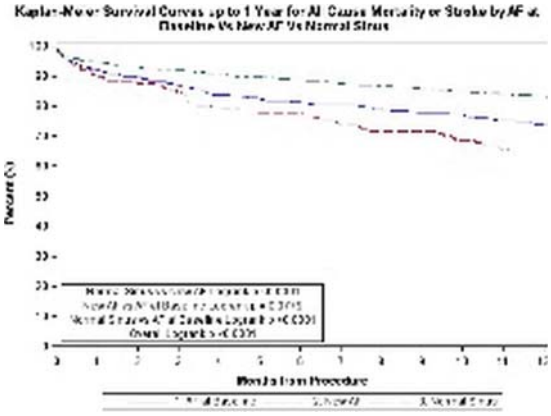
Background: Atrial fibrillation (AFib) is a well-established predictor of adverse outcomes in patients with aortic stenosis. Previous studies have demonstrated increased risk of mortality due to AFib in patients undergoing valve surgery. Data on the impact of AFib in patients undergoing TAVI are scant.
Purpose: To assess prevalence, predictors and outcomes of patients treated by TAVI according to the presence of pre-existing or new onset AFib (AFib occurring within 30 days after TAVI).
Methods: We analysed the dataset of the SOURCE-XT study (Clinicaltrials.gov Identifier: NCT01238497), a multicenter prospective registry of patients treated by TAVI with the SAPIEN XT valve at 99 sites in 17 countries. Follow-up was scheduled at discharge, 1 month and 1 year.
Results: Of the 2688 consecutive TAVI patients, follow-up was complete in 98.7% at 1 year. AFib was reported in 24.6% (n=662) patients, while 5.1% (n=138) developed new onset AFib. Afib patients showed significantly worse 1-year outcome compared to patients without AFib in terms of all-cause mortality and the combination of all-cause mortality or stroke (Figure). In multivariable analysis, total A-fib as well as new onset or pre-existing AFib alone remained independent predictors of 1-year mortality and of 1-year mortality or stroke. Independent predictors of new onset AFib were age (OR 1.1), non-transfemoral access route (OR 3) and balloon post-dilation (OR 1.6). No interaction was observed between paravalvular leak and occurrence of new onset AFib.



Conclusions: The presence of either pre-existing or new onset Afib is a major predictor of increased mortality and of mortality or stroke in patients undergoing TAVI. Non-transfemoral access route and balloon post-dilation are the strongest procedural predictors of new onset AFib after TAVI.

5787 | BEDSIDE
Mitraclip therapy in the setting of advanced heart failure with severe functional mitral regurgitation: pre-operative evaluation and implications in patients selection

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Background: Recurrence of high-grade mitral regurgitation after Mitraclip therapy may occurs in patients with functional mitral regurgitation (FMR) and advanced left ventricular (LV) failure.
Purpose: We sought to investigate the pre-procedural predictors of FMR recurrence after Mitraclip in patients with advanced heart failure (HF) and importantly remodeled left ventricle (LV).
Methods: From April 2012 and October 2014, 25 patients with advanced HF (NYHA III-IV), decreased LV function (median LV ejection fraction 29% (IQR 23–34)) and FMR≥3+ underwent Mitraclip implantation in our institution. FMR degree was systematically reassessed before discharge (median time 4 days, IQR 2–6) and at short-term follow-up (median time 2 months, IQR 1–6).
Results: At the time of procedure the median age was 72 years (IQR 60–76), 46% were ischemic, the median EuroSCORE II was 6 (3–11), 50% had CRT before Mitraclip. Study patients presented a significant LV remodeling (median LVEDV 214 ml; IQR 186–261) and high BNP values (406 pg/ml; IQR 294–1002);

46% had right ventricular (RV) dysfunction, median estimated systolic pulmonary pressure (sPAP) was 56 mmHg (QR 46–64). One patients died before the short-term evaluation. Clip implantation success was obtained in 24/25 patients (96%). Acute procedural success (MR≤2+ before discharge) was obtained in 77% of patients. However MR≥3+ was observed in 9/25 patients (39%) at short-term re-evaluation. Pre-implantation BNP (for 10 pg/ml increase OR 1.041, 95% CI 1.001–1.0234, p=0.049), RV fractional area shortening (OR 1.077, 95% CI 1.002–1.058, p=0.045), sPAP (OR 1.09, 95% CI 1.067–1.104, p=0.049), mitral anulus size (for 1 mm OR 1.49, 95% CI 1.47–1.52, p=0.018) and vena contracta width (OR 1.44, 95% CI 1.42–1.47, p=0.047) were significantly associated with short-term FMR persistence/recurrence. BNP (AUC 0.827, p=0.014) and anulus dimensions (AUC 0.829, p=0.009) showed the best accuracy at the ROC analysis.
Conclusions: Valid predictors of Mitraclip efficacy in patients with advanced HF and LV dysfunction have not yet been identified. Pre-implantation BNP and anulus size might be helpful in the selection of patients eligible for Mitraclip therapy in this setting. Future prospective studies are warranted to test these findings on large populations.

5788 | BEDSIDE
Mortality in transfemoral transcatheter aortic valve implantation: impact of ejection fraction

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Introduction: Reduced LV ejection fraction (EF) is frequently seen in patients with severe aortic stenosis (AS). However, it is not clear to what extent this contributes to procedural risk and overall survival, as there has been conflicting data on this topic. It is also debatable whether EF adequately reflects left ventricular (LV) dysfunction in the setting of diastolic dysfunction typical for severe AS. We examined this issue in a large cohort of patients receiving transfemoral aortic valve implantation (TF-AVI) in our centre.
Methods: EF determined by echocardiography was available in all 1570 patients (pts) receiving TF-AVI between 2006 and 2014, EF at 10 days after intervention was available in 1419 of these pts. Follow-up concerning 1-year-survival was available in 1502 of the pts. We analyzed survival at 30 days and at 1 year, as well as myocardial infarction (MI), bleeding, access site complications, stroke and kidney injury at 30 days, as defined by the Valve Academic Research Consortium (VARC). These were compared between pts with EF >30% and EF ≤30%.
Results: Of 1570 patients, 112 (7.2%) had an EF ≤30%. Mean STS-PROM was 8.5±6.1% with EF>30% and 10.6±7.6% with EF≤30% (p<0.01). Mean logEURO-Score was 18.9±12.6% and 31.8%±17.5, respectively (p<0.01). However, 30-d-mortality was 6.7% with EF>30% and 7.9% with EF≤30%, with no significant difference between groups (p=0.61). 1-year-mortality did not differ significantly, either (21.0% vs. 23.9%, p=0.48). There were no significant differences concerning MI (0.7% in EF>30% vs. 1.1% in EF≤30%, p=0.72) or stroke (4.4% vs. 6.5%, p=0.37). There was also no significant difference concerning kidney injury (14.4% vs. 11.8%, p=0.70) or access site complications (27.7% vs. 18.3%, p=0.05). Life threatening (8.3% vs. 6.5%, p=0.54) or major (29.6% vs. 24.7%, p=0.32) bleeding were not significantly different in incidence, either. In pts with EF≤30%, TF-AVI led to significant improvement of EF, from a mean of 24.9% ±4.5 to 37.5% ±12.2 10 days after TF-AVI (p<0.01).
Conclusion: Although STS and EURO risk scores predicted a significantly higher risk of mortality for patients with severely impaired EF, we could not substantiate significant differences in 30-day- or 1-year-mortality. Also, there were no significant differences in the VARC-defined endpoints MI, stroke, bleeding, access site complications or renal injury. These results, demonstrate that EF, even if severely reduced, is not a useful parameter in the preprocedural evaluation of TF-AVI patients, and patients with severely impaired EF should not be deemed unsuitable for TF-AVI.

5789 | BEDSIDE
Geometry of the aortoventricular annulus as a predictor of pacemaker implantation following transcatheter aortic valve implantation

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Background: One of the causes of conduction abnormalities associated with transcatheter aortic valve implantation (TAVI) is a disruption of atrioventricular (AV) conduction tissue caused by mural tension during positioning and expansion of the prosthetic valve. We sought to evaluate whether a higher difference between the long and short diameters of the elliptic AV annulus is a predictor of pacemaker (PM) need following TAVI.
Methods: We conducted a retrospective analysis of 104 consecutive patients who underwent TAVI during a 1 year period. All patients had the AV annulus analyzed and measured by multidetector cardiac computed tomography up to a month prior to valve implantation. The difference between maximal (Dmax) and minimal diameters (Dmin) of the annulus was considered the elliptic factor (ELFA) which was analyzed using t-test to evaluate whether it significantly differs between the PM receiving group and the group without need for a PM. Then, using a univariate and multivariate model adjusted for other confounders predicting the need for a PM (age, gender, prior right bundle branch block, type of prosthetic valve implanted), we sought to evaluate whether the ELFA is a predictor of PM implantation within 1 month following TAVI.
Results: Mean age was 82±6 and 65% were women. The CoreValve prosthesis was implanted in 63% patients. Mean valve size was 27 mm. Average Dmax, Dmin and ELFA were 25.6 mm, 20.6 mm and 5 mm respectively. Thirteen patients (12.5%) underwent PM implantation. Those patients had an ELFA of 5.7 mm compared to 4.8 mm in those who did not get a PM (p<0.02). In multivariate analysis adjusted for known confounders, a higher ELFA still remained a statistically significant and independent predictor for the need of PM (p=0.04).
Conclusions: Our data shows that ELFA is an independent and significant predictor of the need for PM implantation after TAVI, and suggests further investigation whether it should be considered as a factor in managing TAVI patients.

5790 | BEDSIDE
5-years outcomes after transcatheter aortic valve implantation with the CoreValve prosthesis

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Little is known about long-term outcomes following TAVI. Previous reports of transcatheter aortic valve implantation (TAVI) have focused on short- and mid-term outcomes; however, long-term durability of transcatheter heart valves and long-term clinical outcomes are unknown. The aim of this study was to evaluate clinical and hemodynamic outcomes 5 years after TAVI.
Methods: Between April 2008 and January 2010, 100 patients underwent TAVI for the treatment of severe symptomatic aortic stenosis with the CoreValve prosthesis
Results: The mean age and euroSCORE were 79.7±6.5 years and 20.9±15% respectively. Mean aortic valve gradient decreased from 50.7±15 mm Hg to 9.03±4.2 mmHg after TAVI and 11.3±9.4 mm Hg at 5 years (p for post-TAVI trend 0.03). Mean aortic valve area increased from 0.63±0.2 cm^2 to 1.64±0.41 cm^2 after TAVI and 1.47±0.27 cm^2 at 5 years (p for post-TAVI trend 0.01).Mean left ventricular ejection fraction increased from 62.9±14 mmHg to 66.8±12 mmHg after TAVI and 60.7±8 mmHg at 5 years (p for post-TAVI trend 0.001)
In-hospital mortality was 4%. Late mortality after a mean of 48.8±23 months was 29.2% and in only 7 p was cardiovascular mortality. Survival rates at 1 to 6 years were at %, 78%, 70%, 65%, 63.5% and 57.1% respectively. At 5 years, 2 patients had severe prosthetic valve dysfunction (severe stenosis and moderate transvalvular regurgitation). Survival rates at 1 to 5 years were 83%, 74%, 53%, 42%, and 35%, respectively.
Median survival time after TAVI was 3.6 years (95% confidence interval [CI]: 3.24 to 4), and the risk of death was significantly increased in patients with acute kidney injury (adjusted hazard ratio [HR]: 4.3; 95% CI: 1.3 to 14.1),p=0.016, severe Prosthesis-patient mismatch (P-PM) HR 6.99; 95% CI 2.33 to 20.9)p<0.001 and subclavian approach HR 19.5; 95% CI 3.46 to 10), p<0.001
Conclusions: Our study demonstrated favorable long-term outcomes after TAVI. Signs of prosthetic valve failure were observed in 2% of patients. Complications after procedure, notably acute kidney injury and severe P-PM, were associated with reduced long-term survival.

5791 | BEDSIDE
Transfemoral aortic valve implantation of edwards sapien 3 without predilatation

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Introduction: Transcatheter aortic valve implantation (TAVI) without predilatation may have some advantages and has been demonstrated to be feasible with various transcatheter valves.
Purpose: We sought to investigate whether this concept also applies to transfemoral implantation of the Edwards SAPIEN 3 device.
Methods: Ninety-two consecutive patients from 2 centers with severe aortic stenosis undergoing transfemoral TAVI were enrolled in order to assess the feasibility and safety of TAVI without prior valvuloplasty.
Results: A direct implantation was feasible in 85 patients (92.4%), whereas 7 patients required predilatation. In one patient the crossing of the aortic valve with the device was not possible, and a rescue BAV became necessary. In the remaining 6 patients pre-ballooning was deemed to be beneficial due to considerable difficulties while crossing the aortic stenosis with the wire or catheter. Patients requiring pre-ballooning had significantly higher calcium-score and -density of the aortic valve, higher age, and higher transvalvular gradients. The aortic valve area was

Predilatation versus no predilatation

Characteristics	Predilatation (n=7)	No predilatation (n=85)	p-value
Age	88.2±5.4	80.5±7.5	0.008
Body mass index	24.2±4.7	27.9±5.1	0.07
GFR (ml/min)	50.1±10.2	66.6±28.6	0.09
Mean gradient (mmHg)	61.0 [49.0–74.0]	40.0 [28.5–54.0]	0.005
Aortic valve area (mm^2)	0.5 [0.4–0.7]	0.7 [0.56–0.87]	0.08
AV-calcium score (AU)	5334 [IQR 3435–5736]	2775 [IQR 1727–3632]	0.002
AV-calcium densitiy (AU/cm^2)	912 [IQR 818–1220]	107 [IQR 73–146]	<0.001

Abbreviations: AV, aortic valve; GFR, glomerular filtration rate.

non-significantly smaller in the pre-ballooning group (Table 1). In the logistic regression Analysis only the aortic valve calcium-density remained an independent predictor for the need of pre-ballooning (p=0.008, Exp(B) 1.042 [95% CI 1.011–1.073]).

Conclusions: Transfemoral TAVI without predilatation using the Edwards SAPIEN 3 valve is a feasible concept. However, it should be taken into account that in the situation of severe aortic valve calcification the crossing of the valve may be cumbersome and (rescue) balloon valvuloplasty may become necessary.

5792 | BEDSIDE
Alterations of the platelet pool in the early period after transcatheter aortic valve implantation or surgical valve replacement in patients with aortic stenosis

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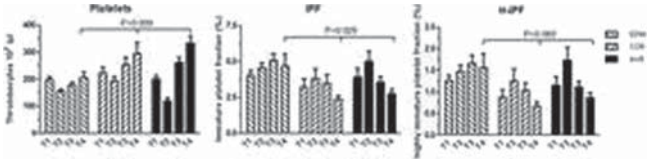
Transcatheter aortic valve replacement (TAVI) is an option for patients with severe aortic stenosis at risk for surgical valve replacement (AVR). Hemorrhagic/ischemic complications are common after both interventions. This study aimed to assess the level of platelet activation and turnover in the periprocedural phase following TAVI or AVR.

Methods: This prospective cohort study enrolled patients undergoing AVR (biological prostheses) or TAVI (balloonexpandable (EDW), selfexpandable (COR)). Blood was drawn before (T1), at day 1 (T2), at days 5–7 (T3) and at days 7–9 (M4) after intervention. Transfusion (blood, platelets, coagulationfactors) and hemodialysis were exclusion criteria for further acquisition. Platelet activation was tested by optical/impedance aggregometry, PFA100 and flowcytometry (PAC1, P-Sel, CD154, CD63, CD31, leukocyte platelet aggregates (LPA)). The immature platelet fraction (IPF) and related parameters were analyzed by Sysmex XE.

Results: 67 patients were enrolled (male=34;mean age 80.5±6.8 years). 27 patients received AVR, 40 patients underwent TAVI (n=25 EDW, n=15 COR). After intervention, ADP and TRAP induced activation decreased over time in all groups with higher levels of activation in AVR patients. In contrast, LPA increased over time in AVR patients whereas no changes were determined in TAVI patients. In COR and AVR patients, IPF and associated parameters showed a transient increase, followed by a decrease on T4 below baseline. Conversely, IPF (p=0.026 T3; p=0.029 T4) and hIPF (p=0.054 T3;p=0.060 T4) remained elevated up to T4 in EDW patients.



Conclusions: Different patterns of activation were found in TAVI and AVR. Compared to AVR and COR, EDW was related with a delayed decrease of IPF and hIPF indicating an increase in platelet turnover in EDW patients.

5793 | BEDSIDE
First-in-human complete filter-based cerebral embolic protection with transcatheter aortic valve implantation

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Background: The occurrence of cerebrovascular events (CVE's) after transcatheter aortic valve implantation (TAVI) has fueled concern for its potential application in younger patients with longer life expectancy. MRI studies, performed after TAVI, show sizable numbers of new ischemic lesions in up to 84% of patients. Embolic protection devices may limit periprocedural CVE's. Currently available filter-based EPD's cover all extracranial contributories to the brain yet leave the left vertebral artery unprotected.

Purpose: We present the first-in-human use of a novel filter-based EPD in the left vertebral artery in addition to the existing dual-filter based device that covers the brachiocephalic trunk and the left common carotid artery to assess both safety and feasibility of complete filter-based brain protection.

Methods: Eight patients underwent TAVI with Dual-filter protection and additional Wirion filter in the left vertebral artery. After TAVI all filters were retrieved and sent for histopathologic evaluation.

Results: All filters were successfully deployed except for the Wirion left vertebral filter in one patient that was complicated by a dissection and required stenting of the proximal segment of the left vertebral artery. Seven Wirion left vertebral filters were available for histopathologic evaluation, which all showed traces of either native or foreign body material. The amount of encountered material per patients varied from two to forty-one separate fragments. Foreign body material was found in five patients, with diameters ranging from 0.04 to 0.65mm. Thrombus and fibrin were found in four patients (size: 0.05 to 1.10mm). In four patients tissue components were found, namely: endothelium, myocardial tissue, calcium fragments, collagen or multiple. Endothelium was found in three patients (size: 0.10 to 1.50 mm), myocardial tissue was found in two patients (size: 0.07 to 1.60 mm), calcium fragments were found in one patient (size: 0.16mm), and collagen was found in one patient (size: 0.09mm).

Conclusion: Our findings confirm that current embolic protection devices, covering the brachiocephalic trunk and the left common carotid artery, are suboptimal in the protection from CVE's during TAVI. Right now, one important access route to the Willis polygon is routinely left untouched. The left vertebral artery seems an important access route for material to enter the brain. This pilot study warrants further research to explore the value of left vertebral artery protection during TAVI.

ECHO-IMAGING PREDICTORS OF CARDIOVASCULAR OUTCOME

5801 | BEDSIDE
Mechanics and prognostic value of left and right ventricular dysfunction in patients with systemic sclerosis

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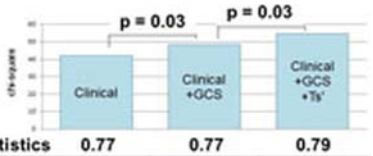
Background: Impairment of myocardial function is an important potential complication of systemic sclerosis (SS) and associated with poor prognosis. The detection of subclinical left (LV) and right ventricular (RV) dysfunction may permit therapeutic intervention.

Purpose: To investigate the prognostic value of both LV and RV deformation in pts with SS.

Methods: We studied 112 pts with SS and 112 age- and gender-matched controls who underwent echocardiography from July 2005 to June 2014. LV strain parameters (global longitudinal and circumferential strain (GLS, GCS)) and tricuspid annular peak systolic velocity (Ts') were measured using speckle tracking. Subjects were followed for a median of 2 years for all-cause admission or death, and the association of the study parameters with outcome was assessed using Cox proportional hazards model.

Results: GLS, GCS, and Ts' were significantly impaired in pts with SS, even in SS pts without pulmonary hypertension, compared to controls. GCS (p=0.03) but not GLS (p=0.11) was associated with systolic pulmonary artery pressure. During follow-up, comparable numbers of SS pts (n=45, 40%) and controls (n=38, 34%) had events (p=0.33). In SS pts, GCS (but not GLS), Ts', and 6-minute walk distance (6MWD) were significantly associated with outcome. A model based on age, gender and 6MWD was significantly improved by sequential models adding GCS and additionally by adding Ts'. However, 6MWD and Ts' (but not GCS) were independently associated with outcome (Figure).



Variable	Model 1 (Clinical) Chi-square=42.0 HR (95%CI), p Value	Model 2 (Clinical+GCS) Chi-square=48.4 HR (95%CI), p Value	Model 3 (Clinical+GCS+Ts') Chi-square=54.7 HR (95%CI), p Value
Age (per 1yr increase)	0.97 (0.94-1.00), p=0.06	0.96 (0.94-0.99), p=0.02	0.97 (0.94-1.00), p=0.03
Male	2.91 (1.43-5.95), p<0.01	2.57 (1.27-5.23), p<0.01	2.68 (1.33-5.40), p<0.01
6-min walk distance (per 1m increase)	0.99 (0.99-0.99), p<0.01	0.99 (0.99-0.99), p<0.01	0.99 (0.99-0.99), p<0.01
GCS (per 1% increase)		1.08 (1.01-1.16), p=0.03	1.04 (0.97-1.12), p=0.28
Ts' (per 1cm/s increase)			0.81 (0.68-0.98), p=0.03

Sequential model

Conclusion: RV dysfunction was associated with adverse outcome, independent of and incremental to clinical and LV deformation parameters in SS. Subclinical LV dysfunction appears to have less prognostic relevance than RV dysfunction.

5802 | BEDSIDE

Long-term prognostic value of the Doppler derived ejection intraventricular pressure gradient in patients with dilated cardiomyopathy

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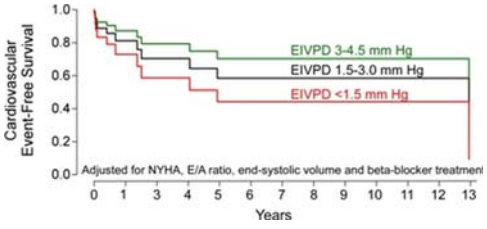
We have recently demonstrated that the Doppler-derived peak ejection intraventricular pressure difference (EIVPD) between the apex and the LV outflow tract is a sensitive and load-independent index of global systolic function that best correlates with invasive maximal elastance. This index could provide additive prognostic information in patients with dilated cardiomyopathy (DCM).
Methods: 200 pts with DCM (61 females, 61±13 years old, 40% ischemic) were prospectively included and underwent an echocardiographic exam including measurement of the EIVPD from outflow color-Doppler M-mode recordings. 20% pts were in NYHA class III, 88% on beta-blockers (BB) and 95% on ACE inhibitors ARB.
Results: After a median follow-up period of 4.1 years (n=191 pts), the composite end-points of any cardiac event (cardiac death, transplantation or hospital readmission for heart failure) or hard cardiac events (cardiac death or transplantation) were recorded in 74 and 35 pts, respectively. Values of EIVPD were similar between ischemic and non-ischemic (2.8±1.2 vs 2.8±0.9 mm) and did not correlate with EF (R=0.2). By multivariate proportional-hazards modeling, stratified to the use of BB,age and sex-adjusted risk of any cardiac event (n=57) was directly related to NYHA (HR=2.5 [95% CI: 1.6 to 3.7], p<0.001), E/A ratio (HR=1.4 [1.2–1.6], p<0.001), end-systolc volume (HR=1.3 [1.0–1.7]), and inversely to EIVPD (HR=0.64 [0.4–0.9] per 1.5 mm Hg, p=0.04; Figure 1; bootstrapped area under the ROC curve= 0.60. The same factors were predictors for hard cardiac events. EF was not related to outcome (HR=0.8 [0.5–1.3], p=0.4)



Conclusions: The Doppler-derived EIVPD is the first noninvasive index of global systolic function which proves to be useful to predict long-term outcome of patients with DCM

5803 | BEDSIDE

Echocardiographic deformation analysis for the prediction of atrial fibrillation and stroke development after ST-elevation myocardial infarction treated with primary percutaneous coronary intervention

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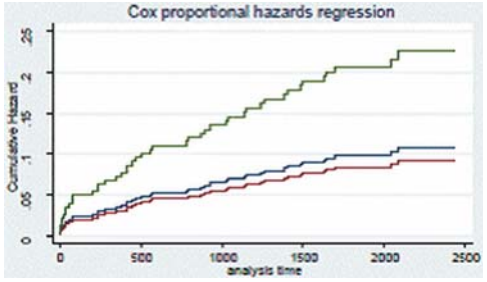
Background: Patients with acute myocardial infarction are at increased risk of developing atrial fibrillation (AF) and stroke. Speckle tracking echocardiography may serve as a way of selecting patients at high risk of developing such outcomes.
Methods: The study comprised of 373 patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention. Patients had an echocardiogram performed a median of 2 days after their STEMI. The echocardiogram consisted of conventional imaging, tissue Doppler, and myocardial strain analysis by speckle tracking. Endpoint was a composite of new-onset AF and ischemic stroke.
Results: At a median follow-up time of 5.5 years 44 of the patients developed AF (n=24) or stroke (n=24), four of which developed both.
Patients who developed AF and/or stroke had significantly reduced systolic function by left ventricular ejection fraction (LVEF) (43% vs 46%, p=0.042) and global longitudinal strain (GLS) (10.9% vs 2.6%, p=0.004), both being univariable predictors. However, only GLS remained a significantly independent predictor (HR=1.12, 95% CI [1.00;1.25], p=0.042, per 1% decrease) after multivariable adjustment for baseline predictors (age, gender, diabetes, hypertension, diastolic dysfunction, and LVEF) in a cox regression model. Furthermore, GLS yielded significantly higher c-statistics for prediction of outcome compared to LVEF<45% (0.63 vs 0.52, p=0.026). When stratified into tertiles of GLS, it became evident that patients in the lowest tertile mediated this signal (figure) with a 2–fold increased risk compared to the highest tertile (HR=2.10, 95% CI [1.04;4.25]).
Conclusion: GLS improves risk stratification for AF and stroke in patients with STEMI, particularly in those with markedly depressed systolic function.



5804 | BEDSIDE

Diastolic dysfunction and adverse diastolic remodelling as predictors of infarct scar and cardiovascular events following acute myocardial infarction

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Background: Severe diastolic dysfunction, or restrictive filling (RF), is a powerful prognostic marker identifying high risk patients post AMI; however it may only identify a small proportion of patients at-risk. Over time, there are dynamic changes to diastolic function following AMI, altered by left ventricular (LV) remodelling, myocardial scar size, and viability. However, there is a paucity of literature on diastolic "remodelling" post AMI and its prognostic value. Furthermore, the relationship between infarct scar size and diastolic function has not been well described.
Purpose: The study aimed 1) to determine the optimal marker of diastolic function that would best predict cardiac magnetic resonance imaging (CMRI) measured LV infarct scar size, 2) evaluate adverse diastolic remodelling (ADR) as a predictor of infarct scar size and 3) the prognostic value of ADR following reperfused STEMI.
Methods: 218 patients with acute reperfused STEMI were prospectively recruited. Serial transthoracic echocardiography (TTE) and CMRI were performed "early" at 4 days (IQR 3–7 days) and at "follow up (FU)" 55 days (IQR 46–64 days) after STEMI. Infarct characteristics were evaluated on late gadolinium enhancement images. Measures of diastolic function including E/A, mitral deceleration time, A wave duration, E/E' and diastolic grade (1=impaired relaxation, 2=pseudonormal and 3=RF), were performed by TTE. Patients were stratified into the "ADR group" (those whose diastolic grade had worsened or persistent RF from early to follow-up scans) and non "ADR group". The primary endpoint consisted of major adverse cardiovascular events (MACE) including mortality, reinfarction, heart failure, stroke and ventricular arrhythmias.
Results: Diastolic grade, at FU, showed the best correlation with FU infarct total and core scar size (r=0.51, p<0.001), gray zone (GZ) scar size (r=0.46, p<0.001), and microvascular obstruction (MVO) size (r=0.33, p<0.001). Patients with ADR (n=50) predicted FU total scar (AUC 0.85), core scar (AUC 0.86), GZ scar (AUC 0.77) and MVO (AUC 0.75). These predictors were similar in patients who had RF at FU (n=33). Over a FU period of 602 days (IQR 437–730 days), the primary endpoint occurred in 40 patients. Multivariate Cox regression analysis showed that infarct core scar size at FU (HR 1.10, p<0.001) and ADR (HR 2.88, p=0.009) were independent predictors for MACE.
Conclusion: Larger Infarct size is associated with worse diastolic function grade and ADR. ADR, on serial TTE, identifies a larger cohort of at risk patients than RF alone, and is a prognostic marker for MACE post AMI.

5805 | BEDSIDE

Reversible abnormal right ventricular function at follow-up is associated with better survival in patients with chronic systolic heart failure

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Background: Longitudinal annular systolic excursion of the tricuspid annular plane (TAPSE) has been widely used to assess right ventricular (RV) function noninvasively. An impaired TAPSE has been associated with a worsen survival in patients with chronic systolic heart failure (SHF) secondary to dilated cardiomyopathy. However, it is not known whether a reversible abnormal TAPSE predicts survival in patients with chronic stable SHF.
Aim: To test the hypothesis that a reversible abnormal TAPSE is associated with a better survival in patients with chronic stable SHF.
Methods and results: A complete echocardiographic examination was performed in 570 patients with chronic SHF and left ventricular ejection fraction (LVEF) <45%. RV systolic function was evaluated by M-mode echocardiography using the TAPSE. Mean age of the study population was 66±12 yrs (21% female). Baseline TAPSE was 19±4 mm. At six-months, TAPSE was 20±4 mm. During a median follow-up of 39 months, 78 patients died. At 60 months, patients with TAPSE ≤14 mm exhibited a survival of 64%, whereas survival was 68% in

those with a moderately depressed TAPSE (between 15 and 17 mm) and 89% in those with normal TAPSE (≥18 mm) (log rank 38.9, p<0.0001). When patients were stratified according to the reversibility of compromised RV function, survival was 91% in patients with persistently normal TAPSE, 86% in those with reversible abnormal TAPSE, and 69% in those with either worsened TAPSE or persistently abnormal TAPSE (log rank 38.8, p<0.0001). Cox regression analysis showed that presence of persistently normal or reversible abnormal TAPSE normalized for age, gender, LVEF and diastolic function was independently associated with improved survival (HR 0.43, 95% CI 0.26–0.72, p=0.001).
Conclusion: These results showed that patients with chronic stable SHF who exhibited reversibility of an abnormal TAPSE during follow-up have a better survival than patients with either worsened TAPSE or persistently abnormal TAPSE.

5806 | BEDSIDE
Novel echocardiographic and clinical score predicts 3-year mortality in coronary care unit patients

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Background: At present there is no clinically available prognostic score that incorporates echocardiographic and clinical data for patients hospitalized in the coronary care unit (CCU).
Purpose: The aim was to develop and validate an integrated model, comprised of clinical and echocardiographic data, to predict 3-year mortality of patients admitted to the CCU.
Methods: We reviewed the records of 8,219 consecutive patients admitted to a tertiary care CCU between 2004 and 2011. From these, we identified a training cohort of 1,993 patients with a complete set of echocardiography parameters recorded at some point during their CCU stay; left ventricular ejection fraction (LVEF), LV diastolic function, right ventricular (RV) size, RV systolic function, RV systolic pressure (RVSP), and stroke volume index. Using multivariate analysis we developed a prognostic model for predicting 3-year mortality. We tested this model in a separate validating cohort of 2,424 patients and compared it to other established prognostic scores (APACHE III, SOFA, SAPS and Charlson score).
Results: Of 1,993 patients in the training cohort, the mean age was 69±16 years. The primary diagnosis was acute coronary syndrome (66%), heart failure (38%) and ~50% had more than one primary diagnosis. 3-year mortality was 28%. Age (OR 1.7, 95% CI 1.6–1.8), diabetes (OR 1.3 95% CI 1.1–1.5), chronic lung disease (OR 1.2 95% CI 1.1–1.5) and chronic kidney disease (OR 1.4 95% CI 1.2–1.8) were independently associated with mortality. Among 6 echocardiography parameters, only LVEF (OR 0.9, 95% CI 0.8–0.9) and RVSP (OR 1.3 95% CI 1.2–1.3) were prognostic of mortality. Integration of clinical data, LVEF and RVSP yielded a better prognostic value, with AUC of 0.78 (95% CI 0.76–0.80), compared to clinical (AUC 0.72; P<0.0001) or echocardiographic data alone (AUC 0.71; P<0.0001). This formula represents the suggested CCU model: 3*Diabetes + 4*Lung + 5*Age in years/10 + 6*LVEF≤40 + 7*RVSP≥40 + 8*chronic kidney disease. 3-year mortality in patients with a score <21, 21–30, 31–40, 41–50, and≥51 were 0.3%, 5%, 15%, 35and 45%, respectively (p<0.0001). The AUC of the model in the validation cohort was 0.77, which was equal to APACHE III (AUC 0.76) and better than SOFA (AUC 0.72), SAPS (AUC 0.72) and Charlson score (AUC 0.71).
Conclusion: We describe an integrated score to predict 3-year mortality of patients admitted to the CCU that is comprised of fewer variables (age, diabetes, pulmonary and kidney disease, LVEF and RVSP) and has better/equal predictive value compared to existing APACHE, SOFA, SAPS and Charlson scores.

5807 | BEDSIDE
Left ventricular contractile reserve as a new prognostic factor in systemic sclerosis patients?

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Introduction: Several studies evidenced high prevalence of myocardial systolic and diastolic dysfunction among patients with systemic sclerosis (SSc), related either to myocardial fibrosis or in some cases to a myocardial microvascular dysfunction. Exercise echocardiography has been used to identify a subset of SSc patients with an inappropriate exercise-induced increase in PASP but the diagnostic and prognostic role of this test is still unclear. We previously showed that a reduced global longitudinal strain under stress test (S-GLS) characterizes SSc patients with a more extensive cardiovascular impairment in terms of left ventricular (LV) diastolic function, pulmonary pressures and exercise tolerance.
Purpose: The aim of our study was to evaluate LV impairment under exercise and its long term prognostic value among patients with SSc.
Methods: We studied 25 patients (age 62,1±10 years; 2 male, 23 female) with SSc. Patients with Interstitial Lung Disease were excluded from the study. All patients performed a clinical evaluation, a 2D echocardiography associated with Tissue Doppler (TD) and speckle tracking (ST) to evaluate LV deformation indexes, exercise echocardiography to evaluate LV contractile reserve (measuring S-GLS) and exercise pulmonary pressures, and a 6 minute walking test (6MWT) to evaluate the exercise tolerance. All patient performed a clinical evaluation and a 2D echocardiography associated with TD and ST at a follow up of 4,2±0,2 years.
Results: We evidenced a significant correlation between basal S-GLS and 6MWT (r 0.63; p<0.001) and Δ PASP (r –0.53; p<0.01). Most importantly a basal S-GLS cutoff <17.2%, computed with ROC analysis, identified SSc patients who showed a decrease in exercise tolerance at follow up [AUC 0.81 (95% CI 0.67 to 0.94), sensitivity 78% (95% CI 63–92), specificity 71% (95% CI 50–91)]. Moreover patients with basal S-GLS <18% demonstrated higher pulmonary pressures at FU (PAPS 34,8±8,4 vs 26±3 mmHg; p<0,05).
Conclusions: Our data demonstrate that in SSc patients a reduced LV contractile reserve is strictly related to an inappropriate pulmonary pressure response to exercise and a reduced exercise tolerance. Moreover a reduced LV contractile reserve showed to be able to identify SSc patients who show a decrease in exercise tolerance at follow up and develop higher pulmonary pressures.

5808 | BEDSIDE
Better prognostic values of longitudinal strain of sub-epicardial myocardium in hypertension

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Background: Global longitudinal strain (GLS) derived from speckle tracking echocardiography is widely used for assessment of occult systolic dysfunction. However, the prognostic value of GLS has not been well studied in hypertension.
Objective: This prospective observational study investigated the prognostic value of GLS as well as sub-endocardial (EndLS) and sub-epicardial (EpiLS) longitudinal strain in regular treated uncomplicated hypertensive patients.
Methods: This study included 95 patients (57 men, age 65±12 years) with uncomplicated hypertension who have been regularly treated for more than 1 year. Speckle tracking echocardiography was used for measurement of longitudinal deformation from 3 apical views of left ventricle. GLS was measured by automated function imaging (AFI). We further divided into sub-endocardial and sub-epicardial myocardium and measured their longitudinal strain by manual click-and-draw method and averaged from 3 apical views. End-points for this study were any admission for stroke, acute coronary syndrome, heart failure, and cardiovascular death.
Results: After a mean follow-up period of 88±24 months, 20 (21%) patients reached end-points. The significant differences between patients with and without end-points included status of diuretic use (75 vs. 93%; p=0.018), age (71±12 vs. 64±12 years; p=0.020), and EpiLS (–16.0±2.0 vs. –17.7±3.0%; p=0.040). There were no difference between groups in GLS (–16.5±1.6 vs. –17.6±3.3%; p=0.263) and EndLS (–21.4±2.1 vs. –22.9±4.1%; p=0.105). After multivariate Cox regression analysis controlling age, body mass index, systolic blood pressure, and status of diuretic use, EpiLS was an independent factor for prognosis (HR 1.241, 95% CI 1.030–1.496, p=0.023). By dividing subjects into 2 strata with the cut-off value of median value –17.57% for EpiLS, the Kaplan-Meier survival curve revealed significant differences (p=0.016) for endpoints.
Conclusions: In regular treated hypertensive patients, EpiLS was an independent prognostic factor for worse outcome but not GLS and EndLS. Our results indicated involvement of sub-epicardial myocardium had important contribution in hypertensive heart disease.

5809 | BEDSIDE
Predictive value of local prolonged electro-mechanical interval by echocardiography in the concealed stage of arrhythmogenic right ventricular dysplasia/cardiomyopathy

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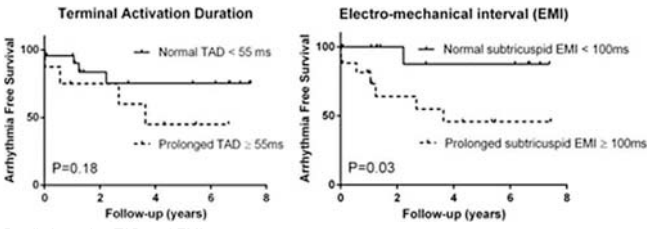
Introduction: The concealed stage of ARVD/C is associated with increased risk of sudden death. However, at this stage risk stratification is hampered by paucity of criteria. Activation delay (AD) is a hallmark of arrhythmogenesis. Deformation imaging may unmask AD in the absence of ECG and structural abnormalities.
Methods: Three groups were compared 1) mutation-positive definite ARVD/C patients (n=44), 2) asymptomatic mutation carriers (AMC) not fulfilling Task-Force criteria (TFC) and without history of ventricular arrhythmias (n=31) and 3) healthy controls (n=30). All underwent echocardiographic examination inclusing deformation imaging and ECG according TFC. As surrogate for local AD the electro-mechanical interval (EMI) was measured, defined as time between first ECG-detected deflection and local onset of shortening. Arrhythmic outcome (ventricular tachycardia, PVC count) of AMC was correlated to EMI and ECG TFC.
Results: EMI was prolonged in all RV segments in ARVD/C patients, >100msec



Predictive value TAD and EMI

was defined as abnormal based on fidings in controls. In AMC prolonged EMI was detected in the subtricuspid area in 17/31 subjects (55%). Terminal Activation Duration ≥55ms was the only ECG abnormality found in this group in 8/31 (26%). Isolated prolonged EMI occurred in 10/31 AMC. After a mean follow-up of 3.8±2.8yrs, 8/31 subjects experienced an increase in ventricular arrhythmia burden. Prolonged subtricuspid EMI was the only parameter significantly correlated to arrhythmogenesis during follow-up (Figure 1).
Conclusion: Deformation imaging reveals abnormal AD both ARVD/C patients and in AMC. In AMC prolonged EMI in the subtricuspid area is often detected without any additional abnormalities. Prolonged EMI is a new parameter unmasking AD in the concealed stage and may contribute to risk stratification.

5810 | BEDSIDE
Right ventricular function assessed by 2D longitudinal strain independently predicts mortality in chronic heart failure patients

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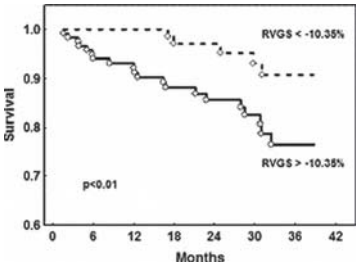
The aim of this study was to evaluate the role of two-dimensional (2-D) speckle tracking measures of right ventricular systolic function in predicting mortality of patients affected by chronic heart failure (CHF).
We enrolled 274 outpatients (77% males, 64±14 years, NYHA class 2.2±0.7, left ventricular ejection fraction, LVEF, 34±9%) with CHF (ESC criteria), in stable clinical conditions (>1 month) and in conventional therapy (91% ACE-inhibitors and/or ARBs, 94% betablockers). By echocardiogram (Echo-PAC, GE), a 4-chamber view (frame rate 50–70/sec) was obtained to evaluate global strain of the right ventricle by 2-D speckle tracking (RVGS).
Tricuspid annulus systolic excursion peak (TAPSE) was also calculated.
During follow-up (21±12 months), 26 patients died (19 for cardiovascular causes and 7 for non cardiovascular causes). Seven patients underwent heart transplantation. RVGS was associated to mortality at the univariate (HR: 1.16; 95% CI: 1.068–1.26; p<0.001; C-index: 0.69) as well as at the multivariate analysis (HR: 1.11; 95% CI: 1.012–1.217; p: 0.01; C-index: 0.82) in a model including age, NYHA class, LVEF. On the other hand, TAPSE was not associated to mortality.
Figure shows Kaplan-Meier curves for survival of patients dichotomized according to RVGS median value.



In conclusion, our findings demonstrate the independent role in predicting mortality of right ventricular function assessed by 2D strain as well as its superiority in comparison to the traditional monodimensional parameter. These data strengthen the clinical usefulness of this echocardiographic approach in daily management of CHF outpatients.

HOT TOPICS ON STEMI

5813 | BEDSIDE
Impact of acute infarct-related artery patency before PCI on 30 day outcomes in patients with ST-segment elevation myocardial infarction treated with primary PCI in the EUROMAX trial

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Background: Early infarct-related artery (IRA) patency has been associated with improved outcomes in STEMI patients treated with primary PCI. However, it is unknown whether this relation persists in contemporary practice with pre-hospital initiation of treatment, use of novel P2Y12 inhibitors, and frequent use of thrombectomy and drug-eluting stents.
Purpose: To determine the impact of early IRA patency on outcomes in the contemporary EUROMAX trial.
Methods: A total of 2218 patients were enrolled. The current analysis was done on 1,863 patients who underwent PCI and had IRA patency data. Thirty-day outcomes were compared according to IRA flow before PCI (TIMI flow 0/1 vs. TIMI flow 2/3) and interaction with antithrombotic strategy was examined.
Results: A patent IRA (TIMI flow 2/3) was present in 707 patients (37.9%) and was associated with lower risk for procedural complications and a shorter hospital stay. At 30 days, a patent IRA was also associated with lower rates of cardiac death, MI and sub-acute stent thrombosis (Table). There were no interactions between antithrombotic treatment and the impact of IRA patency on cardiac death, MI or the composite death/MI (Breslow-Day interaction p-values of 0.21, 0.33 and 0.46 respectively).

Outcomes according to baseline TIMI flow

	Baseline TIMI 0/1 (N=1156)	Baseline TIMI 2/3 (N=707)	P value
Procedural outcomes			
Any complication (%)	8.0	4.4	0.002
Bailout GPI (%)	32.2	11.8	<0.001
Final TIMI flow 3 (%)	92.6	98.9	<0.001
Length of hospital stay (days)	6.2±6.3	5.9±7.3	0.023
30-day outcomes			
Cardiac death (%)	2.9	1.3	0.026
Death/MI (%)	4.6	2.7	0.039
Acute stent thrombosis (%)	0.6	0.8	0.57
Subacute stent thrombosis (%)	0.8	0.0	0.016

Conclusions: Despite evolution in primary PCI strategies (including pre-hospital pharmacotherapy), early IRA patency is still associated with higher procedural success and improved clinical outcomes. The choice of antithrombotic strategy did not interact with the benefits of a patent IRA at presentation.
Acknowledgement/Funding: The EUROMAX Trial was sponsored by The Medicines Company, Parsippany, USA

5814 | BEDSIDE
In-hospital prognosis of eltderly patients undergoing primary angioplasty: results of a national multicenter registry

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Background: Eldery patients (pts) are underrepresented in studies evaluating the revascularization strategies in the acute phase of myocardial infarction with ST-segment elevation (STEMI); however, they now account for a significant part of pts refered for primary angioplasty (P-PCI).
Aim: Based on the National Register of Interventional Cardiology (NRIC) we evaluated the short-term prognosis of the elderly over 75 years with STEMI submitted to P-PCI, compared to younger patients (<75 years).
Methods: From 86 334 pts prospectively included in the NRIC in 2002–2013, 22 national centers, we analyzed 9787 pts with STEMI treated with P-PCI, of which 2038 (21%) were elderly ≥75 years. By logistic regression analysis we evaluated the impact of age on hospital mortality adjusted to other demographic, clinical, angiographic and procedural factors and we analyzed the evolution of mortality in the elderly over the study period.
Results: The elderly undergoing P-PCI were more likely to be women (44% vs 20%, p<0.001), diabetic (26% vs 22%, p<0.001) and hipertensive (71% vs 54%, p<0.001). They showed more comorbidities (prior cerebrovascular disease 9% vs 4% and renal disease 6% vs. 3%, p<0.001 for both) and a more extensive cardiovascular disease (multivessel disease 59% vs 46% and left ventricular dysfunction 26% vs 15%, p<0.001 for both). The time to reperfusion was higher in elderly patients (median 243 vs. 282 min, p<0.001), mainly due to a longer delay of the patient (increase 59 min in median vs. in younger patients, p<0.001). Evolution in Killip IV was also more frequent (11% vs 7%, p<0.001). The lower use of thrombectomy (25% vs 32%, p<0.001), GP IIb/IIIa inhibitors (18% vs 33%, p<0.001) and stents (86% vs 90%, p<0.001) was reflected in a lower rate of TIMI 3 flow in the elderly (90% vs 95%, p<0.001). After adjusting for clinical and procedure variables, the elderly have a worse prognosis in the short term, with 3.1 times greater risk of in-hospital death (6.1% vs 1.8%, 95% CI 1.78–5.54, p<0.001). In-hospital mortality decreased during the registration period: 2002–2005 18.8%, 2006–2008 3.1%, 2009–2013 6.1%.
Conclusions: These NRIC data suggest that despite the elderly are a high risk group, reperfusion can be achieved in a high percentage and in-hospital mortality rate is relatively low and has declined in recent years.

5816 | BEDSIDE
Nyctohemeral variations in hour of STEMI onset in relation with time to first call. The e-MUST registry

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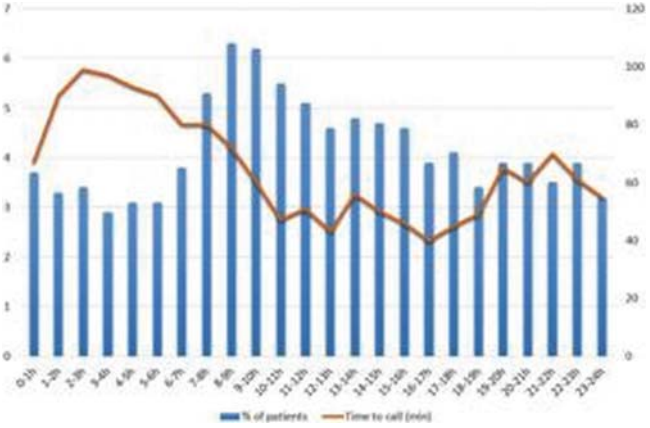
Background and aim: Time from symptom onset to first call is the first component of total ischemic time in STEMI patients, and should therefore be as short as

possible. The aim of the present study was to assess time to first call in relation with timing of onset of pain, in a large cohort of patients having called the French emergency medical system (SAMU: Service d'Aide Médicale Urgente).
Methods: The e-MUST registry was set-up by the regional health authority of the greater Paris region in France to prospectively collect data on all STEMI patients transported by the physician-staffed mobile intensive care units (MICU) dispatched by the SAMU. The registry has been ongoing since 2003 and all data up to 2013 were used for the present analysis, excluding only inter-hospital transfer patients.
Results: Complete data on time of onset and time to first call were available in 17,789 patients. One third of STEMI cases occurred in the morning (from 6:00 am to 12:00 pm), with fewer occurring during the night (from 12:00 am to 6:00 am) (Figure). Overall, median time from onset to call was 60 minutes (25; 167 min), with considerable nyctohemeral variations: the longest time to call was found during the night (88 [33; 258] minutes from 12:00 a.m. to 6:00 a.m.), and the shortest in the afternoon from 12:00 p.m. to 6:00 p.m. (46 [19; 123] minutes).



Time to first call by time of onset

Conclusion: Though fewer STEMI cases had their onset during the night, but their time to first call was much longer. Also, time to first call in the morning hours, where a higher proportion of STEMI occurred, was longer than when STEMI occurred in the afternoon. Media campaigns and public information should therefore specifically focus on reducing time delays when AMI occurs at night or, to a lesser extent, in the morning.

5817 | BEDSIDE
Culprit vessel versus multivessel intervention at the time of primary percutaneous coronary intervention for patients with multivessel disease: insights from the British Columbia Cardiac Registry

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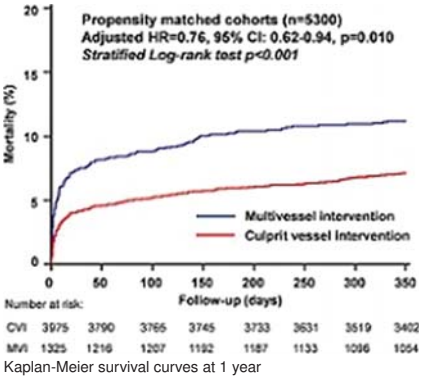
Background: Up to two thirds of patients with ST elevation myocardial infarction (STEMI) have multivessel disease (MVD). Current guidelines discourage percutaneous coronary intervention (PCI) of non-infarct-related arteries at the time of primary PCI in patients without cardiogenic shock. The optimal strategy for treating non-culprit disease continues to be debated.
Methods: We analyzed all patients undergoing primary PCI (n=12,105) between 2008–2013 who were enrolled in the British Columbia Cardiac Registry. Of these 7,337 patients had MVD. Patients with cardiogenic shock and bystander left mainstem disease (>50% stenosis) were excluded. We compared culprit-vessel intervention (CVI) versus multivessel intervention (MVI) at the time of primary PCI and analyzed mortality at 1 year. Cox proportional hazard models were built to determine independent predictors for mortality, and confounding was addressed using propensity score methods.
Results: Of the 6503 patients included in the final analysis, 5178 patients (80%) had CVI. CVI was associated with lower 1-year mortality (7.1% vs. 11.2%, p<0.001). In the unmatched cohort, CVI was not a predictor for 1-year mortality (HR=1.08, 95% CI: 0.84–1.39, p=0.540). However, when addressing measured confounders, CVI was an independent predictor for reduced 1-year mortality in propensity-matched cohorts (n=5300) (HR=0.76, 95% CI: 0.62–0.94, p=0.0120) and in inverse-probability treatment weighted analyses (HR=0.53, 95% CI: 0.41–0.69, p<0.001).
Conclusions: In this study of unselected patients with STEMI and MVD disease, CVI was associated with lower 1-year mortality. When adjusting for confounding, CVI was an independent predictor for survival at 1 year. Acknowledging the limitations of registry data, our findings support current recommended practice guidelines.



Kaplan-Meier survival curves at 1 year

5818 | BEDSIDE
ST-segment elevation myocardial infarctions in younger patients: is there a specific risk profile?

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Introduction: Despite its socio-economic impact acute myocardial infarction in young patients are less studied than for older populations. Aim of this study was to compare ST-segment elevation myocardial infarctions (STEMI) in younger vs. older patients with regard to risk profile, severity of myocardial infarction and trends between 2006 and 2013.
Methods: All patients with STEMI admitted between 2006 and 2013 at a western german heart center were included in this study. The heart center is exclusively responsible for emergency-PCI for a metropolitan region of approximately 1 million inhabitants.
Results: Of the 5632 patients which entered analysis 417 (7%) were younger than 45 yrs. Although mean age increased between 2006 and 2013 (2006: 63.5±13 to 2013: 64.5±13 yrs, ANOVA p<0.01) the proportion of patients <45 yrs. remained constant (p(for trend)=0.8). Pts <45 yrs. were more likely to be male and had a higher prevalence of active smoking (85 vs 40%, p<0.01) and of a positive family history for cardiovascular disease (44 vs. 21%, p<0.01). While hypercholesterolemia was not associated with a specific age, the prevalence of diabetes mellitus and art. hypertension was significantly lower in young STEMI-patients. The results were confirmed in a multivariate logistic model (Table 1). Young STEMI-patients were more likely to suffer larger myocardial infarctions ((creatinine kinase (CK)>3000 U/l): OR 1.7, 95% CI 1.3–2.1) or a prehospital resuscitation event (OR 2.5, 95% CI 1.6–3.9). While the proportion of young smokers was constant during the study period (2006–09:85%, 2010–13: 84%,p=0.8), the proportion of obese (BMI >30 kg/m^2) patients <45 yrs. increased significantly: 2006-09: 23%, 2010-13: 32%, p<0.01.
Conclusion: The results of this large registry-study demonstrate that STEMI in younger patients occur at a relative constant rate (approx.7% of all pts.) over time. STEMI in young patients are distinguished by more extensive myocardial infarctions and higher rates of prehospital resuscitation events. The dominating risk factor for young STEMI-patients was active smoking with a prevalence of 85%, followed by a positive family history for cardiovascular disease and obesity.

5819 | BEDSIDE
In-hospital outcome in octogenarians with acute coronary syndrome undergoing invasive coronary procedures

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Background: Limited data are available in octogenarian patients, and most of these studies excluded older patients with significant co morbid conditions. This is an observational study of octogenarians admitted for acute coronary syndrome (ACS).

Abstract 5818 – Table 1. Independent predictors of age <45 years

	Smoking	Pos. family history for CAD	BMI ≥30 kg/m^2	Male Gender	Total cholesterol ≥240 mg/dl	No risk factor for CAD	Diabetes mellitus	Art. hypertension
Odds ratio (95% CI)	6.0 (4.3–8.4)	2.6 (2.0–3.3)	1.6 (1.3–2.1)	1.3 (1.03–1.5)	1.1 (0.7–1.6)	1.3 (0.7–2.5)	0.6 (0.4–0.9)	0.5 (0.4–0.6)
p	<0.01	<0.01	<0.01	0.03	0.8	0.8	<0.01	<0.01

Purpose: We sought to investigate clinical characteristics, treatment and outcome of octogenarian patients during hospital stay for ACS in transitional country.
Methods: Data were collected in the ISACS-TC registry (ClinicalTrials.gov, NCT01218776) from October 2010 to February 2015: there were 992 patients ≥80 years old, consecutive admitted with a diagnosis of ACS at 58 hospitals in 11 Eastern European countries. Patients who had undergone fibrinolysis and coronary artery bypass grafting (CABG), were also excluded. In-hospital mortality was the primary end-point.
Results: Octogenarian patients represent 7.5% of ISACS-CT population. Among these, 56.7% were admitted with a diagnosis of ST segment elevation myocardial infarction (STEMI). The mean age of the study population was 83.5±3.5 years and 51.6% of the patients were women.
Female, less frequently than male, had history of myocardial infarction, peripheral artery disease (PAD), prior CABG and chronic kidney disease. They were less likely to have smoking and former smoking status. There was no difference in the rates of death between male (18.5%) and female (19.2%) patients. Octogenarian patients undergoing invasive coronary procedures had significantly lower rate of death (12.5% vs 22.2 P<0.001). In multivariable regression analysis, cardiovascular death in the octogenarians was associated (p<0.05) with age ≥85 years (odds ratio [OR] 1.82), prior PAD (OR: 4.92) and Killip class ≥2 (OR 4.41). Invasive coronary procedures was an independent significant protective factor on hospital mortality (OR 0.43).
Conclusions: Octogenarian ACS patients have a high mortality rate which can be reduced by invasive coronary procedures. Age is relevant in the prognosis of ACS, but its importance should be considered not secondary to other clinical factors.

5820 | BEDSIDE
Impact in the prognosis of the utilization of thrombectomy devices in primary angioplasty in patients with ST-elevation acute myocardial infarction

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Introduction: Thrombus embolization and no-reflow phenomena continue to be one of the factors that influence the success of primary angioplasty in the treatment of ST-elevation acute myocardial infarction (STEMI).
Purpose: To evaluate the impact on morbidity, in-hospital mortality and mortality at one year of patients (P) with STEMI that underwent thrombus aspiration (TA) in the moment of primary angioplasty (PPCI).
Methods: We studied 3209 P with STEMI submitted to PPCI included in a multicenter national register. We consider two groups, P submitted to TA and P not submitted to TA. We registered age, sex, co-morbidities, clinical and electrocardiographic presentation, in-hospital therapy, coronary angiography results and ejection fraction (EF). We defined the following in-hospital complications: heart failure (HF), cardiogenic shock (CS), re-infarction, mechanical complications, sustained ventricular tachycardia (TV), high grade atrioventricular block (AV block) and major bleeding. We compared in-hospital mortality and mortality at 1 year follow-up. We performed multivariate analysis to assess the impact of the use TA in-hospital mortality and in the development of HF.
Results: Thrombus aspiration was utilized in 39,4% of P with STEMI undergoing PPCI (1265P). These P were younger (61±14 vs. 64±13 years, p<0,001), had a lower prevalence of hypertension (57,5% vs 62,5%; p=0,005), Diabetes (2,4% vs 23,8%, p=0,026), prior angina (16,2% vs 9,7%, p<0,001) and prior HF (1,0% vs 2,2%, p=0,016). There were no differences in Killip-Kimball class or electrocardiographic at STEMI presentation. There were no differences in the number and type of vessels with lesions, however the number of total occlusions of the left anterior descending artery (LAD) and right coronary artery (RCD) was higher in P undergoing TA (LAD: 41,8% vs 35,6%, p<0,001 and RCD: 39,8% vs 34,0%, p=0,001). Patients submitted to TA had more HF (20,8 vs 17,2%, p=0,01), CS (7,8% vs 5,6%, p=0,013), worse EF (48±11 vs 53±13%, p<0,001), TV (4,8% vs 1,7%, p<0,001), AV block (8,3% vs 4,9%, p<0,001), greater need for invasive mechanical ventilation (4,9 vs 3,4%, p=0,04) and intra-aortic balloon (2,7 vs 1,3%, p=0,004). There were no differences in in-hospital mortality or mortality at 1 year. By multivariate analysis, TA per se is not a predictor of mortality or HF.
Conclusions: In our population, the use of thrombectomy devices seems to be conditioned by the presence of total occlusions of coronary arteries and is associated with an increase of CS, arrhythmias, but not with increased in-hospital mortality or mortality at 1 year.

VASCULAR REMODELLING IN AGEING AND DISEASE

5846 | BENCH
Insulin receptor substrate 2 (IRS2) overexpression in vascular smooth muscle cells (VSMC) blunts neointima formation in mice

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Objective: Insulin resistance (IR) is a major risk factor of neointima formation after percutaneous coronary interventions (PCI), which is mainly due to PDGF-BB related VSMC proliferation and migration. During IR, insulin signal relay by IRS proteins is diminished.
Purpose: To elucidate the impact of IRS2 signalling in VSMC on neointima formation.
Methods: Mice overexpressing IRS2 in VSMC were generated and screened for body weight, morphology of inner organs, and insulin and glucose tolerance. Male mice 3–5 months of age were subjected to wire injury of the common carotid artery (ACC), and intima/media ratio was assessed after 4 weeks. VSMC were isolated from aortas: PDGF-BB induced migration was quantified in modified Boyden chambers, and glucose induced apoptosis by MTT and TUNEL assays. PDGF-BB induced proliferation was measured by colorimetric BrdU and membrane-staining based FACS assays. Abundance of proteins was assessed by Western Blotting and, for GLUT4, additionally by immunocytofluorescence. βPDGFR/PI3K interaction was assessed by co-immunoprecipitation of the activated βPDGFR and the PI3K subunit p110α.
Results: IRS2OE mice were undistinguishable from controls in terms of body weight, insulin and glucose tolerance, and inner organ morphology - except for the heart, which was larger (left ventricular weight/tibia length: 7.8±0.45 vs 5.5±0.05mg/mm, p=0.012, all data expressed as mean ± SEM). No alteration of native ACC's of IRS2OE mice was detected. The intima/media ratio was lower in IRS2OE versus control mice 4 weeks after wire injury (0.11±0.036 vs 1.1±0.76, p=0.039). Isolated IRS2OE VSMC migrated faster in a PDGF-BB gradient (86.6±8.5 vs 17.5±1.5 cells per field, p<0.001), and showed higher susceptibility to glucose induced apoptosis (survival in MTT test: 26.9±0.031% vs 50.9 ±0.024%, p<0.001, TUNEL positive: 96±4% vs 0, p<0.001). There was an increased abundance of anti-apoptotic BCL proteins, MnSOD, but also GLUT4. IRS2OE VSMC proliferated less to PDGF-BB in vitro (BrdU (3.6±0.11 fold vs 4.7±0.39 fold increase compared to unstimulated cells, p=0.040) and FACS (2 vs 5 divisions, n=3). There was less p110α bound to the βPDGFR after PDGF-BB stimulation.
Conclusions: IRS-2 overexpression in VSMC blunts neointima formation in vivo. It increases the rates of glucose induced apoptosis and reduces PDGF-BB induced proliferation by disturbing βPDGFR/PI3K interaction, while it augments PDGF-BB related VSMC migration. During IR, these effects should be mitigated, resulting in increased neointima formation after PCI.

5847 | BENCH
Hnrnpa1 is a critical regulator in vascular smooth muscle cell functions and neointima hyperplasia

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Background: RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1) plays various roles in transcriptional and posttranscriptional modulation of gene expression. Our previous study has demonstrated for the first time that hnRNPA1 plays an important role in vascular smooth muscle cell (VSMC) differentiation from stem cells in vitro and in vivo. However, little is known about the functional involvements of hnRNPA1 in VSMC functions and neointima hyperplasia.
Purpose: In this study, we aimed to investigate the functional roles of hnRNPA1 in the contexts of VSMC functions, injury-induced vessel remodelling, and human atherosclerotic lesions.
Methods and results: Studies used mouse aorta VSMCs showed that hnRNPA1 expression levels were consistently modulated during VSMC phenotype switching. Moreover, VSMCs with hnRNPA1 knockdown had an increased migratory and proliferative ability, but a reduced VSMC-specific gene expression level. Consistently, over-expression of hnRNPA1 significantly reduced VSMC migration and proliferation. Furthermore, our data shows that hnRNPA1 exerts its effects on VSMC functions through modulating IQ motif containing GTPase activating protein 1 (IQGAP1) gene, a well-known important regulator of VSMC migration and proliferation. Mechanistically, hnRNPA1 up-regulates microRNA-124 through regulating microRNA-124 biogenesis. Compelling evidence also suggests that IQGAP1 is the authentic target gene of microRNA-124. Importantly, the expression levels of hnRNPA1 were significantly down-regulated during neointimal lesion formation induced by wire injury, suggesting a role for hnRNPA1 in vessel injury-induced neointimal development and progression. In accordance, perivascular ectopic overexpression of hnRNPA1 greatly reduced VSMC proliferation, and inhibited neointima formation in wire-injured carotid arteries. Translationally and consistently, lower expression levels of hnRNPA1 and microRNA-124, while higher expression levels of IQGAP1, were observed in human atherosclerotic lesions.
Conclusions: We have identified hnRNPA1 as a critical regulator in VSMC functions and neointima hyperplasia. Our data provide new insight into the roles of hnRNPA1-microRNA-124-IQGAP1 regulatory axis in VSMC functions and the pathogenesis of neointima formation and/or angiographic restenosis, and aid the development of novel therapeutic agents for the prevention of these diseases.

5848 | BENCH

Selective inhibition of the histone lysine methyltransferase G9a preserves differentiation and inhibits calcification in vascular smooth muscle cells

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Introduction: Activation and de- or transdifferentiation of smooth muscle cells (SMCs) at sites of vascular injury is regulated by epigenetic mechanisms. Epigenetic histone methylation has been recognized as a dynamic mark controlling many biological processes in health and disease. Here we have identified a histone methyltransferase inhibitor as a selective modulator of SMC differentiation.

Methods and results: We studied the effects of the several epigenetic modifiers on smooth muscle cell proliferation, inflammation and TNFα-mediated dedifferentiation. UNC0638 a specific inhibitor of the G9a histone methyltransferase controlling histone h3 lysine 9 dimethylation was found to selectively modulate SMC differentiation. UNC0638 had no effect on TNFα-induced MCP-1 expression or PDGF-induced SMC proliferation as detected by cell counting and BrdU incorporation. However, UNC0638 treatment significantly attenuated TNFα-induced down regulation of the SMC marker gene SM22α, suggesting that UNC0638 reduces SMC dedifferentiation.

This effect was detectable up to 72h after the initial treatment and associated with a strong and equally sustained reduction of the respressive histone mark (h3k9me2) at the SM22α promoter. Based on these data we analyzed the impact of UNC0638 treatment on $CaPO_4$-induced SMC-calcification, an in vitro model of SMC transdifferentiation. Consistent with the previously observed preservation of the SMC-differentiation status, UNC0638 treatment significantly attenuated SMC calcification as detected by von Kossa-staining. This was associated with a reduced expression of SMC calcification markers including ALPL, Runx2, BMP-2 and osteocalcin while anti-calcification markers including PPAR-γ and MGN were upregulated.

Conclusion: In summary, our data suggest pharmacologic modulation of histone methylation as a promising approach to target SMC phenotypes and differentiation status in vascular diseases like in-stent restenosis or atherosclerosis and warrant further research to dissect histone methylation dependent mechanisms in SMCs and to investigate in vivo applications of small molecule inhibitors.

IMPROVING CARDIOPULMONARY RESUSCITATION

5884 | BEDSIDE

FirstAED emergency dispatch, global positioning of first responders with distinct roles - a solution to reduce response times and ensuring early defibrillation on a bridge connected island area

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Background: The national survival rate for out-of-hospital cardiac arrest is approximately 11%. Guidelines recommend cardiopulmonal resuscitation (CPR) within 5–6 minutes and early defibrillation with an automated external defibrillator (AED) with the purpose to increase survival rates. Shortening the ambulance response time to less than six minutes in the rural areas, is however unrealistic.

Purpose: FirstAED is an auxiliary to the public emergency services and enables the dispatcher to send an organized team of first responders to the scene. FirstAED organizes three first responders in a team: no. 1 reaches the patient to give CPR; no. 2 brings the AED; no. 3 is the on-site coordinator. The aim is to shorten the first responder response time at emergency calls and the time to the AED on-site to below 5–6 minutes in both public/residential/rural settings in a bridge connected island area.

Methods: CPR and first aid is provided by 175 trained lay first responders who use their smartphone (iPhone 4S/5). The island is characterized by 13,000 inhabitants and long distances to the nearest hospital. The population purchased 95 AED's which are available around the clock and placed less than two kilometres apart. FirstAED global positioning system (GPS)-track the nearby first responders who can accept or reject the alarm. FirstAED chooses the three most optimally placed first responders who accepted the alarm.

Results: During the first 24 months the FirstAED GPS system was used 718 times. FirstAED entailed a security for first responder CPR and a significant reduction in median response time from more than 8 minutes before to 4 minutes 9 seconds after. The response time was faster than the comparable median ambulance response time at 13 minutes and 20 seconds. The AED was on-site in more than 99% of the cases and with a median on-site time of 5 minutes and 47 seconds. The first responder response times were short all over the island (public/residential/rural settings). Thirty first responders accepted the alarm more than 25 times. Three first responders arrived in 89.1%, two first responders in 7.1%, one first responder in 3.0% of the cases. The first responders arrived before the ambulance in 94.3% and at the same time in 2.4% of the cases. The first responders were involved in cardiac arrests, respiratory arrests and a patient with subarachnoid hemorrhage.

Conclusion(s): Global positioning tracking and a team structure with distinct roles reduces the response times and ensures the possibility for CPR and early defibrillation in public/residential/rural settings of the island.

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5885 | BEDSIDE

Clinical comparison of off-hours versus regular hours extracorporeal cardiopulmonary resuscitation for cardiac arrest

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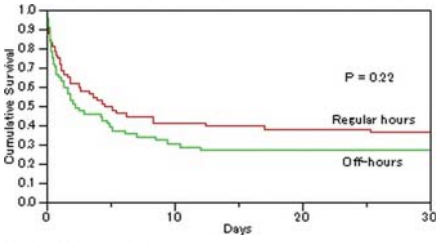
Background: There is a potential delay to perform extracorporeal cardiopulmonary resuscitation (ECPR) during after-hours because of cath lab activation and off-shift. We aimed to evaluate the relationship between ECPR timing and mortality in patients with cardiac arrest.

Methods: We studied 130 consecutive patients (mean age=62.4±15.2 years, 83.1% Male) who underwent venoarterial extracorporeal membrane oxygenation (VA-ECMO) due to refractory circulatory collapse between January 2008 and February 2015 in our hospital. The primary endpoints were in-hospital death and neurological impairment.

Results: A total of 62 patients (47.7%) were treated during off-hours (Monday-Friday, 6:30 pm-8:30 am and weekends) and 68 patients (52.3%) during regular hours. Acute myocardial infarction was the most common cause of cardiac arrest (53.2% during off-hours vs 52.9% during regular hours, P=0.20). The frequency of bystander cardiopulmonary resuscitation was 72.1% during off-hours and 76.4% during regular hours (P=0.57). Time of day was not related to pre-hospital delay (28.3±3.1 minutes during off-hours vs 25.5±3.0 minutes during regular hours, P=0.53). There was a statistically significant delay for the interval between patient's arrival at the hospital to initiation of VA-ECMO (door-to-ECMO) between the off-hours group and the regular hours group (48.2±4.2 minutes vs 27.2±4.2 minutes, P=0.001). In-hospital mortality was 77.4% and 67.7% in the off-hours and regular hours groups, respectively (P=0.21). Neurological impairment was observed in 78.1% of the off-hours group and 77.3% of the regular hours group (P=0.80).



Kaplan-Meier survival curves

Conclusion: There is time delay in door-to-ECMO during off-hours, but off-hours ECPR still provides similar survival as patients who present during regular hours.

5886 | BEDSIDE

Predictive value of neuron-specific enolase for clinical outcome in cardiac arrest survivors depends on the time of sample collection: results of a prospective study

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Background: Despite marked advances in intensive cardiology care, current options for outcome prediction in cardiac arrest survivors remain significantly limited.

Purpose: The aim of our study was, therefore, to compare the day-specific predictive values of neuron-specific enolase (NSE) in cardiac arrest survivors treated with endovascular hypothermia.

Methods: Eligible patients were out-of-hospital cardiac arrest survivors alive for more than 24 hours from hospital admission. All were treated with endovascular hypothermia (33℃ for 24 hours). NSE was measured using immunoturbidimetric assay and samples were collected at day 1, 2, 3, and 4, respectively, after hospital admission, Clinical outcomes were evaluated at 30 days according to the Cerebral Performance Category.

Results: One-hundred-and-thirty-two cardiac arrest survivors (mean age 64.3 years) were included into the study. Using ROC analysis, optimal cut-off values of NSE for prediction of CPC 1–2 at respective days were determined as: Day 1: ≤22,3 mcg/l (sensitivity 85,2; specificity 58.3; P<0.0001), Day 2: ≤27.3 mcg/l (sensitivity 91.3; specificity 72,4; P<0.0001), Day 3: ≤32.9 mcg/l (sensitivity 96,6; specificity 74,1; P<0.0001), and Day 4: ≤25.4 mcg/l (sensitivity 92.5; specificity 86,9; P<0.0001). Values >57.2 mcg/l measured at any time predicted poor outcome (CPC 3–5) with 100% specificity.

Conclusion: Our results indicate that NSE estimation might be useful for neurological outcome prediction in cardiac arrest survivors treated with endovascular hypothermia. The highest predictive values of NSE measurement were observed at Day 3 and Day 4 after cardiac arrest.

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THE CHALLENGE OF INFLAMMATORY CARDIOMYOPATHIES

5898 | BENCH
High number of CD45RO positive cells in endomyocardial biopsies is associated with increased mortality of patients with Inflammatory cardiomyopathy

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Background: Intramyocardial inflammation is considered as an adverse prognostic factor in inflammatory cardiomyopathy (CMi). However, the precise nature of immune cells relevant for the prediction of long-term course remains elusive. We analyzed the correlation of increased inflammatory infiltrates (CD45RO-activated memory T-lymphocytes, CD3) to mortality in a large cohort of patients with CMi.
Methods: We investigated 1811 consecutive patients with suspected CMi, undergoing endomyocardial biopsies (EMBs), and examined the mortality of these patients for a 10-year follow-up period. In EMBs myocardial inflammation was assessed by histology and immunohistology including digital imaging analysis. In total, 82 (4.5%) patients met the endpoint of death (31.9±21.8 months).
Results: Multivariable statistical analysis of mortality in all patients revealed that a high number of CD45RO or CD3 cells in EMBs at the point of the initial biopsy is an important predictor of mortality (9.3%/10.5% respectively). The analyzed cohort was divided by the number of measured CD45RO cell number higher than 50/60 cells/mm^2 myocardial tissue with an increasing rate of mortality and significance (p=0.0001/ p=0.0002). For CD3 positive lymphocytes the mortality is significantly higher starting from a cell number higher than 20 cells/mm^2 ($p<0.0004$). Since the cell numbers of both cellular infiltrates are highly correlated ($p<0.0001$), we found a significant group ($p<0.0001$) of patients dying in the 10-year follow-up with an increased number of CD45RO cells but a normal value of CD3 infiltration. This finding pronounces CD45R0 cells as an independent predictor of mortality in inflammatory cardiomyopathy.
Conclusion: In this EMB-based analysis of the long-term course of CMi we identified, for the first time, that high numbers of CD45RO positive inflammatory cells in the myocardium predict increased mortality.

5899 | BEDSIDE
T2 mapping increases diagnostic accuracy in patients with clinically suspected acute myocarditis - a prospective, endomyocardial biopsy controlled study

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Background: Myocarditis has been reported in up to 20% of sudden cardiac death in young adults and is regarded as precursor of dilated cardiomyopathy. Recent European consensus recommendations endorse the use of endomyocardial biopsy (EMB) in the diagnostic workup of myocarditis. Besides EMB, cardiac magnetic resonance (CMR) offers the advantage of analysing the whole myocardium without being prone to sampling errors. However, late gadolinium enhancement (LGE) as well as T2-weighted (T2w) CMR exhibit inadequate sensitivity, especially during early stages of inflammation.
Purpose: To investigate diagnostic accuracy of quantitative T2 relaxation mapping in clinically suspected acute myocarditis.
Methods: We carried out a prospective biopsy controlled study in 60 patients with clinically suspected acute myocarditis defined by recent ESC recommendations: clinical symptoms <5 days plus diagnostic criteria like ECG abnormalities or hsTNT-elevation or new global/ regional wall motion abnormalities and exclusion of coronary artery disease. All patients underwent CMR at 1.5 T including T2-mapping with a Gradient and Spinecho sequence (GRASE: 15 T2 echos separated by 10ms, res: 1x1x10 mm^2, 3 short axis slices). Two patients had non-diagnostic T2 maps and 23 patients refused EMB. The remaining 37 patients underwent EMB within 24h after CMR. Sixty-five age- and sex-matched volunteers served as controls for T2 value dependent ROC curve analysis.
Results: EMB confirmed acute myocarditis in 70% of the patients presenting with suspected myocarditis and agreed biopsy. Applying quantitative CMR strategies with T2-mapping, patients with biopsy-proven myocarditis displayed significantly increased areas of global myocardium with prolonged T2 times compared to controls (14.68±9.4% vs. 3.3±2.7% myocardium with T2 time >80ms). A segmental T2 time analysis displayed significantly elevated T2 times predominantly in lateral myocardial segments. ROC analysis revealed that a threshold of 7.6% myocardial area with absolute T2 times above 80ms displayed optimal sensitivity of 0.92 and a specificity of 0.90 in patients with biopsy proven myocarditis. Applying this threshold to patients with clinically suspected myocarditis, a sensitivity of 0.85 and a specificity of 0.90 could be reached. Combined with T2w imaging and LGE the sensitivity rose towards 96%.
Conclusions: Conventional CMR and EMB are of additive diagnostic value in patients with clinically suspected acute myocarditis. T2 mapping increases diagnostic accuracy in CMR-based diagnosis of acute myocarditis.

5900 | BEDSIDE
Long-term arrhythmic prognosis in patients with biopsy-proven myocarditis, studied by cardiac magnetic resonance imaging and electroanatomic mapping

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Background: Data on long-term follow-up (FU) in patients (pts) with biopsy-proven myocarditis are conflicting, particularly those regarding ventricular events.
Purpose: To determine the prognostic variables for ventricular arrhythmias (VA) in pts with biopsy-proven myocarditis.
Methods: We prospectively studied consecutive pts with endomyocardial biopsy (EBM)-proven myocarditis (M1 Group). Control group was represented by pts presenting with suspected myocarditis, without EBM evidence of myocarditis (M0 Group). All pts underwent cardiac magnetic resonance imaging (MRI), coronary angiography, electrophysiological study (EPS) and electroanatomic mapping (EAM). Implantable cardioverter defibrillator or loop recorder was implanted in a subgroup of pts, following guidelines. The primary endpoint was the occurrence of sustained VA at FU.
Results: 49 pts with biopsy-proven myocarditis were enrolled in Group M1, and 10 patients in Group M0 (mean age 41±15 vs 42±13 years respectively, p=0.87; men 59% vs 70% respectively, p=0.52). There were no statistically significant differences between the 2 groups regarding clinical variables and imaging parameters. Group M1 showed greater involvement of the right ventricle (RV), expressed as wider low-voltage area, compared to group M0, both at bipolar and unipolar mapping (Table 1). At 37±24 months of FU, there were 12 VA in group M1 vs 1 VA in group M0 (24% vs 10% respectively, p=0.44). VA predictors among Group M1 were the presence of left ventricular systolic dysfunction (HR 3.5, 95% CI 1.3–9.4, p=0.01) and ventricular tachycardia (VT) induction at EPS (HR 5.3, 95% CI 1.9–14.9, p=0.001). At multivariate analysis, inducible VT remained the only independent predictor of VA in pts with myocarditis (HR 4.1, 95% CI 1.3–12.6, p=0.015).

Table 1. Right ventricle EAM

	Group M1 (n=49)	Group M0 (n=10)	P value
Bipolar low voltage (<1.5 mV) area (%)	10.0±10.4	2.4±3.2	0.04
Bipolar scar area (<0.5 mV) (%)	3.9±6.9	0.4±0.6	0.015
Unipolar low voltage (<5 mV) area (%)	21.1±20.1	6.7±10.7	0.01

Data are expressed as mean ± standard deviation.

Conclusions: A higher degree of RV unipolar and bipolar mapping alterations was observed in pts with biopsy-proven myocarditis, confirming that substrate alteration at EAM reflects histological abnormalities in these pts. VT inducibility was the only independent predictor for VA in pts with biopsy-proven myocarditis.

NON-CODING RNAS IN HEART FAILURE

5903 | SPOTLIGHT
A crucial role of miR-195 in pressure overload-mediated cardiac remodeling

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Background: Cardiac angiogenesis plays a crucial role in adaptive hypertrophy to pressure overload. We previously showed that impaired angiogenesis in heat shock transcription factor 1 (HSF1) knockout (KO) mice under increased workload manifested maladaptive hypertrophy and heart failure. However, the potential mechanism is still incompletely understood.
Purpose: Here we investigate the function of microRNAs involved in HSF1-dependent angiogenesis and cardiac hypertrophy in response to pressure overload.
Methods and results: 10 weeks old HSF1 KO mice and wild-type (WT) C57BL/6J mice as control were subjected to transverse aorta constriction (TAC) for four weeks, microRNAs array analyses from the heart samples of these mice revealed that the level of miR-195 was significantly upregulated in HSF1 KO hearts when compared with that in WT hearts. In addition, HSF1 deficiency reduced the AMP-activated protein kinase (AMPK) α2 but without affecting AMPKα1. In vitro, we showed that overexpression of AMPKα2 but not AMPKα1, enhanced p53 phosphorylation and its nuclear export in endothelial cells stimulated by mechanical stretch. AMPKα2 overexpression also significantly increased the level of HIF-1α and promoted endothelial angiogenesis. Importantly, AMPKα2-mediated p53 suppression and HIF-1α-dependent angiogenesis were abolished by mimic transfection of miR-195. Further experiments, we confirmed that HSF1 induction could suppress the enhanced miR-195 level in endothelial cells with mechanical stress, which strengthened the AMPKα2 expression, and attenuated the nuclear accumulation of p53. Furthermore, we demonstrated that transfec-

tion of Ad-AMPKα2 in HSF1 KO mice effectively improved cardiac angiogenesis, reduced cell apoptosis and alleviated myocardial remodeling in response to TAC.
Conclusions: Our findings indicate that miR-195 is critically involved in cardiac remodeling via impairment of HIF-1α-dependent angiogenesis. Induction of HSF1 might be a novel and effective target for therapeutic approaches to pressure overload-induced heart failure through regulating the miR-195/AMPKα2 pathway.

5904 | BENCH
Transcoronary gradient of circulating microRNAs in heart failure

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Background: Circulating levels of microRNA (miRs) are emergent promising biomarkers for cardiovascular disease. In particular, altered expression of miRs has been related to heart failure and cardiac remodeling.
Purpose: To identify the heart as a potential source for miRs released into the circulation, we measured the concentration gradients across the coronary circulation for the miR-34a (whose levels have been associated to LV-remodeling and prognosis); miR-126 (whose decrease has been associated to an impaired cardiac repair capacity); the miR-21*, that was recently shown to be actively involved in mediating HF and LV-hypertrophy, and the miR-423 that was recently shown to be highly regulated in HF patient.
Methods: Circulating miRs were measured by TaqMan polymerase chain reaction in EDTA-plasma simultaneously obtained from the aorta (Ao) and the coronary venous sinus (CVS) in patients with non-ischemic heart failure (nonICM-HF, n=12), or ischemic heart failure (ICM-HF) (n=32).
Results: Circulating levels of the miR-34a (2.3-fold increase), the miR-423 (4.4-fold decrease), the miR-21* (1.6-fold decrease), and the miR-126 (1.3-fold decrease) were differently modulated in nonICM-HF compared to ICM-HF patients. Interestingly, there was a positive transcoronary concentration gradient for the miR-34a in the nonICM-HF group ($p<0.05$) as well as of the miR-423 in the ICM-HF group ($p<0.05$), suggesting a release of a specific microRNA into the coronary circulation of HF patients with different etiology.
Conclusions: Circulating levels of miRs are differentially expressed in circulating blood from patients with HF of different etiologies. Interestingly, the miR-34a is released from the heart into the coronary circulation in patients with non ischemic HF as its levels in the CVS are higher than in the Ao. Similarly, the miR-423 is released from into the coronary circulation in patients with ischemic HF. The differential regulation of circulating miRs during the transcoronary passage in HF might provide important information to better understand their role in HF and foster their use as cardiac biomarkers, especially to differentiate between HF of different etiologies.

5905 | BEDSIDE
MiR-21 and miR-133 levels in peripheral blood mononuclear cells in patients with heart failure with preserved ejection fraction

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Purpose: MicroRNAs (miRs) are essential regulators of gene expression implicated in cardiovascular function and disease. MiR-21 and miR-133 have been shown to play a role in heart hypertrophy and fibrosis. They have also been shown to regulate proliferation and phenotypic switch of vascular smooth muscle cells. However, there are limited data regarding their role in left ventricular (LV) diastolic dysfunction. The aim of this study is to investigate miR-21 and miR-133 levels in peripheral blood mononuclear cells in patients with heart failure with preserved ejection fraction (HFPEF).
Methods: We included 39 patients with symptoms and signs of heart failure who had an LVEF >50% and evidence of LV diastolic dysfunction (19 males, aged 68±10 years. Blood samples were also obtained from 29 healthy volunteers for comparison (17 males, aged 52±8 years). All subjects underwent a complete echocardiographic study.
Peripheral blood mononuclear cells (PBMCs) were isolated and microRNA levels were determined by quantitative real time reverse transcription PCR.
Results: MiR-21 levels were found to be higher (4.6±0.45 versus 2.05±0.31, $p<0.05$), while miR-133 levels were found to be lower (11.5±6.9 versus 37.03±8.18, $p<0.05$) in patients with HFPEF compared to healthy controls. MiR-21 levels showed strong negative correlations with E/E' ratio ($r=-0.42$, $p<0.001$) while miR-133 levels showed strong positive correlations with E/E' ratio ($r=0.41$, $p<0.001$)
Conclusions: MiR-21 and miR-133 levels in PBMCs differentiate in patients with HFPEF compared to normal individuals. In addition, they show a strong relationship with LV diastolic dysfunction in those patients. Our findings contribute to the understanding of pathogenesis of HFPEF and might offer a future therapeutic target.

NEW INSIGHTS IN DEVICE THERAPY

5914 | BEDSIDE
Feasibility, safety, and acute hemodynamic effect of a new approach for anti-bradycardia pacing: left ventricular septum pacing by transvenous approach through the inter-ventricular septum

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Introduction: Conventional right ventricular apex (RVA) pacing causes left ventricular (LV) dyssynchrony which can lead to LV dysfunction. Previous animal studies have shown that LV septum (LVS) pacing results in less ventricular dyssynchrony than RVA pacing and maintains LV pump function. We investigated the feasibility, safety, lead stability, and hemodynamic effects of LVS pacing in patients.
Methods: Ten patients (5 men; age 72±10 years; LV ejection fraction 57±8%) with sinus node dysfunction scheduled for dual chamber pacemaker implantation were selected. Right ventricular (RV) angiography and intra-cardiac echocardiography (ICE) were performed to visualize the inter-ventricular septum. A custom pacing lead (Medtronic 09066) with extended helix (4 mm) was introduced via the subclavian vein, and after positioning against the RV septum (RVS) using a preshaped guiding catheter guided by fluoroscopy and ICE, driven through the inter-ventricular septum to the LVS. The acute hemodynamic effects of RVA, RVS and LVS pacing were evaluated by invasive LVdP/dtmax measurements.
Results: The lead was successfully delivered to the LVS in all patients in a single attempt without complications. Lead implant procedure time shortened with experience (90 min at first to 12 min at last procedure). This also applied to total fluoroscopy time (44 min at first to 10 min at last procedure). In the last 2 patients, lead implantation was accomplished without guidance by ICE. QRS duration was shorter during LVS pacing (147±21 ms) than during RVA pacing (172±33 ms, $p=0.02$ compared to LVS pacing) and RVS pacing (165±17 ms, $p=0.04$ compared to LVS pacing). RVA and RVS pacing reduced LVdP/dtmax compared to baseline atrial pacing (–7.1±4.1% and –8.7±2.1% respectively), whereas LVS pacing maintained LVdP/dtmax at baseline level (+0.63±4.45%, $p<0.01$ compared to RVA and RVS pacing). R-wave amplitude and pacing threshold were 13.3±7.7 mV and 0.5±0.3 V at implant and remained stable during follow-up (mean 4.8±1.5 months; minimum 3; maximum 6), without lead related complications.
Conclusion: LV septum pacing by transvenous approach through the inter-ventricular septum is a new, feasible, safe, and hemodynamically preferable approach for anti-bradycardia pacing therapy.

5915 | BEDSIDE
Exercise detection with 3-Axis accelerometer of a total intracardiac leadless pacemaker

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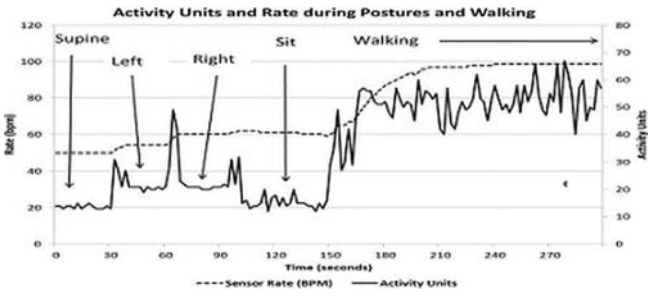
Background: Conventional pacemaker systems use accelerometers or other extracardiac sensors to adapt stimulated heart rate to actual patient activity. The Micra Trans-Catheter Pacemaker (TCP) is implanted in the right ventricle and incorporates a 3-axis accelerometer to detect patient (pt) activity. The TCP incorporates filtering to accentuate physical motion over cardiac motion.
Purpose: To describe the performance and stability of the activity detection during exercise and different body positions.
Methods: Pts underwent postural and hallwalk testing at pre-discharge, 1 month, 3 month and 6 month. The activity units were measured in each accelerometer vector during different postures and activity (Figure). An excellent vector was defined as having activity units at least >10 above the highest resting posture, >5 units was considered adequate.
Results: Overall 40 pts (76±7.8 yrs, 10 female, 30 atrial fibrillation) were implanted with the TCP. At least one vector testing was available in 39 pts; repeated testing was available in 27 pts. Although activity detection occurred at rest (due to cardiac motion) and position differences were observed in 23 pts, 38 of 39 had either one excellent (20 pts) or adequate (18 pts) vector. In repeat testing, if an



excellent vector was programmed initially, this vector remained excellent (15/15). In pts programmed to an adequate vector at baseline, 10/12 patients were still adequate and 2 were programmed to a different vector.
Conclusions: Although posture dependent activity differences were observed, detection of physical exercise and appropriate rate response with intracardiac accelerometer in a TCP was demonstrated. A simple exercise test allows selection of the accelerometer vector with the greatest activity to rest ratio.
Acknowledgement/Funding: Medtronic Inc

5916 | BEDSIDE
Right ventricular lead placement in a pacemaker population: comparison of apical and septal positions. The right pace study

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Introduction: Chronic right ventricular (RV) apical pacing induces mechanical left ventricular (LV) dyssynchrony and may cause heart failure at long-term follow-up. Septal RV site could induce less variation in the temporal pattern of LV mechanical activation.
Methods: The RIGHT PACE study is a trial comparing pacing from RV apex and septal area. Patients with indications for cardiac pacing and no indications for implantable-defibrillator and/or resynchronization were enrolled in 14 centers. The primary objective was to acutely evaluate the pacing-induced LV dyssynchrony, calculated as the delay between septum and lateral wall contraction (SLD), as recorded with tissue-Doppler echocardiography.
Results: 437 patients were enrolled. 274 patients received an RV lead in the apex and 163 in the septal area (high-septum 21, mid-septum 111, low-septum 31). The two groups were similar in terms of ejection fraction (57±9% versus 58±9%), prevalence of coronary artery disease (24% versus 29%), QRS duration (98±25ms versus 92±24ms, all $p>0.05$). During spontaneous LV activation, SLD was comparable between groups (48±27ms versus 52±28ms) and the proportions of patients with spontaneous LV dyssynchrony (i.e. SLD>41ms) were 25% and 28%, respectively (all $p>0.05$). During RV pacing, SLD increased to 54±27ms in Apex group and 57±25ms in Septal group (p=0.281). The proportions of patients with pacing-induced LV dyssynchrony were 48% and 51% (p=0.579). Nonetheless, the QRS increased to 145±30ms versus 141±31ms in Apex and Septal groups, respectively (p=0.285). After X-rays central adjudication, the apical positioning was not confirmed in 56 (20%) patients of the Apex group. Similarly, in 21 (16%) patients of the Septal group the adjudicated pacing site was the apex. According to on-treatment analysis, the proportion of patients with pacing-induced LV dyssynchrony was 47% with apical and 52% (p=0.331) with septal pacing. The QRS increased to 146±31ms versus 139±29ms in Apex and Septal groups, respectively (p=0.041).
Conclusions: Although pacing at the RV septal area resulted in shorter QRS duration than the RV apex, it did not reduce the pacing-induced LV dyssynchrony.

5917 | BEDSIDE
Minimized ventricular pacing delays first onset of AF in pacemaker patients without AF history

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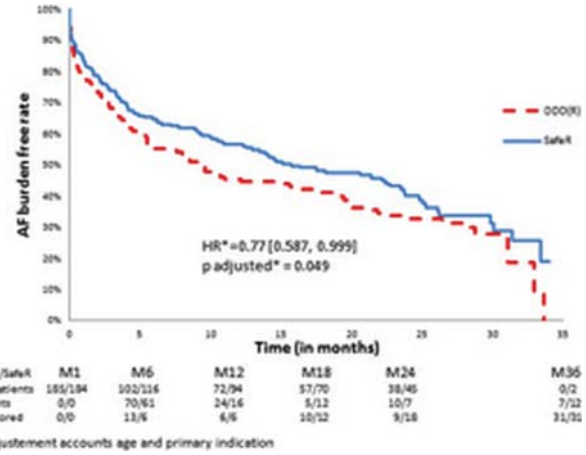
Introduction: Atrial fibrillation (AF) is a frequent comorbidity in the pacemaker (PM) population and has been associated with high risk of heart failure, stroke and death. ANSWER is a randomized (1:1), multicenter trial comparing the SafeR mode, designed to reduce unnecessary right ventricular pacing (Vp), with standard DDD in patients (pts) with sinus node disease (SND) or AV block (AVB), with or without atrial arrhythmia (AA). The aim of this post-hoc analysis was to (1) identify predictors of AF and (2) evaluate the incidence of first onset of AF according to the pacing mode, within 3 years after implantation in patients without AA history.
Methods: First onset of AF was ascertained from the PMs memories. Onset of AF according to the pacing mode was evaluated using Kaplan-Meier statistics. Predictors of AF were identified using a Cox model in pts without previous AA history among 13 parameters (age, indication, gender, NYHA class, LVEF, coronary disease, cardiomyopathy, valvular disease, HF history, diabetes, arterial hypertension and pacing mode).
Results: Out of the 650 pts enrolled in the ANSWER study, 380 pts (58.6%) were without history of AF at baseline (71.4±11.8 years, 61.5% males, 41% SND and 59% AVB). Among them, 369 pts were randomized (184 in SafeR and 185 in DDD). A 23% risk reduction in AF onset was associated with SafeR (HR=0.766, 95% [0.587, 0.999], adjusted p value=0.049) (Figure). Old age (p=0.035) and SND (p=0.004) were identified as predictors of AF onset.



Conclusion: In ANSWER patients without history of AA, younger age and primary indication of AVB were independently associated with a reduced risk of first onset of AF. In addition, SafeR mode proved to be superior to standard DDD pacing to prevent the first onset of AF.

5918 | BEDSIDE
Are DDD/AAI mode switch algorithms worthwhile to prevent unnecessary right ventricular pacing in sick sinus rhythm patients? Results from a randomized cross-over study

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Background: Two algorithms designed to prevent unnecessary right ventricular pacing (RVP) were tested in the "Ventricular Pace Suppression (VPS) Versus Intrinsic Rhythm Support (IRS)" enrolling patients with sick sinus syndrome (SSS) and investigating their effect on RVP percentage, arrhythmic burden and left ventricle (LV)/atrium size. The VPS algorithm automatically switches from a dual-chamber mode to a single-chamber atrial mode or vice versa, when stable atrio-ventricular (AV) conduction is detected (6 out 8 beats) or is no longer confirmed; the IRSplus algorithm simply prolongs the pacemaker AV interval up to 400ms at the first ventricular sensed event, spontaneously occurred or detected during periodic searches.
Methods: SSS patients with indication to cardiac pacing without evidence of II/III degree AV block were 1:1 randomized after pacemaker implant either to IRSplus or VPS algorithms crossing-over after 6 months. The study was designed with a 90% power to detect a least difference in RVP percentage of 3%. Data were collected at 6 and 12 months. Non-normal distributions were generally obtained and described with median (interquartile range). Wilcoxon signed-rank test was used for intra-individual comparisons.
Results: A total of 230 patients (62% males, age 75 (69–79) years) were enrolled: ejection fraction, 57 (50–60)%; NYHA class I 57%, II 40%; CHA2DS2VASc score, 2 (1–2). IRSplus and VpS were respectively associated to a RVP percentage of 1 (0–11)% and 3.5 (0–27)%, (p=0.001) with non-significantly different atrial pacing percentages of 58 (27–82) and 54 (34–78). At the end of respective 6-month periods, variation rate of LV end-diastolic (–22% vs. –18%, p=0.4), end-systolic (25% vs. 20%, p=0.1), atrium end-diastolic (4% vs. 2%, p=0.4) and atrium end-systolic (4% vs 0%, p=0.9) volumes were not significantly different between IRSplus and VPS. No difference in AF burden was observed. In the subgroup of patients with baseline with baseline AV interval >270ms, RVP percentage was lower during the IRSplus period (3 (0–20)%) than during VPS (23 (1–63)%, p=0.01))
Conclusions: Our data showed that automatically prolonging the pacemaker AV delay to 400ms (as with the IRSplus), is at least as effective as DDD/AAI switch algorithms in preventing unnecessary RVP, with no relevant effects on arrhythmic burden and cardiac volumes. IRSplus was even superior in patients with prolonged intrinsic AV conduction, likely including undocumented paroxysmal AV blocks.
Acknowledgement/Funding: BIOTRONIK SE & CO. Kg

5919 | BEDSIDE

Outcome of epicardial pacing in neonates with isolated congenital complete atrioventricular block. A bicentric study

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Background: Isolated congenital atrioventricular block (CAVB) is a rare disorder, and the only treatment is the early implantation of pacemaker (PM). Few data are available, more specifically in neonates.
Purpose: The aim of our study is to assess the feasibility and the long term outcomes of epicardial pacing in this high risk population. We also sought to identify the predictive factors of development of dilated cardiomyopathy.
Methods: This is a bicentric retrospective study. Neonates with CAVB diagnosed in utero or at birth, who underwent pacing during the first month of life were included. They were hospitalized at the Lille University Hospital and at "Necker Enfants Malades" hospital between 1993 and 2014.
Results: A total of 47 neonates were included. Median term at birth was 37 (35–38) weeks of amenorrhea. Median age and weight at implantation were 3 (2–7) days and 2550 (2030–3110) grams, respectively. Ventricular pacing was performed in the majority of patients (74%), most often by subxiphoid approach (63%). Futhermore, left ventricular lead (46%), more physiologic, was also implanted by subxiphoid approach in 65% of them. Follow up was 5 (2–10) years. Epicardial ventricular lead survival was 83% at 5 years, with low median ventricular threshold (0.96V (0.93–1)). 30% of patients had developed dilated cardiomyopathy (DCM) at different time during the follow up. 75% of early DCM were cured by pacing, suggesting multifactorial etiology. Significant risk factors of DCM identified were the increased cardiothoracic index (p=0.075) and the decrease of hemoglobin during hospitalization (p=0.035). Overall mortality rate was 6.5% (one cardiogenic shock and two respiratory distress). There were no mortality due to PM implantation.
Conclusion: There is a clear improvement of prognosis CAVB. Early epicardial PM implantation can be performed in the first days of life safely through minimally invasive subxiphoid approach. The epicardial PM should and could be left in place as long as possible. Some predictive factors of DCM have been identified and a larger cohort could be used to establish a risk score.

5920 | BEDSIDE

Pacemaker implantation using ultrasound guided axillary vein puncture compared to conventional techniques

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Introduction: Venous access during pacemaker implantation can be challenging and result in serious complications. Current approaches consist of subclavian vein puncture using bony anatomical landmarks, surgical cut down to the cephalic vein and fluoroscopy guided axillary vein puncture.
Purpose: This study compares a novel approach for axillary vein puncture using ultrasound guidance with standard techniques.
Methods: Group A consisted of 100 consecutive patients where a single operator (DR) used the subclavian anatomical landmark technique as the primary approach. The same operator subsequently switched to ultrasound guided axillary vein puncture as the primary approach in 248 consecutive patients (Group B). A vascular ultrasound transducer was used to image the axillary vein and adjacent artery in cross section over the first rib. The axillary vein was punctured percutaneously with real time ultrasound visualisation. Group C comprised 228 consecutive patients where 2 operators used the cephalic technique as the primary approach. All 3 operators had 5–20 years experience in pacemaker implantation.
Results: The clinical characteristics and outcomes are shown in the table. The subclavian landmark technique and fluoroscopy guided axillary vein puncture were used as secondary approaches in 43.4% and 11.0% respectively by cephalic operators. In the single case where ultrasound guided puncture of the axillary vein was unsuccessful the cephalic vein was accessed percutaneously using ultrasound guidance. Pneumothorax occurred in 8 patients; the subclavian anatomical landmark approach was used in 7 and the cephalic in 1.

	Group A (n=100)	Group B (n=248)	Group C (n=228)
Age /yrs	78±9	78±11	79±11
Male (‰)	65	59	59
BMI (kg/m^2)	26±4	26±6	26±5
Dual chamber pacemaker (‰)	46	66	69
Successful primary approach (‰)	93.0	99.6	45.1
Pneumothorax (‰)	4.0	0	1.8

Conclusion: Ultrasound guided axillary vein puncture allows safe and swift venous access. It sets a new standard for improving the quality of care of patients undergoing implantation of cardiac rhythm devices.

5921 | BEDSIDE

Feasibility and safety of concurrent atrioventricular junctional ablation in patients undergoing a transcatheter pacemaker implantation: a single-center experience

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Introduction: Atrioventricular junctional (AVJ) ablation is often required when pharmacotherapy fails to attain ventricular rate control during permanent atrial fibrillation (AF) and is accompanied by simultaneous pacemaker implantation as it leaves the patient pacemaker dependent. A newly developed miniaturized leadless permanent single chamber rate responsive pacemaker (MPP) can be implanted via catheter in the right ventricle with a novel fixation mechanism comprised of retractable tines, thus potentially eliminating many of the recognized acute risks of standard pacemaker implantation We report the outcomes of the first patients in the FDA trial of this device who received concurrent AVJ ablation.
Methods: We retrospectively assessed patients who were enrolled in the study and underwent concurrent MPP implantation and AVJ ablation for management of rapid rates associated with AF. Patients and devices were followed per the trial protocol.
Results: Total six patients (median age 76.5 [range: 63–84], female 100%, median BMI 25 [range: 19–39]) underwent MPP implantation and AVJ ablation via a specialized 23F introducer sheath and transfemoral delivery catheter and all were successful. The median times for MPP implantation, duration of fluoroscopy use, and duration of radiofrequency application were 30 mins [range: 21–74], 5.5 mins [range: 3–13], and 210 secs [range: 66–480], respectively. There were no in-hospital complications. There was no device dislodgement or malfunction during the 30-day follow-up. Pacing thresholds were within the trial's prescribed range at implant and remained in range at 30-day follow-up. A total of 3 patients were re-hospitalized within 30 days of the procedure, one of whom died due to breast carcinoma related pneumonia and sepsis unrelated to the device. Other 2 patients were hospitalized for diastolic heart failure which was present prior to implantation.
Conclusions: This first series of patients undergoing AVJ ablation with concurrent transcatheter pacemaker implant suggests reasonable safety and feasibility of this approach. There was no device dislodgement, malfunction or significant pacing threshold increase during the 30-day follow-up. Despite the novel device and fixation mechanism, this combined approach can be considered for drug refractory AF with suboptimal rate control and may potentially provide a lower risk of in-hospital complications.
Acknowledgement/Funding: None

5922 | BEDSIDE

Cardiac implantable devices: an invaluable tool for the diagnosis of sleep apnea

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Introduction: The Sleep Apnea/Hypopnea Syndrome (SAHS) is characterized by the absence or reduction of ventilation during sleep and its diagnosis is based on polyssomnography, which is seldom available. There is a high prevalence of SAHS in patients with cardiovascular disease, and it is a marker of cardiovascular risk in healthy individuals. Amongst patients with cardiac implantable electronic devices (CIED) the prevalence of SAHS can reach 60%. Our objective was to evaluate the presence of SAHS on patients with CIED and to evaluate the value of CIED on the screening of SAHS.
Methods: This prospective single-center study included 28 adult patients with CIED with rate responsive function. Sleep study was conducted on all patients and was compared to the data collected from the CIED on the following morning. Baseline demographic, clinical and echocardiographic data was collected.
Results: Most patients were male (69%) with a mean age of 75,9 years. The prevalence of SAHS was 77% (14 patients with apnea-hypopnea index (AHI)>15; 9 with AHI>30) and 5 patients presented with Cheyne-Stokes respiration. No correlation was found between body mass index and AHI. The number of snoring events was positively correlated with the AHI (ρ(28)=0,548, p=0,004). The data collected by the CIED strongly correlated with the AHI evaluated on the sleep study (ρ(28)=0,704, p<0,01). For the diagnosis of severe SAHS (AHI >30), CIED showed a specificity of 64,7% and a sensitivity of 100% with a negative predictive value (NPV) of 100% and positive predictive value (PPV) of 60%.
Conclusion: SAHS is a highly prevalent disease in the population with CIED. The data obtained through the CIED monitorization data has a strong positive correlation with the AHI and its sensitivity, specificity, NPV and PPV make it a valuable tool for severe SAHS diagnosis and treatment monitoring.

5923 | BEDSIDE

Persistence of left bundle branch block within periinterventional pacemaker implantation after transcatheter aortic valve implantation

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Introduction: Interventional transcatheter aortic valve implantation (TAVI) has become an established alternative to surgical aortic valve replacement for patients with severe aortic stenosis and a high perioperative risk. Aim of the study was to determine the persistence of new-onset LBBB in the context of periinterventional pacemaker implantation.
Material and methods: The study included a total of 975 patients who underwent TAVI due to severe aortic stenosis between July 2008 and October 2013. 477 (48.9%) pat. received an Edwards SAPIEN valve, USA, 76 pat. (7.8%) a Medtronic CoreValve USA, 92 pat. (9.4%) a JenaValve, Germany and 75 pat. (7.7%) a Symetis prosthesis, Switzerland). In 178 pat. (n=168;17.2%) a peri- or postinterventional pacemaker implantation was performed.
Results: There were no significant differences in the patients baseline characteristics (median age: 80.9±7.6 years, male gender: n=80;44.9%, BMI: 26.7±4.9 kg/m^2). The use of CoreValve bioprosthesis was associated with a significantly higher incidence of peri- or postinterventional pacemaker implantation ($p<0.001$). The most frequent indication for a PPM implantation was the development of a third-degree atrioventricular (AV) block (n=80;47.6%), followed by a LBBB (n=51;30.4%). During 12 months of follow-up (n=29), LBBB could no longer be detected in 12 of the PM-supplied patients (n=12;41.4%).

Table 1. Comparison between different bioprosthesis of patients who received a periinterventional pacemaker implantation after TAVI or not

Prothesis	Total	PM implantation	No PM implantation
SAPIEN, n (%)	477	83 (17.4%)	394 (82.6%)
CoreValve, n (%)	76	48 (63.16%)	28 (36.8%)
JenaValve, n (%)	92	18 (19.6%)	74 (80.4%)
Symetis, n (%)	75	19 (25.3%)	56 (74.7%)

Conclusion: There is a significantly higher incidence of permanent pacemaker implantation following TAVI with a Medtronic CoreValve bioprosthesis. During follow-up a resolution of LBBB could have been detected in almost 40% of the patients who underwent PPM implantation. In order to perform a predictive statement regarding a stricter indication of pacemaker implantation further studies are necessary.

VENTRICULAR ARRHYTHMIAS: STRATIFICATION AND TREATMENT

P5924 | BEDSIDE

Real World Experience with Wearable Cardiac Defibrillators

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Background and introduction: The wearable cardioverter defibrillator (WCD) has emerged as a non-invasive therapy for sudden cardiac death. There are several clinical scenarios when a WCD may be prescribed, however no standardized criteria to guide its use exist. In addition, there is limited data regarding the frequency of treatments delivered.
Purpose: Our study sought to delineate WCD indications in practice and frequency of therapies delivered by WCDs.
Methods: We retrospectively reviewed indications and therapies of all WCD prescriptions in a 2 year period from 2 large academic medical centers. Data on compliance of patients wearing the WCD and WCD treatment events was provided by ZOLL Medical Company.
Results: Among the 147 patients prescribed a WCD between January 2012 and December 2013, 76% were male with a mean age of 59. A variety of WCD indications were cited: newly diagnosed cardiomyopathy with an ejection fraction $\leq$35% was most common (n=42 nonischemic [28%], n=34 ischemic [23%]); implantable cardiac defibrillator (ICD) extraction (n=33 [22%]); current contraindication to ICD implantation (n=19 [13%]); and bridge to an ICD decision based on further work up (n=19 [13%]). Among the 134 patients who wore the WCD for at least one day, the median WCD wear time was 40 days (range 2–355). The device detected 11,000 high ventricular rate events (average of 1.4 per patient per day) over a total wear-time of 7,888 person-days. High-voltage treatment was delivered in 3 separate patients. One patient had two shocks for ventricular fibrillation, each converting to a wide complex bradyarrhythmia, yet the patient subsequently died. A second patient was shocked for polymorphic ventricular tachycardia, however salvos of the arrhythmia rapidly recurred and the patient died. The third patient was shocked for a regular wide complex tachycardia, subsequently deemed to be supraventricular in origin, which converted the rhythm to ventricular fibrillation ultimately resuscitated by emergency medical responders. In 30 patients, ICD implantation decisions were made by unaffiliated providers and are not known. In the remaining 104 patients, 54 (52%) ultimately had an ICD implanted.
Conclusions: WCDs are becoming a commonly prescribed device in patients at high risk for ventricular arrhythmias. In this limited sample, both events requiring therapy and inappropriate shocks were rare, and no patients were saved by the WCD. Future efforts are warranted to improve identification of patients most likely to benefit from a WCD and efficient utilization of therapies to minimize sudden death.

P5925 | BEDSIDE

Lack of an additional prognostic value of programmed electrical stimulation for risk stratification in Brugada patients without previous cardiac arrest: J-IVFS study

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Background: The HRS/EHRA/APHRS Expert Consensus Statement 2013 indicates that positive inducibility of ventricular tachy-arrhythmias (VT/VF) by programmed electrical stimulation (PES+) is classified as class IIb for the indication of ICD implantation in Brugada syndrome (BrS) patients. The recent Japanese report, however, indicated that syncope, spontaneous type 1 ECG (spType1), and PES+ were important risk factors and the combination of these 3 indices could stratify the risk of later arrhythmic events in BrS patients without previous cardiac arrest.
Purpose: To evaluate any additional prognostic value of PES+ for risk assessment in BrS patients without previous cardiac arrest and having clinical history of syncope and/or spType1 in a large Japanese cohort of BrS (The Japan Idiopathic Ventricular Fibrillation Study [J-IVFS]).
Methods: A total of 338 consecutive BrS patients without previous cardiac arrest (mean age 52±14 years, 317 males), who were performed PES, were enrolled. Clinical outcomes during the follow-up period were compared between the groups with and without PES+ in patients showing clinical history of syncope and/or spType1.
Results: The incidence of cardiac events (sudden cardiac death [SCD] or VF) during a mean follow-up period of 63±37 months was not different in patients with and without PES+ (0.7 and 0.9%/yr, respectively, p=0.72). In patients with syncope (n=45), spType1 (n=125), and both (n=66), incidences of cardiac events in cases with and without PES+ were not different (0.6 vs 0, 0.4 vs 1.8, 2.2 vs 2.0%/yr, respectively; p=n.s). The incidence of cardiac events was significantly higher in patients with Class IIa (syncope + spType1, 3.2%/yr) than those with Class IIb indication (PES+ in patients except for Class IIa indication, 0.6%/yr) (p=0.009), as determined by the Kaplan-Meier method.
Conclusions: We confirmed no additional prognostic values of PES+ for risk assessment in BrS patients without previous cardiac arrest and having clinical history of syncope, spType1, or both. Combination of syncope and spontaneous Type 1 ECG is enough for risk assessment in BrS patients without previous cardiac arrest.

P5926 | BEDSIDE

Critical progressive activation delay after premature stimulation is associated with polymorphic ventricular tachycardia in nonischemic cardiomyopathy: results from the Leiden NICM Study

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Background: Progressive activation delay after premature ventricular stimulation has been associated with ventricular fibrillation in nonischemic cardiomyopathy (NICM).
Purpose: In this study, we (1) investigate prolongation of the paced QRS duration (QRSd) after premature stimulation as a marker of global activation delay in NICM, (2) assess its relation to induced ventricular arrhythmias, and (3) analyze its underlying substrate by late gadolinium enhancement CMP (LGE-CMR) and endomyocardial biopsy.
Methods: Patients with NICM were prospectively enrolled in the Leiden Nonischemic Cardiomyopathy Study, and underwent a comprehensive evaluation including LGE-CMR, electrophysiological study (EPS) and endomyocardial biopsy. EPS data were compared with control patients without structural heart disease.
Results: A total of 40 patients with NICM (age 57±14 years, 83% male, LVEF 30±13%) were enrolled and compared to 20 controls. After the 400 ms drive train and progressively premature stimulation, the maximum increase in QRSd was larger in NICM than in controls (35±18ms vs. 23±12ms, p=0.005) and the coupling interval (CI) window with QRSd prolongation was wider (47±23ms vs. 31±14ms, p=0.005). The maximum paced QRSd exceeded the ventricular refractory period allowing for pacing before the previous QRS offset in 20/39 NICM patients vs. 1/19 controls ($p<0.001$). In NICM, QRSd prolongation was associated with polymorphic VT inducibility (16/39 patients), and was related to long thick strands of fibrosis on biopsies but not to focal enhancement on LGE-CMR (all $p>0.05$).
Conclusion: QRSd is a simple parameter to quantify global activation delay after premature stimulation and its prolongation is associated with the inducibility of polymorphic VT and with the pattern of myocardial fibrosis on biopsies.

P5927 | BEDSIDE
PainFree SST trial: T-wave oversensing algorithm performance

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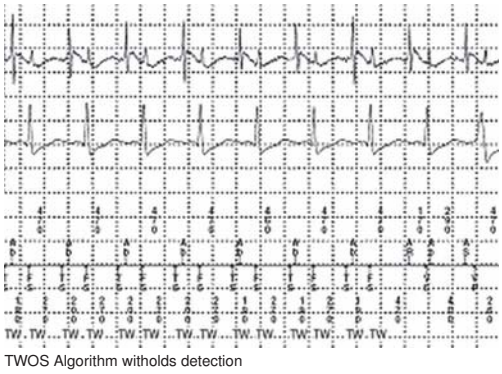
Introduction: T-wave oversensing (TWOS) may cause inappropriate shocks in patients with implantable cardioverter-defibrillator (ICD). A suite of new detection algorithms, SmartShock Technology (SST), has been shown to reduce the rate of inappropriate shock. This analysis was focused on the performance of the TWOS algorithm designed to prevent shocks caused by TWOS.
Methods: PainFree SST was a prospective international clinical trial to estimate inappropriate shock rate after implant of Medtronic Protecta ICDs with SST. TWOS algorithm withholds detection when the frequency content of alternating sensed beats is consistent with a pattern of TWOS. "TW" in figure indicates detection withheld by TWOS algorithm. Episodes were adjudicated by an independent physician committee.
Results: 2770 patients (pts) were included with mean follow up of 22 months. There were 257 TWOS episodes in 14 pts. Of these, 4 episodes in 4 pts received inappropriate shock and 1 episode in 1 pt received inappropriate ATP. The remaining 252 episodes were appropriately withheld for an incremental specificity of 98.1% (CI: 93.5%, 99.4%). Only 50 episodes in 11 pts contained EGM and were adjudicated, all as due to TWOS. Logs contained an additional 104 episodes w/o EGM, all in the same 11 pts. These are presumed to also be true TWOS for which detection was withheld. The remaining 98 episodes were by device counter only and occurred in 3 of the same 11 pts. These, too, were presumed to be appropriate withholding of detection by the TWOS algorithm. There were no instances of appropriate detection of VT/VF being withheld by the TWOS algorithm.



TWOS Algorithm witholds detection

Conclusion: The TWOS algorithm is designed to reduce shocks for TWOS. The PainFree SST trial showed TWOS reduces inappropriate detection by 98% without loss of sensitivity.

P5928 | BEDSIDE
Arrhythmia treatment and survival of patients wearing the cardioverter defibrillator vest

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The wearable cardioverter defibrillator (WCD) is established as a tool to protect patients with a temporary risk for sudden cardiac death or a contraindication toimplant an ICD. It is widely accepted in these cases.As the WCD is not only a therapeutic tool in preventing sudden cardiac death from malignant ventricular arrhythmias it also has a potencial to be used as a diagnostic tool by storing ecg data of arrhythmias.
The aim of the present study is to evaluate the outcome of unselected patients fitted with a wearable cardioverter defibrillator during the prescription period and after returning the WCD.
The data is being collected and pooled in a multicenter retrospective approach from patients wearing the cardioverter defibrillator from 07/10 until 01/2015 from three University hospitals and one Cardiovascular Centre in Germany.
In total data of 459 patients could be collected. Indication for WCD in our data: 162 patients (35.3%) dilated cardiomyopathy with highly reduced ejection fraction <30%, 77 patients (16.8%) with ischemic cardiomyopathie and 63 patients (13.7%) with myocarditis. Other indications were: explantation of ICD, ventricular tachycardia, congenital heart disease or peripartum cardiomyopathie. From all the patients the mean left ventricular ejection fraction was 26% when WCD was prescribed. Relevant side diagnosis: 101 (22%) patients with atrial fibrillation and 67 (15%) with chronic kidney failure.
14 (3.0%) patients received lifesaving treatment from the WCD during the prescribed period. 8 patients (1.7%) were treated because of ventricular flutter, 4 (0.9%) because of asystolie alarm. In total 1 patient (0.2%) received inadequate therapie and 1 patient (0.2%) held back the therapy in the situation of a haemodynamic stable period. At the end of the WCD period 183 (40%) had ICD implantation.
In this large heterogenous cohort of patients equipped with the wearable cardioverter defibrillator life saving shocks occured in a relevant proportion of 3.0% in non ischemic as well as ischemic cardiomyopathies and in patiens with myocarditis. Real asystolies occured. 1 inadequate shock occured in atrial fibrillation in a septic and unconscious patient. The wearable cardioverter defibrillator is a safe and efficacious tool to bridge patients until ICD implantation is feasible and permanently indicated.

P5929 | BEDSIDE
Prevalence and significance of electroanatomical and ultrastructural abnormalities in patients with Brugada syndrome

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Background: Brugada syndrome (BrS) is considered a pure electrical disorder mainly affecting the epicardium, but the presence of structural abnormalities is still controversial. Unipolar electroanatomic mapping has been demonstrated an accurate tool to detect epicardial abnormalities in myocardial diseases.
Purpose: To assess the prevalence of electroanatomical and ultrastructural abnormalities in BrS, we performed 3D-electroanatomic unipolar and bipolar mapping (EAM), and EAM-guided right ventricular endomyocardial biopsy (EMB) in a series of consecutive patients (pts) with BrS.
Methods: We enrolled 23 pts (18M, 43±10 years) with a diagnosis of BrS according to current criteria. All pts had a type 1 ECG pattern spontaneously (n=19) or after flecainide challenge (n=4). All pts underwent EAM with bipolar and unipolar mapping. In 12 cases EAM-guided EMBs were also performed. Low-voltage areas (LVA) were defined as ≥3 adjacent points with amplitude <1.5 mV (bipolar) and <5.5 mV (unipolar). Scar was defined as ≥3 adjacent points with amplitude <0.5 mV at bipolar mapping. All pts were also submitted to programmed electrical stimulation (PES).
Results: Twenty pts (87%) showed LVA at unipolar mapping; of them, 10 (43%) showed LVA also at bipolar mapping. Mean low-voltage areas were 36±31 cm^2 and 12±4 cm^2 at unipolar and bipolar map respectively. Right ventricular outflow tract was the most commonly involved area (n=16) (70%). During the invasive study 12/19 (63%) pts exhibited the spontaneous type 1 pattern. Ventricular fibrillation or syncopal sustained ventricular tachycardia were induced at PES in 10/23 (43%) pts. Ventricular arrhythmias induction was associated with the presence of a spontaneous type 1 pattern during PES ($p<0.001$). The detection of scar at bipolar map was associated with the presence of spontaneous type 1 pattern ($p=0.02$). Histology showed myocardial inflammation in 10/12 pts (83%). In 8 pts, EMBs showing myocardial inflammation had been drawn from outflow tract areas with both unipolar and bipolar LVA. Two pts with myocardial inflammation and the two pts with normal biopsy had normal bipolar map but LVA at unipolar map.
Conclusions: We observed a high prevalence of unipolar map abnormalities among BrS pts, supporting the hypothesis that BrS is not a pure electrical disorder. Myocardial inflammation, as shown in pts with both unipolar and bipolar LVA, suggests a disease progression from epicardium to endocardium. Larger studies with long-term follow-up will clarify the prognostic significance of these findings and the role of myocardial inflammation in the pathogenesis of the syndrome.

P5930 | BEDSIDE
Reproducibility of repetitive T-wave alternans measurements in the EUTrigTreat study

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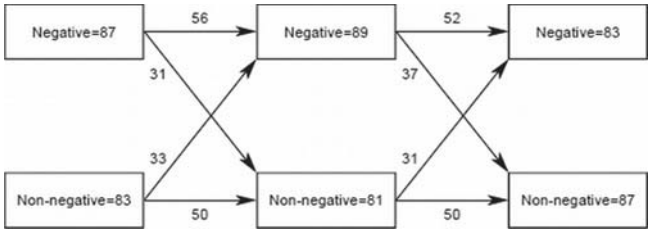
Background: Microvolt T-wave alternans (TWA) has been proposed as a useful predictor of ventricular arrhythmias to guide ICD therapy. The timing and the necessity for repeated testing remain unclear.
Purpose: To study the reproducibility of repetitive TWA and its correlation with ICD shocks.
Methods: The EUTrigTreat study is a prospective trial aiming to risk stratify ICD patients for mortality and shocks. The underlying cardiac disease is diverse including ischemic and non-ischemic cardiomyopathies and arrhythmogenic heart disease. TWA was performed using the Cambridge Heart exercise method (target heart rate of 110–120 bpm). Only patients with ≥3 consecutive TWA were included.

Results: In total, 632 patients were analyzable with a follow-up of 2.4±1.2 y. Of these, 170 had ≥3 consecutive TWA results with a follow-up of 2.9±0.8 y. TWA was reproducible in 73 patients (43%; 3x negative (neg) in 36, 3x non-negative (n-neg) in 37). In 97 patients (57%) results were variable (Figure).
3/36 (8%) 3xneg patients received shocks during follow-up vs 8/37 (22%) 3xn-neg and 12/97 (12%) with mixed results. There was no statistical difference for shock, nor for mortality between the 3 groups, probably due to the small number of events. Predominantly neg (n=90), ie ≥2 neg tests, however received significantly less shocks during follow-up than predominantly n-neg patients (n=80, ≥2 n-neg tests).
Logistic regression for worsening of the first TWA was associated with lower baseline left ventricular ejection fraction (p=0.02).



Conclusions: In this diverse population of ICD recipients TWA results were reproducible in less than half of the patients. Patients with predominantly negative TWA have a longer shock-free survival, corresponding to the baseline predictive value of a negative TWA result in the entire cohort.

REPERFUSION OF STEMI

P5931 | BEDSIDE
Cardiogenic shock in elderly patients with acute myocardial infarction. The FAST-MI programme

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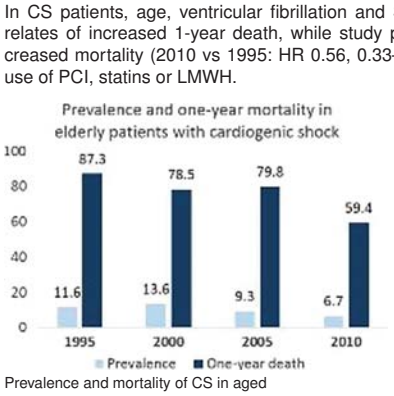
Rationale: Though cardiogenic shock (CS) after AMI is more common in the elderly, information on its prevalence, determinants and prognostic factors in the aged is scarce.
Methods: We analysed incidence and 1-year mortality of CS in 4 nationwide French surveys carried out 5 years apart from 1995 to 2010, including consecutive STEMI and NSTEMI patients over one-month periods.
Results: Among the 10,610 patients, 3,389 were aged ≥75 years, of whom 9.9% developed CS. Incidence of CS decreased from 11.6% in 1995 to 6.7% in 2010, P=0.02. Use of PCI ≤3 days from admission increased for both patients with and without CS (11% to 48% and 5% to 55%, respectively), as did statin use (1% to 70% and 4% to 82%, respectively). Occurrence of atrial and ventricular fibrillation decreased in patients without CS (22% to 9%, and 3.6% to 1.5%, respectively, P<0.001), but not in those with CS (19% to 20%, and 10% to 8%, respectively). Conversely, AV block decreased in patients with (30% to 11%) or without CS (9% to 3%). One-year mortality was 77% in CS patients, versus 22% in patients without CS. From 1995 to 2010, mortality decreased from 87% to 59% in CS patients and from 30% to 17% in patients without CS (P<0.001).
In CS patients, age, ventricular fibrillation and STEMI, were independent correlates of increased 1-year death, while study period was associated with decreased mortality (2010 vs 1995: HR 0.56, 0.33–0.94 P=0.03), along with early use of PCI, statins or LMWH.



Prevalence and mortality of CS in aged

Conclusion: The prevalence of CS is higher in elderly patients but has decreased in the past 15 years. One-year mortality remains considerable, but decreased by 32%, a decrease potentially mediated by broader use of PCI, statins and LMWH. Occurrence of ventricular fibrillation in patients with CS is a correlate of increased one-year mortality.

P5932 | BEDSIDE
Reperfusion in elderly patients with acute ST-elevation myocardial infarction: results from the RENAU-RESURCOR STEMI network

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Background: Elderly patients with acute ST-elevation myocardial infarction (STEMI) remain undertreated.
Purpose: To evaluate the management of elderly STEMI patients treated in a formal regional network of care.
Methods: This prospective analysis, based on data from the ongoing RESURCOR coronary emergency network, involved 6169 patients presenting with an acute STEMI between 2002 and 2011 in the French Alps. Patients were divided into age groups: <65, 65–74, 75–84 and ≥85 years. Reperfusion rates, types, timing and adjunctive medications were compared. The RESURCOR network advocates primary percutaneous coronary intervention (PPCI) over fibrinolysis and bivalirudin over glycoprotein inhibitors (GPI) in the elderly.
Results: Lack of reperfusion therapy increased with age (Table). The rate of fibrinolysis was higher than that for PPCI in younger patients whereas the situation was reversed in elderly patients.In patients who had PPCI, use of bivalirudin increased and GPI decreased with age, system delays were similar,

Cares among the age groups

	<65 years n=3476	65–74 years n=1238	75–84 years n=1147	≥85 years n=308	P-value
No reperfusion, n (%)	3.8	5.6	8.0	13.6	<0.001
Fibrinolysis, n (%)	1853 (53.3)	593 (47.9)	449 (39.2)	87 (28.3)	<0.001
Primary PCI, n (%)	1492 (42.9)	576 (46.5)	606 (52.8)	179 (58.1)	<0.001
Delay (first medical contact to PPCI), median (IQR), min	80 (58–123)	85 (60–125)	85 (64–130)	84 (60–124)	0.1
Bivalirudin*, n/N (%)	81/1197 (6.8)	30/429 (7.0)	48/373 (12.9)	28/121 (23.1)	<0.001
GPI*, n/N (%)	1375/2695 (51.0)	493/963 (51.2)	435/879 (49.5)	85/222 (38.3)	0.003

*Calculated among patients undergoing a coronarography. Bivalirudin has been used since 2008.

Conclusion: These regional French data indicate that elderly STEMI patients receive appropriate management with timely delivered PPCI and bivalirudin; however, a substantial proportion are still undertreated.

P5933 | BEDSIDE
Management of young STEMI patient with mono truncular coronary artery occlusion based on minimum intravascular material implantation and guided by optical coherence tomography

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Background: Bioresorbable vascular scaffold (BVS) is a new therapeutic option for patients requiring PCI in simple, focal lesions. Potential advantages of BVS include restoration of endothelial function and decrease in adverse events after foreign material disappearance from the vessel wall.
Purpose: The aim of this study was to evaluate a new strategy for STEMI management involving BVS treatment of culprit lesion under optical coherence tomography (OCT) guidance.
Methods: This is a pilot, non-randomized clinical trial screened for inclusion patients with ongoing STEMI<12 hours, single vessel lesion at baseline angiography and successful thromboaspiration (restoration of TIMI 3 flow + chest pain cessation + EKG normalization) under GPIIb-IIIa infusion. Patients included in the study benefited from a postponed control coronary angiography + OCT analysis performed between day 2 and 7 following the initial procedure.
The decision of stenting was based on the presence of a significant residual culprit stenosis ((reference lumen area-minimal lumen area)/reference lumen area >70%) or threatening ruptured lesion based on OCT analysis. In case PCI was needed, BVS was implanted. Patients not requiring stenting were managed medically (double anti-platelet therapy+ B blockers+ statins). Control coronary angiography + OCT was performed for all patients at 6 months. The primary end point was the occurrence of any major adverse clinical event (death, myocardial infarction and re hospitalisation) at 6 months.
Results: 37 consecutive patients (mean age=42,7; 75,6% males; smoking in 86%) have been included. STEMI were anterior in 42%, inferior in 49% and lateral in 9%. Median time between onset of symptoms and PCI was 212 min. 27 patients were treated by BVS and 10 medically treated. No event occurred between the two angiographies. No event occurred (MACE) at 6 months (mean follow up = 1 year). At 6 months, 36 patients were controlled by OCT. In BVS group, no malapposition is described and all struts are reendothelialized (no polymer resorption). Initial Minimal Lumen Area (MLA) is 3,36±0,56mm versus 3,29±0,78 at 6 months. In medical group, MLA is also statistically similar at 6 months (3,23±0,68 vs 3,27±0,57mm).
Conclusion: In a selected population of young STEMI patients with monotrun-

cular coronary artery occlusion, a management guided by OCT and based on minimal intra arterial device implantation (implantation of BVS which is resorbed in approximately 24 months or continuation of medical treatment alone) could be used safely to avoid metal stenting late complications.

P5934 | BEDSIDE
Prognostic significance of the culprit vessel in patients with ST-segment elevation myocardial infarction treated with primary coronary intervention

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Background: Patients (pts) with ST elevation myocardial infarction (STEMI) could benefit from primary percutaneous coronary intervention (pPCI). We have very few data on prognostic significance of culprit vessel (CV) treated with pPCI.
Aim: Our aim was to study the prognostic significance of CV in pts with STEMI treated only one CV with pPCI
Methods: A total of 10763 STEMI pts undergoing pPCI were found in the National Myocardial Infarction Registry in whom only one CV was treated with successful intervention. The pts were allocated to four groups, according to localization of the CV. All pts were followed for one year and the vital status were collected from the national data.
Results: Pts characteristics according to CV were summarized in Table 1. The LM group was significantly older, the prevalence of PAD and previous myocardial infarction were significantly higher than in the LAD and RCA group. During hospitalization, cardiogenic shock was more often (26.7%) in the LM group compared to LAD, LCx RCA groups (6.7%, 5.7%, 5.5% respectively). Thirty days mortality was highest in LM group (25%) compared to LAD, LCx, RCA groups (9.2%, 6.3%, 6.4% respectively). One-year mortality was also highest in LM group (32%) compared to LAD, LCx and RCA groups (15.5%,12.3%, 11.1% respectively). Both date the mortality was significantly higher in LM and LAD groups compared to all others (p=0.013).

Pts groups according to culprit vessel

	LM	LAD	LCx	RCA	Difference (p)
Number of pts	107	4765	1481	4404	
Age year±SD	66.3±12.8*	63.1±13.4	62.7±12	63.3±12.1	*LM vs. all others (p<0.05)
Male (%)	72	62.1	66.4**	61.6	**LCx vs. (LAD, RCA p=0.002)
Hypertension %	73.7	71	73.1	72.7	NS
Diabetes %	30.5	25.5	25.6	26.2	NS
PAD %	19.8***	8.6	10.1	10.7	***LM vs. all others (p=0.006)
Previous MI%	24.7****	14.2	18.5	14.8	****LM vs. LAD, RCA p=0001
Previous stroke %	10.4	7.7	8.1	8.8	NS

LM, left main; LAD, left anterior descendens artery; LCx,left circumflexus artery; RCA, right coronary artery; PAD, periferal artery disease, MI, myocardial infarction, SD,standard deviation.

Conclusion: CV has prognostic significance in patients with STEMI in spite of successful pPCI. Pts have the worst prognosis if the CV the LM or LAD artery in spite of pPCI.

P5935 | BEDSIDE
Benefit of thrombaspiration for patients admitted with ST-elevation myocardial infarctions on post-interventional coronary flow, extension of myocardial infarction and mortality

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Introduction: Previous studies on the benefit of thrombaspiration during percutaneous coronary intervention (PCI) in patients with myocardial infarction have had contradictory results. Aim of the present study was to analyse whether an increased use of thrombaspiration (TA)-systems has led to better post-PCI-results and/or lower mortality rates in patients with ST-elevation-myocardial-infarctions (STEMI).
Methods: All patients with STEMI and primary percutanous intervention (PCI) admitted between 2006 and 2013 were included in this study. Our heart-center, situated in northwest Germany is exclusively responsible for emergency PCI for a metropolitan region of approximately 1 million inhabitants.
Results: A total of 4880 pts. with STEMI and primary PCI entered analysis. While thrombaspiration from 2006–2008 was done only in 1.7% of cases (31 of 1850 pts.) its rate increased between 2009–2013 to 19% (577 of 3030 pts.). TA-systems were more likely to be used in pts.<65 yrs, males and those with initial TIMI-0-flow or 1-vessel-disease (table). A multivariate model showed that TA-usage did not lead to better post-PCI-results or lower 30-day or 1-year mortality-rates (table). However the usage of TA-systems was independently associated with more extensive myocardial infarctions (peak creatine kinase (CK)>3000 U/l). A multivariate comparison with the control-population (2006–2008) to rule out bias by patient selection confirmed the findings.
Conclusions: These registry data indicates that thrombaspiration in STEMI-patients was more likely to be carried out in men, young patients and those presenting with single vesssel-disease and initial TIMI-0-flow. However the usage of TA-systems did not lead to better post-PCI-results, nor to lower short or long-term mortality rates. Peak-CK-values were higher for patients undergoing TA indicating a higher deployment-rate in pts. with proximal coronary thrombotic occlusions or a more extensive myocardial "washout".

P5936 | BEDSIDE
Circadian variation of intracoronary thrombus aspiration efficacy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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Introduction: The clinical benefit of intracoronary thrombus aspiration (TA) during primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) remains controversial. Different studies have suggested a circadian variation of myocardial infarction size (IS) among patients with STEMI depending on the time of the day at symptom onset.
Purpose: We aimed to investigate whether the clinical efficacy of manual TA varies according to circadian rhythms.
Methods: We analyzed data from a large, nationwide, prospective, multicenter registry of patients admitted with acute coronary syndrome in Switzerland (AMIS Plus). Patients undergoing primary PCI for STEMI with (TA+) or without (TA-) manual TA within 12 hours of symptom onset were included. Time of the symptom onset, peak creatine kinase (CK), a proxy measure for myocardial IS and clinical outcome were retrospectively obtained. We divided 24 hours into 4 time groups based on the time of symptom onset: group 1 (00:00–05:59), group 2 (06:00–11:59), group 3 (12:00–17:59) and group 4 (18:00–23:59). The primary endpoint was in-hospital all-cause mortality.
Results: Between 2008 and 2014, a total of 3,648 patients (TA+, n=1,800; TA-, n=1,848) were included. In-hospital death of any cause occurred in 3.8% of the patients in the TA+ group, as compared with 3.7% in the TA- group (p=0.44). In-hospital mortality was not statistically different between the 4 time groups in TA+ and TA- patients (2.1%, 4.6%, 2.9% and 5.1% respectively in TA+ group, p=0.082 and 3.1%, 3.0%, 5.6% and 2.9% respectively in TA-group, p=0.098). We observed a circadian variation of myocardial IS in patients undergoing TA with larger myocardial IS occurring during the night period (group 1: 2,833±2,304 U/l; group 2: 2,449±2,336 U/l; group 3: 2,542±2,114 U/l; group 4: 2,995±2,424 U/l, p=0.001). Of note, there was a statistically significant net benefit of manual TA in terms of myocardial salvage in patients with symptom onset between 06:00 and 18:00 (groups 1 vs. 2: p<0.001; groups 1 vs. 3: p<0.05; groups 4 vs. 2: p<0.001; groups 4 vs. 3: p<0.05).
Conclusion: In a real-world registry of patients with STEMI, intracoronary TA during primary PCI was not associated with improved in-hospital all-cause mortality, independently of the time of symptom onset. However, our results suggest a circadian variation of the efficacy of manual TA with a significant reduction of myocardial IS in patients with symptom onset between 06:00 and 18:00.

P5937 | BEDSIDE
Association of changes in patients' characteristics and management with decreasing mortality rates of men and women with STEMI in Poland from 2005 to 2011

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Background: Mortality rates in STEMI have been decreasing in recent decades. It is related to numerous advances in management as well as to temporal changes in patients' risk profiles. Women with STEMI have generally higher death rates than men and there are concerns about sex-disparities in treatment.
Purpose: To estimate how much of the decrease in in-hospital and 1-year mortality in STEMI patients in Poland from 2005 to 2011 can be attributed to improved

Abstract P5935 – Table 1. Predictors of TA and impact on outcome

2009–2013	Predictors for usage of TA-systems (multivariate model)				TA-impact on outcome (multivariate model)			
	Age <65 yrs (%)	Male gender (%)	Initial TIMI-0-flow (%)	1-vessel-disease (%)	Post-PCI: TIMI ≥2 (%)	CK >3000 U/l (%)	30-day mort. (%)	1 year mort. (%)
TA (n=577)	57	75	91	45	95	32	10	12
No TA (n=2453)	50	70	77	38	95	18	9	12
OR (95% CI)	1.3 (1.1–1.5)	1.5 (1.0–2.6)	2.5 (1.5–4.1)	1.6 (1.1–2.3)	1.0 (0.6–1.7)	1.7 (1.3–2.2)	1.4 (0.8–2.8)	1.2 (0.8–1.9)
p	0.05	0.05	<0.01	<0.01	0.8	<0.01	0.2	0.2

treatment strategies and how much it is related to changes in baseline clinical characteristics, and compare these findings for men and women.
Methods: We analysed 32790 patients with STEMI form Polish nationwide registry of acute coronary syndromes PL-ACS. All available baseline characteristics were incorporated into a regression model to estimate a propensity score (PS) of each individual. Patients from 2005 and 2011 were nearest neighbour matched on their PS (a total of 22059 patients in two separately matched groups of men and women). Observed in-hospital and 1-year death rates were compared with results in groups matched on PS.
Results: For in-hospital mortality relative risk reduction (RRR) was 37% for women and 35% for men; for 1-year it was 23% for women and 15% for men. After matching on propensity score RRR for in-hospital mortality was 21% in women and 27% in men; for 1-year it was 11% and 10% respectively. Around 57% of observed mortality reduction in women and 77% in men was related to improved in-hospital management while the remaining part to changes in patients' clinical profiles. For 1-year death rates 43% of total reduction in women and 69% in men was associated with improved management strategies.

Table 1

Mortality rates (%)	Men observed		Men after PSM		Women observed		Women after PSM	
	2005	2011	2005	2011	2005	2011	2005	2011
In-hospital	12.3	7.7	10.8	8.5	7.1	4.6	6.3	4.6
1-year	23.1	17.7	20.9	18.8	15.1	12.7	13.8	12.2

PSM, Propensity Score Matching.

Conclusions: Over the study period higher RRRs were observed for in-hospital than 1-year death rates and in women compared to men. Men benefit more from improved in-hospital treatment strategies but in 1-year observation changes in management had similar overall benefit to both sexes. Higher mortality rate reductions observed in women can be explained by relatively more positive changes in their baseline characteristics.

NEW TECHNIQUES AND NEW APPLICATIONS IN ECHOCARDIOGRAPHY

P5938 | BEDSIDE
A new 2D semi-quantitative echocardiographic tool to detect myocardial scar

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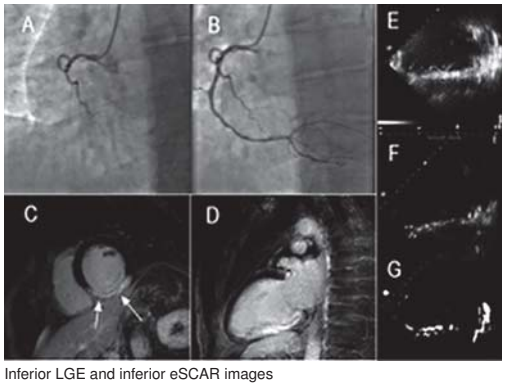
Background: The presence of myocardial scar is a critical feature impacting patient's management and prognosis. Nowadays CMR-LGE is the gold standard for the detection of myocardial scar. However we lack a bedside, easy tool to be used in our daily practice.
Purpose: To test an echocardiographic technique exploiting pulse modulation/inversion mode to detect myocardial scars in patients with recent STEMI and to compare it with CMR-LGE images.
Methods: We enrolled a) twelve patients who presented with STEMI and were treated with timely primary angioplasty and b) twelve patients who underwent CMR for a clinical indication and who demonstrated no CMR-LGE. In the STEMI-group transthoracic echocardiography was performed between 28 and 32 days after the STEMI using both standard 2D and a commercially-available pulse cancellation ultrasound technique (eSCAR). Visual analysis of eSCAR images was used to assess the presence of scar. eSCAR was defined as any myocardial area demonstrating a continuous series of non-black pixels, not including the pericardium, valve leaflets, or other fibrous/calcific structure. CMR-LGE was performed within 72 hours of the echocardiogram. In the negative CMR-LGE group echocardiography was performed within 72 hours after their CMR study.
Results: Ten STEMI patients completed the protocol for both echo and CMR-LGE. Nine demonstrated detectable scar at CMR-LGE, while all of the 10 patients demonstrated eSCAR at echocardiography. In the 9 STEMI patients in whom CMR-LGE was detectable, regional matching between eSCAR and CMR-LGE was total, but the segmental extension of the scar was not always perfectly superimposable.
Conclusion: eSCAR is a promising new tool for the detection of myocardial scar which reliably matches the presence of CMR-LGE when assessed at 30 days after STEMI.



Inferior LGE and inferior eSCAR images

P5939 | BEDSIDE
Blood-flow propagation in LA by Doppler echocardiography depend on elevation of LA pressure

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Background: Transmitral flow (TMF) and pulmonary vein flow (PVF) profiles are closely related to left ventricular (LV) diastolic property, left atrial (LA) pressure, and other cardiac dynamics. The onset of early diastolic TMF (E) leads to the onset of diastolic PVF (D) in the almost same period of the cardiac cycle. However, it is unknown whether the time difference between the peak E and the peak D (E-D delay) is related with LV diastolic function and LA pressure.
Methods: A total of 147 normal subjects (N group, 59±18y.o, m=78) and 20 patients with heart failure (HF group, 62±14y.o, m=13) were studied. TMF and PVF, early diastolic mitral annular velocity (e') was recorded by Doppler echocardiography. We measured the time intervals from R wave on electrocardiography to TMF peak E (tRE) and PVF peak D (tRD), and then the E-D delay (=tRD-tRE) adjusted by R-R interval (E-D delay/RR) was calculated (Figure 1). We compared E-D delay/RR between N-group and HF group and investigated the relationship between E-D delay/RR and Doppler indexes.
Results: In HF group, E-D delay/RR was significantly shorter than N group (Figure2) and correlated with E/A ratio, peak D, E/e' and pulmonary artery systolic pressure ($r=-0.53$ $p<0.05$, $r=-0.47$ $p<0.05$, $r=-0.61$ $p<0.01$, $r=-0.59$ $p<0.01$).

Figure 1

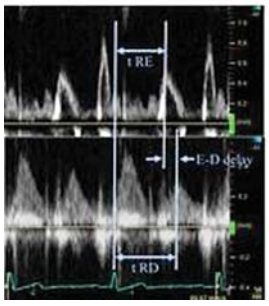
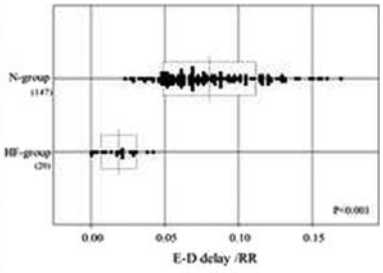


Figure 2



Conclusion: We proposed a novel index "E-D delay" combined the E wave and D wave derived by Doppler echocardiography. Our results indicate that this novel index may play a new role to provide additional information in predict the elevation of LV preload, that is shown as LV filling pressure, LA pressure and pulmonary artery systolic pressure.

P5940 | BEDSIDE
Echocardiographic predictors of postoperative atrial fibrillation after high-risk abdominal surgery

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Background and purpose: Postoperative atrial fibrillation (POAF) is a frequent complication post high-risk surgery in elderly patients. We examined the use of preoperative echocardiography to predict POAF in these patients.
Methods: We performed a prospective study and enrolled 300 consecutive patients, age ≥65 years (mean age 72±6 years, 61% men) who underwent elective duodeno-pancretic surgery, liver resection or bile duct surgery under general anesthesia between April 2013 and September 2014. Preoperative echocardiography was performed in all patients, including tissue Doppler imaging (TDI). We measured left atrial (LA) volumes (maximal, minimal and pre-systolic) and indexed to body surface area and the time interval between the onset of the P-wave on ECG and a point of the peak-A wave on TDI from the lateral mitral annulus (PA lateral), septal mitral annulus (PA septal), and right ventricular tricuspid annulus (PA tricuspid). Left atrial dyssynchrony was measured by subtracting the PA septal from PA lateral. Interatrial dyssynchrony was measured by subtracting PA tricuspid from PA lateral. Right ventricular systolic pressure was assessed by the tricuspid regurgitation jet (TRJ) Doppler velocity method.
Results: Thirty-seven (12.3%) patients developed POAF. They had a higher prevalence of hypertension (95% vs. 11.4%; p=0.04) and type 2 diabetes (41% vs. 19%; p=0.05). Patients with POAF had higher LA maximum volume >40 mL/m^2 ($p<0.0001$), LA minimal volume >25 mL/m^2 (p=0.002), LA pre-systolic volume >33 mL/m^2 ($p<0.0001$), left ventricular mass index >165 g/m^2 (p=0.04) as well

as prolonged PA lateral, PA septal duration, left atrial and interatrial dyssynchrony time. Preoperative echocardiography in patients who devleoped POAF demonstrated significant elevation of TRJ Doppler velocity (p=0.001). Based on our results, we defined the following cutoff points predictive of POAF: PA lateral >139 ms (69% sensitivity, 92% specificity), left atrial dyssynchrony >35 ms (78% sensitivity, 89% specificity), and TRJ Doppler velocity >2.6 m/s (89% sensitivity, 64% specificity).
Conclusion: Our results demontrate that PA lateral, LA dyssynchrony and TRJ Doppler velocity are independently associated with the incidence of POAF after high-risk abdominal surgery. These findings demonstrate that some of the typical structural and functional changes in the atria in chronic AF in the elderly are also common in surgical patients who develop POAF, suggesting that POAF and chronic AF may have similar pathophysiology.

P5941 | BENCH
Effect of afterload increase on left ventricle mechanical dispersion and electromechanical window

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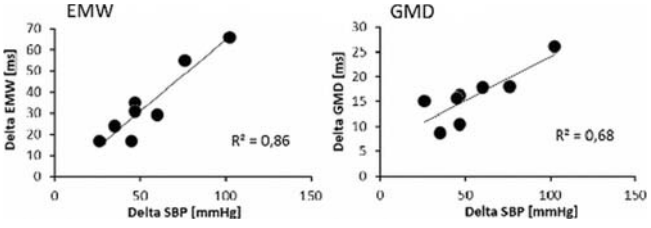
Purpose: Mechanical dispersion and electromechanical window have shown potential as risk predictors for arrhythmias. Given the close relationship between diurnal variation in arrhythmic events and blood pressure rise, we sought to investigate the relation between acute increases in blood pressure and these parameters in a controlled animal model.
Methods: Afterload increase was induced by balloon inflation in the descending aorta in eight anaesthetised pigs. Two dimensional (2D) echocardiographic LV apical (2–3-4 Chamber) views and pulsed wave (PW) Doppler recording of the LV outflow were obtained trans-diaphragmatically using a Vivid 9 system (GE Healthcare). Global mechanical dispersion (GMD) was defined as the standard deviation of time to peak longitudinal shortening obtained by Speckle tracking in all 18 LV segments. EMW is the interval between the end of the T wave (ECG) and aortic valve closure (PW Doppler, LV outflow).
Results: Balloon inflations raised BP by an average of 53.9±24% (P<0.01) and heart rate decreased significantly (P<0.01), while QT remained unchanged. LV end-systolic and end-diastolic volumes enlarged significantly during inflation (p<0.001) and LV ejection fraction decreased (p<0.001). GMD increased during inflation (35.5±9.9 ms vs. 51.5±11.6 ms, p<0.001). Similarly, EMW prolonged during afterload increase (30.6±26.6 ms vs. 64.9±14.1 ms, p<0.001), because of a delayed aortic valve closure. Both parameters showed a strong positive correlation with BP (GMD: r2=0.69 and EMW: r2 =0.87) (Figure 1).



Conclusions: Blood pressure surges consistently increase GMD and EMW. These data would suggest that measuring these risk predictors during an acute raise in blood pressure (e.g. by a handgrip test), could unmask possible afterload-induced arrhythmic risk.

P5942 | BEDSIDE
Validation of 2D strain parameters in the diagnosis of acute rejection after heart trasplantation

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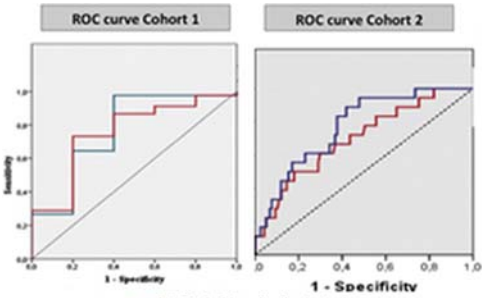
Acute allograft rejection (AAR) is still a relevant complication after orthotopic heart transplantation (HT). Its diagnosis is based on endomyocardial biopsy (EMB), but recent advances in 2D-strain imaging may allow an early non-invasive detection of AAR.
Objective: To analyze the usefulness of conventional and 2D strain parameters to detect AAR after HT and verify them on an internal validation cohort.
Methods: We prospectively included 34 consecutive adult recipients (sample 1) admitted at our center for HT and 21 patients (sample 2) for internal validation. A total of 235 and 148 pairs of EMB and echocardiograms were performed in sample 1 and 2 respectively. We analyzed classic echocardiographic parameters, speckle-tracking derived left ventricular global longitudinal strain (LVGLS) and global and free wall right ventricular longitudinal strain (Free wall RVLS).
Results: In sample 1, AAR was detected in 26.4% of EMBs (n=62), 5.1% (n=12) required specific treatment (AAR≥2R). In sample 2, AAR was detected in 44.6% of EMBs (n=66), 12.8% (n=19) of them ≥2R. In sample 1, Free wall RVLS <17% was associated with a Sp 91.1%, PNV 98.8% and accuracy of 90.7% while LVGLS <15.5% presented a Sp 81.4%, PNV 98.8% and accuracy 81.7% for the diagnosis of AAR≥2R. We applied these cut-off points for internal validation in sample 2 obtaining that free wall RVLS <17% was associated with a Sp 74.6%, PNV 90.7% and accuracy 71.3% while LVGLS <15.5% presented a Sp 82.4%, PNV 92.8% and Accuracy of 79.2%.



	Cohort 1		Cohort 2	
	AUC	p	AUC	p
LV global longitudinal strain	0.769 (0.47-1)	0.05	0.77 (0.67-0.87)	0.0001
Free wall RV longitudinal strain	0.756 (0.52-0.98)	0.06	0.70 (0.57-0.83)	0.0006

Conclusions: We propose the combination of two new echocardiographic measures (global LV and free wall RV Longitudinal strain) to detect AAR after HT. In our internal validation (sample 2) we obtained an excellent PNV, so 2D strain routine measures could be a reliable tool to rule out AAR and potentially reduce EMBs.

P5943 | BEDSIDE
Right atrial volume - a surrogate marker for estimating right atrial pressure

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Introduction: Current guidelines recommend that pulmonary artery systolic pressure (PASP) should be estimated by echocardiography using tricuspid regurgitation (TR) velocity with the addition of right atrial (RA) pressure, assuming no significant right ventricular outflow tract (RVOT) obstruction. The RA pressure is derived from dimensions of inferior vena cava (IVC) and its collapsibility.
Purpose: Our hypothesis is that measurements of maximum right atrial volume (RAV) can be correlated with right atrial pressure (RAP) better than measurements of IVC.
Methods: Fourteen consecutive patients with idiopathic pulmonary arterial hypertension were referred to our clinic. We performed echocardiography and measured right atrial volume (aria-length method and disk summation technique in apical four chamber view) and IVC dimensions and its respiratory variations, according to current guidelines recommendations. All had previously undergone right heart catheterization with measurement of right atrial pressure. Patients with other possible causes of RA enlargement were excluded from the study.
Results: Mean RAV was 109.64 mL (Range: 36–250 mL), mean RAP was 12.42 mmHg. Bivariate correlation analysis revealed an intense positive association between RAV and RAP which is stronger than the association between IVC dimension and RAP. Regression analysis confirmed RAV as a predictor of RAP (R2= 0.85, p=0.0001) (Figure 1). The equation for estimating RA pressure by RA volume is RAP = 0.141 x RAV - 3.045.

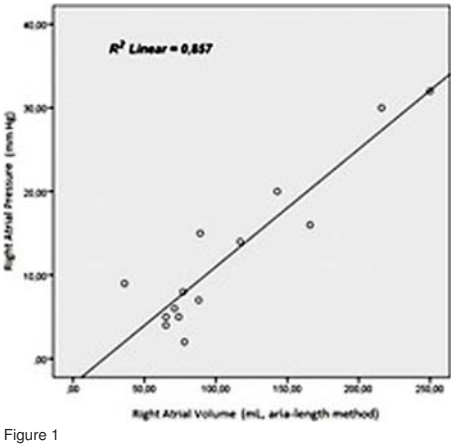

Figure 1

Conclusion: Our pilot study shows a superior correlation between RAV and RAP measured by right heart catheterization compared with IVC size and respiratory variation. We are currently conducting a study on a larger cohort of patients in order to validate these results.

P5944 | BEDSIDE

Detection of clinically stable myocardial ischaemic segments confirmed by invasive fractional flow reserve using resting 2D speckle tracking echocardiographic multi-layer strain: 13 months follow up

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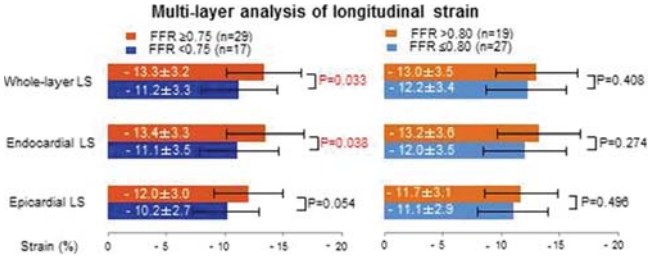
Background: Endocardial layer of left ventricular (LV) wall is more vulnerable to ischemia than epicardial layer. Multi-layer speckle tracking transthoracic echocardiography (TTE) yields quantitative strain measurements of LV endocardial and epicardial layers contributing to early detection of ischemic myocardium without drug or exercise loading.
Purpose: To detect LV myocardial stable ischemic segments using non-invasive multi-layer TTE and confirm actual prognosis.
Methods: This was a retrospective analysis of 39 stable patients (32 males; 65.8±11.9 yr) with 46 coronary arteries with ≥50% stenosis confirmed by invasive coronary angiography undergoing invasive fractional flow reserve (FFR) measurement and TTE (Vivid E9) within 36 days without clinical incident. On TTE, regional longitudinal strain (LS) in whole, endocardial, and epicardial layer supplied by stenotic coronary vessels was calculated. Patients were followed for a median of 13 months. Adverse events included death, myocardial infarction (MI) and urgent revascularization.
Results: Of 46 vessels, FFR was <0.75, ≥0.75, ≤0.80 and >0.80 in 17, 29, 27 and 19 vessels, respectively. Whole- layer and endocardial LS were significantly greater in LV segments with FFR<0.75 than when FFR≥0.75 (both P<0.05). No significant differences of epicardial LS between LV segments with FFR<0.75 and ≥0.75 and of all LS between LV segments with FFR≤0.80 or FFR>0.80 were observed. Endocardial LS showed a slightly negative correlation with FFR (R=–0.299, P=0.044). Adverse events occurred in one patient (MI) whose FFR was 0.56.



Conclusion: In stable subjects with coronary arteries with ≥50% stenosis, regional whole-layer and endocardial, but not epicardial LS distinguished LV segments with FFR<0.75 from those with ≥0.75 using 2D TTE.

ION CHANNEL AND CARDIOMYOPATHY: THE NEGLECTED LINK

P5945 | BENCH

A missense mutation in the transcription factor TBX20 gene causes long QT syndrome

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Introduction: We describe a heterozygous missense mutation in the gene encoding the T-box transcription factor TBX20 found in a proband diagnosed with long QT syndrome. The proband is a 45 aged male who has been asymptomatic so far. Clinical evaluation of the family led to the identification of two sisters who died suddenly and two other diagnosed with long QT syndrome who wear implantable defibrillators. His mother was successfully resuscitated from sudden death and recently died from leukaemia. Next Generation Sequencing of samples from the proband and affected relatives revealed a missense mutation located in the transactivation domain of TBX20 (p.R311C), that was confirmed by Sanger. Screening for mutations in all described long QT syndrome genes was negative.
Purpose: This work aimed to determine the functional consequences of this mutation and the mechanism by which it can lead to QT interval prolongation.
Methods: WT and mutated TBX20 tagged with GFP were expressed in HL-1 cells and endogenous currents were recorded at room temperature using the whole-cell patch-clamp.
Results: Expression of WT or p.R311C TBX20 in HL-1 cells did not significantly modified peak or late sodium current (INa) compared to that recorded in control conditions (–45.9±17.0 pA/pF and –2.1±0.5 pA/pF, respectively). Identical results were obtained when L-type calcium (ICa,L) and inward rectifier (IK1) currents were analyzed. Next, we determined putative effects of the mutation on the IKr measured as the dofetilide-sensitive current. Expression of WT TBX20 significantly increased IKr tail current density (from 2.5±0.3 to 3.6±0.3 pA/pF at +60 mV, P<0.05). Interestingly, p.R311C TBX20 markedly reduced tail current density to 2.0±0.2 pA/pF (P<0.05). However, neither WT nor p.R311C TBX20 modified the density of the dofetilide-insensitive current (IKs). A mathematical model of human ventricular action potential demonstrated that p.R311C TBX20 prolonged action potential duration (APD) measured at 50 and 90% of repolarization by 26.7 and 28.3%, respectively. Analysis of the promoter sequence of the ion channels responsible for IKr (KCNH2) revealed a conserved TBX20 binding motif near the transcription start site. Luciferase reporter assays demonstrated that WT TBX20 significantly increased KCNH2 promoter activity, whereas p.R311C TBX20 mutation completely abrogated this effect.
Conclusions: The present results demonstrate that a missense mutation in TBX20 lead to APD lengthening by means of a reduction in IKr density and allow the identification of TBX20 as a novel gene associated with long QT syndrome.

P5946 | BENCH

VEGF-B induces a unique electrophysiological phenotype in mouse heart

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Background: Cardiac effects of vascular growth factors (VEGFs) have mainly been studied in the context of angiogenic gene therapy to enhance perfusion of the heart. However, the role of VEGFs in the heart seems not to be restricted only to angiogenesis. Recently, VEGF-B has been implicated in myocardial metabolism and is involved in and modulates heart's response to pathological stress. However, the effects of VEGF-B on myocardial function are not known.
Purpose: The purpose of this study was to assess the effects of VEGF-B on the contractile and electrophysiological properties of the mouse heart.
Methods: Echocardiographic and ECG monitoring of cardiac-specific VEGF-B overexpressing mice (TG) and their litter mate controls (WT) were done with Vevo2100 small animal ultrasound. The effect of beta-adrenoceptor agonist, dobutamin, on ECG was studied by i.p. injections. Conventional whole-cell voltage- and current-clamp was used for currents and action potential recordings (Axopatch 200B). Gene expressions were measured with qPCR and Western blot.
Results: In vivo contractile function or the morphology of TG hearts did not differ from WT hearts. However, ECG measurements showed a decrease in the R and S amplitudes as well as in PQ time and an increase in the QRS time in TG mice compared to the WT mice. Isolated TG cardiomyocytes had increased duration (APD90; 55.8%, p=0.005) and rise time (47.1%, p=0.00001) of the action potentials. These were accompanied by a decrease in the density of the sodium current (20.8% at –40mV, p=0.0005) and in the transient outward K+-current (57% at 50mV, p=0.0004), while ultra-rapid (34.8%, p=0.04 at 50mV) and steady state K+-currents (149%, p=0.01, at 50 mV) were both increased. In line with this, expressions of ion-channel subunits were changed; SCN5A, a gene of voltage-gated sodium channel (type V, alpha) was downregulated by 32.2% (p=0.02), Kcnip2 gene (Kv channel-interacting protein 2) downregulated by 42% (p=0.03) and Kcna5 gene (potassium voltage-gated channel) was upregulated by 36% (p=0.03). These electrophysiological changes predisposed TG animals to catecholamine-induced arrhythmias; upon dobutamine injection 60% TG vs. 10% WT mice developed severe arrhythmias.
Conclusion: Cardiac VEGF-B overexpression results in remodelling of cardiomyocyte ion currents, resulting in changes of the action potential waveform and unique ECG changes resembling those seen in long-QT-syndromes. Altogether, cardiac overexpression of VEGF-B induces a unique electrophysiological phenotype predisposing animals to arrhythmias.

P5947 | BENCH

Heart failure is associated with distinct remodelling of atrial repolarising K2P K+ channels in patients with atrial fibrillation

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Introduction - The prevalence of atrial fibrillation (AF) increases with advanced stages of heart failure (HF). Molecular effects of ventricular dysfunction on atrial arrhythmogenesis remain to be elucidated. We hypothesized that repolarising two-pore-domain (K2P) K+ channels are differentially regulated and contribute to proarrhythmic substrate in AF patients with concomitant HF.
Purpose: The purpose of this study was to assess K2P channel remodelling in patients with AF complicated by varying HF stages.
Methods: Right atrial tissue was acquired from a cohort of 135 patients with

paroxysmal (p)AF, chronic (c)AF, and sinus rhythm (SR). Patients were further stratified according to left ventricular (LV) function. K2P channel expression was analyzed by quantitative real-time PCR and Western blot. Membrane currents were recorded from atrial cardiomyocytes using the patch clamp technique.
Results: K2P3.1 and K2P17.1 channels were differentially regulated dependent on rhythm status and LV function. CAF was associated with increased K2P3.1 expression but decreased abundance of K2P17.1 at mRNA and protein levels. By contrast, there was less K2P remodelling in pAF patients. Severely reduced LV function in SR patients was associated with decreased expression of both K2P3.1 and K2P17.1. K2P3.1 remodelling was accompanied by corresponding changes in atrial K+ current. Finally, we observed patient-specific K2P3.1 remodelling in cases with concomitant AF and HF, characterized by cAF-dependent enhancement and by HF-associated suppression of K2P3.1 levels, respectively.
Conclusion: The coexistence of AF and HF is associated with distinct remodelling of atrial repolarising K2P3.1 and K2P17.1 channels. Atrial K2P3.1 levels depend on the individual contribution of AF and LV impairment, respectively, highlighting the need for patient-tailored antiarrhythmic strategies.

P5948 | BENCH
The Na+-Ca2+ exchanger mediates beta-adrenergic increase in heart rate in a beating whole heart mouse model with NCX overexpression

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Introduction: The Na+-Ca2+ exchanger (NCX) generates an inward current (INCX) and is involved in diastolic depolarization in cardiac pacemaker cells. Until now only computational model simulations and single cell models with altered NCX function were available to suggest that NCX may contribute to sinus node activity and beta-adrenergic increase in heart rate. Furthermore, the influence of altered NCX activity on atrioventricular node (AV) is unknown.
Purpose: This is the first study, to use a whole heart mouse model with transgenic NCX-overexpression (NCX-OE) to investigate the properties of NCX on heart rate, SA node and AV node function during beta-adrenergic challenge.
Methods: Beating whole heart Langendorff-perfused hearts of transgenic mice with homozygous overexpression of NCX and wild-type (WT) littermates were studied at baseline and during perfusion with 0.2 μM isoproterenol (ISO). ECGs were recorded from the epicardial surface. Electrical pacing protocols were used to determine sinus node recovery time (SNRT), AV nodal Wenckebach cycle length (AVWCL) and retrograde AVWCL.
Results: ECG recordings showed no significant difference in heart rate between NCX-OE and WT at baseline (Cycle length (CL) in: NCX-OE, 185.9±30.5 ms, n=18; WT, 177.6±40.0 ms, n=20; p=0.21). Perfusion with 0.2 μM ISO resulted in a significantly higher heart rate in NCX-OE hearts as in WT (CL in: NCX-OE, 117.7±14.2 ms, n=18; WT, 133.4±13.4 ms, n=20; $p<0.001$). At baseline and during perfusion with ISO, SNRT was not significantly different between both genotypes. Both AVWCL and retrograde AVWCL were significantly shortened by 0.2 μM ISO compared to baseline within both genotypes (AVWCL, baseline vs. 0.2 μM ISO, NCX-OE, $p<0.001$) (AVWCL, baseline vs. 0.2 μM ISO, WT, $p<0.001$) (Retrograde AVWCL, baseline vs. 0.2 μM ISO, NCX-OE, $p<0.001$) (Retrograde AVWCL, baseline vs. 0.2 μM ISO, WT, $p<0.001$). AVWCL and retrograde AVWCL were not significantly different between NCX-OE and WT.
Conclusions: This is the first study to use a whole heart model with transgenic NCX overexpression to studying the properties of NCX on cardiac pacemaker activity and the specific cardiac conduction system under near physiological conditions. In our model, NCX seems to be required for beta-adrenergic increase in heart rate without affecting resting heart rate, SNRT or conduction properties of the AV node. Our study supports the hypothesis that the "Ca2+ clock" is involved in cardiac pacemaker function, particularly in increasing heart rate during beta-adrenergic stimulation.

P5949 | BENCH
Atrial arrhythmia susceptibilit and electrical remodelling with endurance training in a mouse model of arrhythmogenic right ventricular cardiomyopathy

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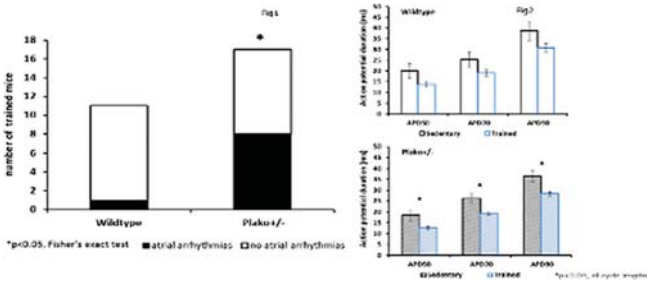
Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited disorder that can cause ventricular arrhythmias and sudden death in endurance athletes. Desmosomal protein mutations including plakoglobin (Plako) deficiency are linked with ARVC.
Purpose: We tested whether endurance training increased atrial arrhythmia susceptibility or caused electrical remodelling in Plako+/– versus WT mice.
Methods: Plako+/– and WT mice group swim-trained (ST) for 5 d/wk, gradually increased from 2 to 90 min/d, with total mean swimming times of 50h over 8 wks. Atrial size and function was assessed by echocardiography. Hearts were Langendorff-perfused and left atrial (LA) monophasic action potentials (MAPs) were recorded. Action potential durations (APDs) were measured during RA pacing at 100ms cycle length (CL). Atrial arrhythmias were provoked by programmed stimulation (S1-S2, arrhythmias >1s). Transmembrane action potentials (TAPs) were recorded from isolated, superfused LA at 100ms CL. All continuous paramaters are expressed as mean±SEM.
Results: ST increased atrial arrhythmia susceptibility in Plako+/– (Fig.1) but not WT mice (WT sedentary (Sed): 3/11 hearts vs ST: 1/11 hearts). ST induced mild left ventricular ventrophy in both genotypes (6–14%, $p<0.05$). ST increased LA size in both genotypes (LA size WT: 3.11±0.14 sedentary vs 3.79±0.17 mm^2 ST, $p<0.05$; Plako+/–: 3.23±0.1mm^2 Sed vs 4.14±0.23mm^2 ST, $p<0.05$). LA APD from MAPs (Fig.2) and RA APD90s measured from TAPs were shorter after ST (WT: 22±1 Sed vs 19±1ms ST; Plako+/– 24±1 Sed vs 18±1ms ST).



Arrhythmias and APDs

Conclusion: Our observations suggest that endurance training shortens atrial APD and increases LA size in both WT and plakoglobin deficient atria. Endurance training increases atrial arrhythmia susceptibility in mice with plakoglobin deficiency.

P5950 | BENCH
Evidence and role of the neuronal sodium channel Nav1.8 in the human failing heart

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In heart failure, persistent current through Na channel (late INa) is enhanced and causes arrhythmias and contractile dysfunction. We have demonstrated that Ca/Calmodulin Kinase IIδ (CaMKIIδ) increases late INa in heart failure via phosphorylation of the Na channel thereby producing arrhythmias. Here, we examined for the first time whether expression of neuronal Nav1.8 channel is increased in the human failing heart and whether CaMKIIδ associates with this channel in human cardiomyocytes thereby regulating its function. Na channel expression was studied by Western blot using mouse monoclonal anti-Nav1.8 antibody. The general expression levels of Nav1.8 channel were significantly increased 2-fold in ventricular myocytes from patients with hypertrophy but preserved ejection fraction (n=9) and end stage heart failure (n=8) compared to healthy control myocardium (n=10) and were not changed in atrial tissue from patients with atrial fibrillation (n=9) versus sinus rhythm (n=9). Association and co-localisation of CaMKIIδ and Nav1.8 were studied by co-immunoprecipitation and immunocytochemistry. CaMKIIδ was immunoprecipitated from human atrial and ventricle homogenate using a rabbit polyclonal Ab against CaMKIIδ and subjected to Western blot with anti-Nav1.8 Ab. There was a significant association of CaMKIIδ with Nav1.8. Co-localisation of CaMKIIδ and Nav1.8 was confirmed by combination of immunocytochemistry and confocal microscopy in human cardiomyocytes. Double-labeling showed that CaMKIIδ and Nav1.8 overlap significantly at both the intercalated disk and T-tubules. Additionally, we measured late INa using whole-cell patch clamp in human cardiomyocytes. There was a significant reduction in late INa after addition of a novel Nav1.8 specific blocker A-803467 (30 nmol/L) in both atrial and ventricular failing myocytes isolated from 9 and 5 patients respectively. In conclusion, we showed for the first time that neuronal sodium channel Nav1.8, which contributes to late INa in the mouse heart, is expressed in the human ventricle and the atria, and its expression level is increased in human failing myocardium. Additionally and importantly this is the first evidence in human that selective inhibition of Nav1.8 reduces the proarrhythmic late INa. We also demonstrate that Nav1.8 associates with CaMKIIδ. This association and increased expression of Nav1.8 might result in increased late INa under conditions of enhanced CaMKIIδ activity such as heart failure and inhibition of this current may be an interesting treatment option which merits further investigation.

P5951 | BENCH
Inducible ventricular arrhythmias and structural heart disease can be identified by determination of heart rate turbulence in mice

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Introduction: Heart rate turbulence (HRT) is a prognostic parameter for cardiac risk stratification in patients after myocardial infarction. Recent studies demonstrated the feasibility to measure HRT as a marker of baroreflex function in healthy mice.
Purpose: The aim of this investigation was to establish the procedure of HRT

measurement in a mouse model with a marked structural heart defect with regard to threshold values and arrhythmogenesis.
Methods: Adult wildtype C57/bl6 mice after transverse aortic constriction (TAC) and after myocardial cryoinfarction (MCI) were compared to the corresponding sham operated animals (control). Parameters of HRT were determined during an in vivo electrophysiological investigation 2 weeks after the operation and calculated according to the established protocols.
Results: Compared to control animals, TAC as well as MCI operated mice did not display an early acceleration in heart rate (i.e. turbulence onset [TO] value ≥0%) after extrastimulus pacing (TO heart disease: 0.29±0.57% vs. controls: –0.16±0.75%; p<0.01). At a cutoff value of >0.25% TO could be used to differentiate between heart disease and healthy animals with a sensitivity of 64.0% and specificity of 88.2% (p<0.01; positive likelyhood ratio [PLR] 5.44). The late deceleration in heart rate as indicated by turbulence slope (TS) did not differ between the groups. However, irrespective of the presence of structural heart disease, the group of animals that was inducible to ventricular tachycardias displayed significant lower values for TS as compared to the non-inducible group (6.5±1.3ms/RR-interval vs. 13.4±2.1ms/RR-interval; p=0.02). TS with a threshold value of <7.79ms/RR-interval could identify inducible arrhythmias with a sensitivity of 75.0% and specificity of 75.8% (p=0.02; PLR 3.09; OR 6.38, 95% CI 1.05 to 38.87).
Conclusion: Measurement of HRT as a marker of baroreflex function in mouse models with structural heart diseases is feasible. Pathological values for TO indicate the presence of structural heart diseases. As in humans, TS appears to be a strong predictor for ventricular arrhythmias.

DIFFERENTIATING PULMONARY ARTERIAL HYPERTENSION FROM OTHER PULMONARY HYPERTENSION GROUPS

P5952 | BENCH
Combined pre-and postcapillary pulmonary hypertension in chronic heart failure: epidemiology, right ventricular function and survival

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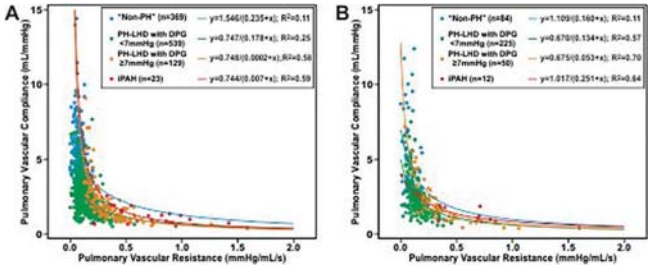
Background: Patients with pulmonary hypertension due to left heart disease (PH-LHD) and a diastolic pulmonary vascular pressure gradient (DPG) ≥7mmHg representing PH out-of-proportion to pulmonary arterial wedge pressure, have pulmonary vascular disease and increased mortality. Little information exists on this condition.
Objectives: We investigated epidemiology, risk factors, right ventricular (RV) function and outcomes in patients with chronic heart failure (HF) and "out-of-proportion" PH.
Methods: The study population was identified from retrospective chart review of a clinical database of 3107 stable patients undergoing first diagnostic right heart catheterization, and from a prospective cohort of 800 consecutive patients at a national tertiary care center.
Results: In the retrospective cohort were 664 patients with systolic heart failure [SHF], and 399 patients with diastolic heart failure [DHF], 12% of which were classified as PHD-LHD with DPG ≥7mmHg, respectively. In the prospective cohort were 172 patients with SHF [14% PH-LHD with DPG ≥7mmHg] and 219 patients with DHF [12% PH-LHD with DPG ≥7mmHg]). COPD and tricuspid annular plane systolic excursion (TAPSE)/systolic pulmonary artery pressure (sPAP) (p=0.015) predicted PH-LHD with DPG ≥7mmHg in SHF. Younger age (p=0.004), valvular heart disease (VHD, p=0.046) and TAPSE/sPAP predicted PH-LHD with DPG ≥7mmHg in DHF (p=0.016). RV-pulmonary vascular (RV-PV) coupling was worse in PH-LHD with DPG ≥7mmHg (SHF: Ees/Ea 1.05±0.25; p=0.002; DHF: Ees/Ea 1.17±0.27; p=0.027) than in those with DPG <7mmHg (SHF: Ees/Ea 1.52±0.51; DHF: Ees/Ea 1.45±0.29).



Conclusions: PH-LHD with DPG ≥7mmHg is rare in HF. RV-PV coupling is poor in PH-LHD with DPG ≥7mmHg, explaining dismal outcomes.

P5953 | BEDSIDE
Venous remodelling in COPD pulmonary hypertension and idiopathic pulmonary arterial hypertension

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Background: Pulmonary arterial remodelling is known to correlate to the severity of precapillary pulmonary hypertension (pPH) in end-stage COPD and idiopathic pulmonary arterial hypertension (IPAH). Scarce information is available regarding venous remodelling in PH.
Purpose: To investigate the extent of venous remodelling in COPD-PH and IPAH.
Methods: 409 end-stage COPD patients with right heart catheterization (RHC) data were evaluated for lung transplantation during 1991–2010 (follow up until 2015) at our university hospital. Of these 301 (74%) underwent transplantation. Four hemodynamic groups were included in an analysis of venous involvement in explanted lungs: 1) non-PH (n=30, mPAP <25 mmHg), 2) mild-moderate pPH (n=30, mPAP 25–34 mmHg, PAWP ≤15 mmHg), 3) severe pPH (n=10, mPAP ≥35 mmHg, PAWP ≤15 mmHg), 4) postcapillary PH (pcPH) (n=33 mPAP ≥25 mmHg, PAWP >15 mmHg), compared to IPAH (n=16, mPAP >50 mmHg). Two–three sections from each lobe were stained with hematoxylin and eosin and for elastin and examined by the same cardiovascular pathologist who was blinded to the hemodynamics.
Results: COPD-nonPH patients had pathological venous remodelling (range 0–1; 40% grade 0, 60% grade 1). COPD-PH had increased venous involvement dependent on hemodynamic group: Mild-moderate pPH (range 0–2; 23% grade 0, 64% grade 1, 13% grade 2); Severe pPH (range 0–2; 20% grade 0, 70% grade 1, 10% grade 2); COPD-pcPH (range 0–2; 30% grade 0, 67% grade 1, 3% grade 2), while IPAH patients had the lowest porportion of unaffected veins and highest proportion of severe remodelling (range 0–2; 13% grade 0, 63% grade 1, 25% grade 2).

Grade 0	No pulmonary venous involvement (thin wall, no prominent muscle layer, indistinct elastic lamina)
Grade 1	Intimal fibrosis or excentric medial hypertrophy/arterialisation (intimal fibrotic thickening, tendency of elastic lamina duplication)
Grade 2	Intimal fibrosis and excentric medial hypertrophy/arterialisation (intimal fibrotic thickening, smooth muscle cell hyper-plasia, usually with more elaborate elastosis)

Conclusion: A novel grading scheme for venous remodelling in pulmonary hypertension is introduced. Myofibroblast proliferation appears in pulmonary veins in both COPD-pPH and COPD-pcPH. Remarkably, IPAH patients presented with advanced forms of venous remodelling, emphasizing that the disease is not restricted to arterial lesions exclusively.

P5954 | BEDSIDE
Impact of atrial contraction on diagnosis of pre- versus post-capillary pulmonary hypertension

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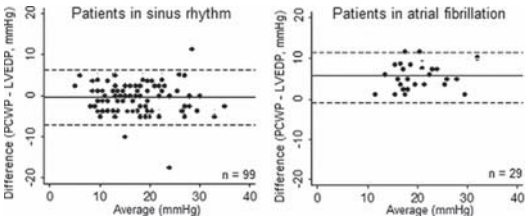
Background: Establishing post-capillary hemodynamics in pulmonary hypertension (PH) is documented by measuring an elevated pulmonary capillary wedge pressure (PCWP >15 mmHg). However, the accuracy of PCWP to reflect left ventricular (LV) diastolic pressures in the PH population is under debate. The aim of the study is to investigate the agreement between PCWP and LV diastolic pressures in PH patients with and without atrial fibrillation.
Methods: Pressure traces of 128 PH patients were reviewed. Mean PCWP was taken at end-expiration. LV diastolic pressure before atrial contraction (pre-A LVDP) was measured at the onset of the LV A-wave and LV end-diastolic pressure (LVEDP) was measured at the nadir of A-wave or at the peak of R-wave on ECG.
Results: In the 99 patients in sinus rhythm (62±15 yrs, 53% male), pre-A LVDP, LVEDP and PCWP were 12±5 mmHg, 17±7 mmHg and 17±6 mmHg, respectively. The sensitivity, specificity, positive and negative predictive values of PCWP to reflect abnormal LVEDP were each 90%. The agreement between PCWP and LVEDP was best in patients with normal LVEDP (mean difference 0.4±2.7 mmHg), while PCWP underestimated LVEDP by 2.6±4.7 mmHg in a subgroup of patients with elevated LVEDP combined with large a LV A-wave (>5 mmHg). In the 29 patients with atrial fibrillation (72±8 yrs, 52% male), PCWP consistently overestimated LVEDP due to the lack of LV A-wave with a mean difference of 4.8±3.1 mmHg. The sensitivity, specificity, positive and negative predictive values of PCWP to reflect abnormal LVEDP were 100%, 8%, 61% and 100%, respectively.



Bland-Altman analysis of PCWP and LVEDP

Conclusion: PCWP reliably reflects pre- and post-capillary PH during sinus rhythm. The poor agreement between PCWP and LVEDP in PH patients with atrial fibrillation may lead to issues with patient classification.

P5955 | BEDSIDE
Differences in the relation between right ventricular function and exercise performance between pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension

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Background: Right Ventricular (RV) function is an important prognostic marker in Pulmonary Hypertension (PH) that can be quantitatively assessed by 2D echocardiography speckle-tracking. It is not known if RV function has the same relation with exercise performance in all pre-capillary PH groups.
Objectives: To assess whether global RV longitudinal strain (RVLS) predicts exercise performance measured by Cardio-Pulmonary Exercise Testing (CPET) in pulmonary arterial hypertension (PAH) and chronic thromboembolic PH (CTEPH). We also related CPET and RVLS to prognostic markers recommended by the American Society of Echocardiography (ASE): Fractional Area Change (FAC), RV myocardial performance index (RVMPI), indexed Right Atrial (RA) area, Systolic and Diastolic left ventricular eccentricity index (EIs, EId) and Tricuspid Annular Plane Systolic Excursion (TAPSE).
Methods: We prospectively recruited 46 consecutive patients with PAH and 42 patients with CTEPH who were referred for CPET and transthoracic echocardiography (TTE) within a month of each other. RVLS was analyzed from an apical four chamber view. CPET parameters included Peak oxygen consumption (PeakVO2), percentage of predicted VO2max, maximum workload, ventilatory equivalent of carbon dioxide (VE/VCO2). Linear then multiple regression analysis was performed with RVLS and prognostic markers as predictors and the CPET parameters as dependent variables.
Results: In PAH, RVLS predicted PeakVO2 (R2=6.6%, $p<0.046$), percentage of predicted VO2max (R2=9.7%, $p<0.02$), maximum workload (R2=7.2%, $p<0.04$), VE/VCO2 (R2=31.7%, $p<0.001$). RVLS was a stronger predictor of VE/VCO2 than all the ASE recommended prognostic markers. With multivariate regression (R2=39.9%), RVLS ($p<0.001$) was an independent predictor of VE/VCO2.
In CTEPH, RVLS did not predict any CPET measurement.
Conclusions: In PAH, RVLS is closely related to function and is an independent predictor of VE/VCO2 a prognostic measure derived from exercise performance. On the other hand, RVLS does not predict any measurement of exercise performance in CTEPH. This implies that RV function and exercise performance may be less closely associated in CTEPH and that other factors such as ventilation-perfusion mismatch may play a role.

P5956 | BEDSIDE
Prognostic value of pulmonary blood volume by contrast-enhanced magnetic resonance imaging in heart failure outpatients

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Background: Assessing and grading congestion in patients with heart failure (HF) is an unmet clinical need. Early diagnosis of subclinical congestion is key to ensure prompt and effective treatment, and to prevent recurrent hospitalizations for worsening HF. Pulmonary blood volume (PBV) has been advocated as a quantitative and non-invasive magnetic resonance (MR) imaging measure of heart failure in animal research.
Purpose: The aim of this study was to prospectively assess the feasibility and the prognostic value of PBV in a cohort of NYHA functional class I and II HF outpatients.
Methods: 44 consecutive asymptomatic or mildly symptomatic patients (34 men, 60±12 years) and 31 age- and sex-matched healthy controls underwent contrast-enhanced cardiac MR on a 1.5 Tesla scanner. PBV was calculated as the product of stroke volume index and number of cardiac cycles for an intravenous bolus of gadolinium contrast to pass through the pulmonary circulation, as determined by cardiac-gated first-pass perfusion imaging. The prognostic value of PBVI was calculated by univariate Kaplan-Meier survival analysis and multivariate Cox proportional-hazard regression analysis.
Results: Compared to healthy controls, PBV indexed to body surface area (PBVI, ml/m^2) and pulmonary transit time (PTT, s), were both significantly higher in HF outpatients (mean±SD: 317±112 vs. 379±146, p=0.03; 6.6±1.8 vs. 8.4±2.9, p=0.004). PBVI was also found to significantly correlate with severity of diastolic dysfunction as assessed by Doppler echocardiography. During a median follow-up period of 40±27 months, 13 patients (29%) reached the combined primary end-point of cardiovascular death, HF hospitalization or sustained ventricular arrhythmias/appropriate ICD intervention. Using a cut-off point of PBVI >541 ml/m^2, corresponding to 2SD above the mean of healthy controls, Kaplan-Meier event-free survival rates were significantly higher in patients below (81%) as compared with patients above (14%) this cut-off (p=0.02). After multivariate adjustment for right and left ventricular ejection fraction, PTT and pulmonary artery pressure, PBVI remained an independent predictor of the composite end-point ($\chi^2=5.76$, p=0.01).
Conclusions: PBVI by contrast-enhanced MR is a novel imaging technique useful to quantitatively determine pulmonary intravascular blood pool. Compared to healthy controls, HF outpatients showed an increased amount of blood in the pulmonary vasculature and a longer PTT. Further studies are warranted to validate PBVI as a non-invasive method to assess and grading congestion, and confirm its prognostic role in the setting of congestive HF.

P5957 | BEDSIDE
Hereditary pulmonary arterial hypertension related to TBX4 mutations: maybe a benign form of heritable PAH?

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T-Box Transcription Factor4 (TBX4)is a pulmonary artery hypertension recently described gene.It can cause childhood-onset PAH and Small Patella Syndrome (SPS).PAH phenotype and prognosis associated to TBX4 mutations (mut) have not been described.We present preliminary results of a Spanish Multi-centric study of genetics of Idiopathic (IPAH) and Heritable (HPAH)patients (pt).
Aim: To describe prevalence of TBX4 mut in adult IPAH&HPAH pt and characterize phenotype compared to other forms of HPAH.
Methods: An Spanish Multi-centric study of genetics of IPAH&HPAH is ongoing since 2011. Genetic analysis was performed looking for BMPR2,KCNK3 and TBX4 mut. After genetic study patients were divided into 3 groups: Idiopathic PAH (no detected mut and no family story), Heritable TBX4 PAH (detected mut in TBX4) and HPAH-non TBX4 PAH (detected mut in BMPR2 or KCNK3 or patients without detected mut but with positive family story). Clinical and survival (SV) data were obtained from Spanish National Registry (REHAP). Screening for SPS was done in TBX4mut carriers.
Results: 117 pt were included.We found 18 mutations in BMPR2 (15,3%), 2 mut in KCNK3 (1,7%) and 2 different missense mutations (p.M452V and p.N475H) in TBX4 in two non-related sporadic PAH pt (1,9%).Both TBX4mut seemed to be pathogenic after bio-informatic analysis and were absent in control population.No other mut in common PAH genes were found in TBX4 mut carriers. Both TBX4mut carriers presented a childhood-onset sporadic PAH with a unique benign course.None of them fullfilled SPS criteria. Characteristics and SV are listed in Chart 1.
Conclusion: HPAH related to TBX4 mut presents as a child-hood onset PAH and may exhibit a more benign course and longer survival than other forms of HPAH.Further investigations are needed to explore the course and prognosis of this new mut.

P5958 | BEDSIDE
Novel strategy for catheter interventional treatment of chronic thromboembolic pulmonary hypertension guided by optical coherence tomography imaging

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by unresolved thromboemboli in the pulmonary arteries. We have previously demonstrated the usefulness of optical coherence tomography (OCT), an interferometer-based imaging modality with a high resolution, to diagnose CTEPH. In the present study, in order to develop an effective and safe treatment for inoperable CTEPH, we examined the effectiveness of our modified methods of

Abstract P5957 – Table 1. Clinical and hemodynamic characteristics

	Age (years)	mPAP (mmHg)	PVR (WU)	NYHA	AVT	Survival (years)	Treatment
TBX4 patient 1 (male) Dx/Present	5/51	1968: 75/68	16,0/ 13,3	III/I	Negative	43,46	Bosentan (since 2010)
TBX4 patient 2 (fem) Dx /Present	10/37	1987: 51/33	NA/5,0	III/I	Positive	28,39	Nifedipine
HAPH non TBX4 (n=25)	33,25±13,2 70,8% female	mPAP: 65,4±14,24	15,44±7,1	54,2% NYHA III	8,3% positive	8,69±0,79	ARE: 41,7% PD5I: 20,8% CCB: 4,2% Prostanoids: 8,3%

mPAP, medium pulmonary artery pressure; mmHg, milimiters of mercury; PVR, pulmonary vascular resistance; WU, wood units; NYHA, New York Heart Association functional class; AVT, acute vasodilator test; ARE, antagonists of endotelin receptor; PD51, phosphodiesterase 5 inhibitors. CCB, calcium channel bloquers;.

percutaneous transluminal pulmonary angioplasty (PTPA) guided by OCT imaging.
Methods: From July 2009 to October 2014, we prospectively enrolled 61 consecutive patients with inoperable CTEPH, including 2 patients with a history of thromboendoarterectomy and residual PH (median age 63 yrs., 78% female). After optimal medical treatment, we performed PTPA in a step-wise manner until mean pulmonary artery pressure (PAP) was decreased below 30 mmHg.
Results: As a vasodilator therapy prior to PTPA, prostacyclin analogues, phosphodiesterase-5 inhibitors, endothelin receptor antagonists and soluble guanylate cyclase stimulators were used in 42 (69%), 45 (74%), 13 (21%) and 10 (16%) patients, respectively. Among them, 42 (69%) received combination therapies of these medications. We performed a total of 279 OCT examinations in order to observe the target lesions for PTPA, which clearly showed meshwork (85%), wall thrombus (10%), and slit (5%) configurations. We also performed a total of 332 PTPA procedures (median 4.5 procedures per patient), resulting in significant improvement of mean pulmonary arterial pressure (42±10 to 27±6 mmHg, $P<0.01$), cardiac index (2.3±0.6 to 2.7±0.5 l/min/m^2, $P<0.01$), pulmonary vascular resistance (742±350 to 321±124 dyne·sec·cm-5, $P<0.01$), and saturation of oxygen (87±6 to 90±6%, $P<0.05$, n=25). OCT showed that PTPA enlarged the lumen diameter (63±90% increase), although some severe thrombotic occlusions were resistant to the procedure. 3D-OCT imaging clearly showed that PTPA destroyed the typical flaps and webs and shifted them to the pulmonary artery walls. Furthermore, cardiac magnetic resonance showed improvement of right ventricular (RV) ejection fraction (39.5 to 51.0%, $P<0.001$), decrease in RV end-diastolic volume index (105 to 84ml/m^2, P=0.03). The complication of PTPA was mild to moderate hemoptysis in 18 out of the 61 patients, which was successfully managed with oxygen and non-invasive positive pressure ventilation without intubation.
Conclusion: OCT-guided PTPA combined with optimal medical treatment markedly ameliorates pulmonary hemodynamics and RV functions in patients with inoperable CTEPH.

WHAT'S NEXT IN CARDIOVASCULAR RISK PREDICTION?

P5959 | BEDSIDE
Coronary artery calcium (CAC) volume, CAC density, and incident coronary heart disease, stroke, and all cardiovascular disease events

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Background: We have reported that coronary artery calcium (CAC) volume by computed tomography (CT) was strongly related to incident cardiovascular disease (CVD) in a multi-ethnic cohort, but that at any given CAC volume, CAC density was inversely related (JAMA 2014;311:271–8). We also noted that CAC density was somewhat more protective at lower levels of CAC volume, though the interaction term was not significant. Longer follow-up has now increased the number of hard CVD events by 47%.
Purpose: To evaluate with longer follow-up 1) whether CAC density remains inversely associated with CVD (CHD and stroke) events, 2) whether the effect of CAC density is modified by the level of CAC volume, and 3) among CVD events, to separately evaluate coronary heart disease (CHD) and stroke events.
Methods: 3398 men and women in the Multi-Ethnic Study of Atherosclerosis with CAC scores >0 at baseline had CAC volume and density calculated from cardiac CT scans. Cox proportional hazards models were adjusted for ethnic group and the new ethnic-specific ASCVD risk score. Hazard ratios (HR) were calculated for CAC volume, CAC density, and for CAC density by quartile of CAC volume.
Results: After an average follow-up of 10.3 years, there were 264 hard coronary heart disease (CHD) events and 126 hard stroke events for a total of 390 hard CVD events. For CHD, the HR was 1.83 ($p<0.001$) for each standard deviation (SD) of CAC volume, and the HR was 0.71 ($p<0.001$) for each SD of CAC density. Results were similar for all CVD. For stroke, the HR was 1.46 (p=0.001) for each SD of CAC volume, and the HR was 0.83 (p=0.13) for each SD of CAC density. CAC volume and CAC density each independently and significantly increased the area under the ROC curves for CHD and CVD. The CHD and CVD HRs for CAC density were similar across the 4 quartiles of CAC volume with no evidence of a trend, and multiplicative interaction terms were not significant.
Conclusions: With extended follow-up, 1) CAC density remained strongly inversely related to incident CHD and all CVD, and 2) this inverse association was similar at all levels of CAC volume. As expected, CAC volume and density showed more modest associations with stroke. CAC scoring systems should include density to improve estimation of CHD and CVD risk.

P5960 | BEDSIDE
Coronary artery calcification improves risk estimation for coronary events in the general population with and without statin recommendation according to ESC and AHA/ACC primary prevention guidelines

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Background: Recently, ESC and AHA/ACC guidelines regarding statin therapy in primary prevention were updated.
Purpose: We aimed to quantify the potential additional role of coronary artery calcification (CAC)-score above the two updated guidelines in the general population.
Methods: Participants from the population based longitudinal Heinz Nixdorf Recall study received non-contrast enhanced EBCT-scanning of the heart for quantification of CAC between 2000 and 2003. For this analysis we excluded subjects with prior cardiovascular disease or lipid lowering therapy at baseline. Subjects remained unaware to their initial CAC-score. Statin indication was assessed according to 2012 ESC as well as 2013 AHA/ACC guidelines based on subjects individual baseline characteristics. After inclusion, participants were followed for occurrence of coronary events, defined as fatal or non-fatal myocardial infarction. We assessed event rates in subjects with and without statin indication according to ESC and AHA/ACC guidelines with respect to CAC-group, using a CAC-score of 100 as threshold.
Results: Overall, 3745 subjects without statin therapy at baseline were included (age 59±8 years, 47% males). During 10.4±2.0 years of follow-up 131 myocardial infarctions occurred. The frequency of statin recommendation was significantly lower when following ESC compared to AHA/ACC guidelines (34% vs. 56%, $p<0.0001$). In contrast, a CAC-score<100 was present in the majority of subjects with statin indication according to both guidelines (59% for statin indication by ESC, 62% for statin indication by AHA/ACC). For ESC recommendations, CAC-score of 100 as threshold differentiated risk for both subjects without (1.6% CAC<100 vs. 6.8 for CAC$\geq$100, $p<0.0001$) and with statin indication (2.9% for CAC<100 vs. 9.5 for CAC$\geq$100, $p<0.0001$). Likewise, for AHA/ACC guidelines, application of CAC-score stratified event rate for coronary events among subjects without (0.9% for CAC<100 vs. 4.2% for CAC<100, p=0.001) and with statin indication (3.2% for CAC<100 vs. 8.9% for CAC$\geq$100, $p<0.0001$).
Conclusion: Quantification of CAC-score in addition to current ESC and AHA/ACC guidelines has the ability to improve discrimination between subjects at high vs. low risk for future coronary events. Therefore it may help to match intensified risk factor modification to atherosclerotic plaque burden as well as actual risk while avoiding therapy in subjects with low coronary atherosclerosis that have low 10-year event rate.

P5961 | BEDSIDE
Biomarker-based risk score for prediction of cardiovascular events in stable coronary heart disease - Experiences from the STABILITY biomarker substudy

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Background: There is no generally used risk score for prognostication of cardiovascular outcomes in patients with stable coronary heart disease (CHD). The biomarkers currently used in routine care for evaluation of these patients are indicators of dysglycemia, dyslipidemia, renal dysfunction and inflammation (C-reactive protein [CRP]).
Purpose: We developed and evaluated a biomarker-based risk score for cardiovascular death (CVD), myocardial infarction (MI), stroke and heart failure (HF) in stable CHD based on clinical characteristics and biomarkers.
Results: Of the 15,828 CHD patients included in the STABILITY trial 13,093 had available information on biomarkers at baseline. Beyond routine biomarkers (listed below), we included markers of cardiac dysfunction (N-terminal pro-B-type natriuretic peptide [NT-proBNP]), high sensitivity cardiac troponin-T [cTnT-hs]), renal dysfunction (cystatin-C), oxidative stress (growth differentiation factor 15 [GDF-15]) and local inflammatory activity (lipoprotein associated phospholipase A2 [Lp-PLA2]). During 3.7 years median follow-up, 1298 CVD, MI and stroke events occurred. A Cox-regression model was constructed, comprising all prognostic clinical variables (age, sex, BMI, smoking, hypertension, diabetes, previous polyvascular disease, previous MI, previous revascularisation, previous multivessel CHD) and the routine biomarkers haemoglobin, white blood cell count, LDL-cholesterol, HDL-cholesterol, triglycerides, estimated GFR (based on creatinine) and cystatin-C, hsCRP, GDF-15, cTnT-hs and NT-proBNP which had C index 0.72. This was then reduced to a smaller parsimonious model, including the variables with the strongest prognostic value. The new model was internally validated us-

ing 100 bootstrap samples. The development of the model followed the recently published TRIPOD statement.
Results: The final reduced model included, in order of importance, NT-proBNP, cTnT-hs, polyvascular disease, smoking, GDF-15 and Lp-PLA2. It was well calibrated and showed good internal validity. The C index was 0.71 for the composite endpoint of CVD/MI/ stroke. Using the same model the C index was 0.81 for CVD, 0.77 for total death, 0.66 for MI, 0.67 for stroke, 0.86 for HF, and 0.82 for CVD/HF.
Conclusion: A biomarker-based risk score, including NT-proBNP, cTnT-hs, GDF-15, Lp-PLA2 and information on polyvascular disease and smoking, accurately predicts risk of fatal and non-fatal cardiovascular events in patients with stable CHD. The use of this score as a decision support tool might further improve secondary preventive treatments in this patient population.

P5962 | BEDSIDE
Increase the predictive capacity of coronary risk with a Genetic Score

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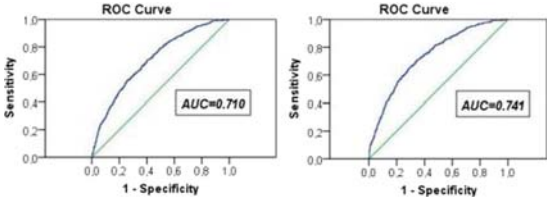
Genes associated with coronary artery disease (CAD) and traditional cardiovascular risk factors (TCRF) present a limited individual predictive value. It is expected that the inclusion in global scores may increase the predictive ability.
Aim: Evaluate the ability of a multifactorial genetic risk score (GRS) be able to add predictive power, for the development of CAD, to the model developed only with TCRF.
Methods: A case-control study was performed with 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. Traditional risk factos were evaluated according to the International criteria. The genetic variants were analyzed with specific primers and the GRS was determined in the population, based on 29 genetic variants previously associated with atherosclerotic disease in general and, in particular, with CAD. A multiplicative model was then used based on risk multiplication (OR) of each genotype of the 29 studied variants. Subsequently, a multivariate analysis was done only with the TCRF or with the TCRF plus GRS. A ROC curve was constructed for both situations.
Results: After multivariate analysis, the GRS was found to be an independent predictor for CAD (OR=2.1; CI: 1.7–2.5; p<0.0001). The AUC increased from 0.71 to 0.74 after the inclusion of GRS to the TCRF in the multivariate analysis (Figure).



ROC Curve model with and without GRS

Conclusions: In our population, the multiplicative GRS was an independent predictor for CAD. When analyzed together with traditional risk factors, it adds little predictive value. Its usefulness, in clinical practice, may be directed to the intermediate risk group, in which a possible risk reclassification can have different therapeutic measures.

P5963 | BEDSIDE
Changes in the Framingham 10-year risk of cardiovascular disease and the European 10-year risk of fatal cardiovascular disease in a large untreated urban population

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Background: Screening of cardiovascular risk factors (CVRFs) is of importance and may lead to detect them and improve patients' life expectancy and functional status. However, surveys measuring effectiveness in reducing CVD incidence have yielded equivocal findings. The aim of this study was to assess the changes in the Framingham 10-year risk of cardiovascular disease and the European 10-year risk of fatal cardiovascular disease in a large untreated urban population.
Methods: Between 2007 and 2012, we conducted a screening campaign for CVRFs in men aged 40 to 65 yrs and women aged 50 to 70 yrs in the western suburbs of Paris. Data were complete for 20,324 participants of which 14,709 were untreated. We systematically calculated the Framingham 10-year risk of cardiovascular disease and the 10-year risk of fatal cardiovascular disease based on the European Systematic COronary Risk Evaluation (SCORE).
Results: The prevalence trend over six years significantly decreased for hypertension (p=0.002 in men and p<0.0001 in women) and for tobacco smoking in men (p=0.0001). We observed a significant decrease in the mean Framingham 10-year risk from 13.3±8.2 in 2007 to 11.7±9.0 in 2012 in men and from 8.0±4.1 in 2007 to 5.9±3.4 in women (both p<0.0001). The 10-year risk of fatal CVD (SCORE) showed a significant decrease in men and in women (1.2±1.1 in 2007 and 0.6±0.7 in 2012, p<0.0001).
Conclusions: Our screening campaign found a significant decrease of the 10-year risk of cardiovascular disease, measured by Framingham or SCORE methods. These results suggest that community prevention programs may improve the control of CVRFs with a potential impact of prognosis in a general population.

P5964 | BEDSIDE
Additional value of a combined genetic score to Framingham risk score

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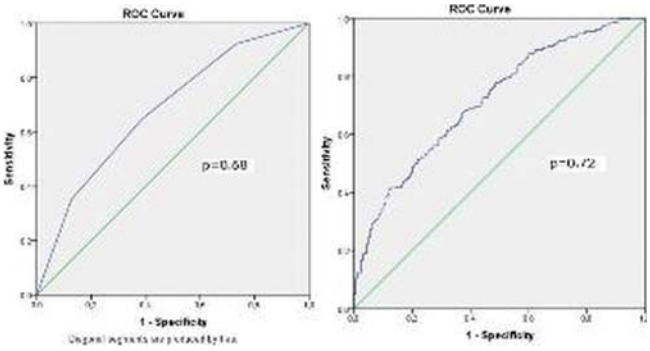
Cardiovascular risk stratification has included traditional risk factors as smoking, cholesterol and blood pressure adjusted to age and gender. The utility of genetic risk scores as independent risk predictors remains inconclusive.
Aim: Evaluate the ability of a multiloci genetic score (GS) to provide additive value to Framingham 10 years risk score (FS) to predict coronary arterial disease (CAD).
Methods: Case-control study of 2555 individuals: 1321 (51,7%) coronary patients and 1234 (48,3%) controls matched for age and gender) divided in three goups according to FS (FS<5%, FS 5%-20% and FS>20%). The multiloci GS was determined with specific primers of 29 different genetic variants associated to atherosclerotic disease. ROC curves and area under curve (AUC) were performed using the traditional risk factos (TRF) and repeated adding GS.
Results: By multivariate analysis GS was an independent predictor for CAD (OR=2,05; 1,66–2,54, p<0.0001). Diabetes, arterial hypertension, dyslipidemia and smoking (OR=3,07 (2,47–3,80); OR=2,07 (1,73–2,49); OR=3,1 (2,37–4,07); OR=3,11 (2,58–3,74); all p<0.0001) were also independent CAD predictors. GS also added predictive value to TRF across all risk subgroups. In individuals within low risk (FS<5) the AUC increased from 0,76 to 0,77, in intermediate risk (FS 5–20) increased from 0,70 to 0,73 and in the high risk (FS>20) subgroup the TRF prediction was lower (AUC=0,68) increasing to 0,72 after the inclusion of the GS.



Conclusion: In our population, GS increased the predictive value of traditional risk factors across all FS risk subgroups. GS proved a better incremental value in intermediate and high risk subgroups. In these subgroups of patients, the inclusion of genotyping may be considered to better stratify cardiovascular risk.

P5965 | BEDSIDE
Clinical Impact of Ankle Brachial Index in patients undergoing successful PCI

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Purpose: To examine the utility of Ankle-Brachial Index (ABI) on major adverse cardiovascular events (MACE) in patients undergoing percutaneous coronary intervention (PCI).
Methods: The subjects were 2052 patients who underwent successful PCI at our institution from July 2007 to May 2010 and simultaneously performed ABI. Of them, we excluded 39 patients due to lack of ABI, 121 patients who underwent previous endovascular therapy for peripheral artery disease or previous surgery for abdominal aortic aneurysm, and 1 patient who did not have sufficient data. Finally, we analyzed 1891 patients and investigated the relationship between ABI and MACE (all-cause death, myocardial infarction, or stroke) in patients who underwent successful PCI.
Results: The mean follow interval was 42.4±13.7 months. MACE occurred in 250 patients (13.2%). At 4 years, compared with normal ABI group, low ABI (<0.90) and high ABI (>1.40) group had significant worse MACE rates (normal 11.4%, low 32.0%, high 28.8%, log-rank p<0.0001). After adjustment, low ABI was still significant predictor for MACE (Hazard ratio (HR) 2.23 [1.66–2.96], p<0.0001). High ABI also had a tendency to be a risk factor of MACE, however it was not

significant (HR 2.07 [0.91–4.09], p=0.08). The HRs for MACE for different levels of ABI compared with a reference ABI of 1.21–1.30 formed a U-shaped curve.

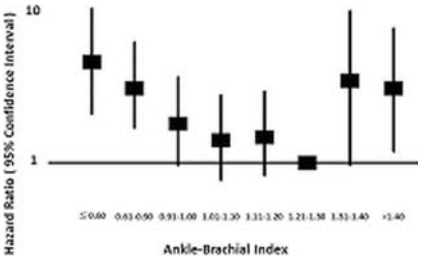

Figure 1. Hazard ratio for MACE by Ankle-Brachial Index.

Conclusions: Our data suggests that ABI which is measurable easily can predict the prognosis of patients with coronary artery disease who underwent PCI.

ANTI-THROMBOTICS IN CLINICAL PRACTICE

P5966 | BEDSIDE
Treatment with cilostazol reduces major amputation after endovascular therapy in hemodialysis patients with critical limb ischemia

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Background: Cilostazol, a selective inhibitor of phosphodiesterase 3, has been reported to have beneficial effects on preventing limb events in peripheral artery disease (PAD) patients. For treatment of PAD in hemodialysis (HD) patients, endovascular therapy (EVT) was widely performed as well as non-HD patients, however, the poor prognosis is consistently clinical problem in HD population. We investigated the effects of treatment with cilostazol on preventing incidence of major amputation after EVT in HD patients with critical limb ischemia.
Methods: This study consisted of 359 HD patients successfully undergoing EVT for treatment of critical limb ischemia. They were divided into two groups: patients receiving treatment with cilostazol in conjunction with standard therapy (n=149 patients, cilostazol group) and those without cilostazol (n=210 patients, control group). They were followed-up for up to 10 years, and data on incidence of major amputation as the primary endpoint were collected. Amputation free survival (AFS), defined as freedom from amputation or all-cause death, was also evaluated. To adjust for baseline differences between the two groups, a propensity score analysis was performed using the multiple logistic regression model including all baseline variables such as gender, age, traditional risk factors, previous cardiovascular diseases, preprocedural ABI, femoropopliteal lesion, TASC type and ulcer/gangrene.
Results: During follow up period (median: 41 months), 27 patients (7.5%) underwent major amputation and 95 patients (26.5%) died. Limb salvage rate for 10-year was significantly higher in the cilostazol group compared to the control group [83.2% vs. 71.4%, propensity score-adjusted hazard ratio (HR) 0.31, 95% confidence interval (CI) 0.11–0.84, P=0.022]. Also, 10-year AFS and all-cause survival was significantly higher in the cilostazol group than in the control group (41.6% vs. 34.5%, adjusted HR 0.48, 95% CI 0.30–0.79, P=0.0033 and 52.2% vs. 37.6%, adjusted HR 0.47, 95% CI 0.28–0.79, p=0.0049, respectively). Even after adjusting for other confounders with propensity score, cilostazol administration (adjusted HR 0.34, 95% CI 0.12–0.92, p=0.034) and ulcer/gangrene (adjusted HR 3.33, 95% CI 1.21–9.16, p=0.019) were independent predictors for major amputation.
Conclusion: Treatment with cilostazol improves long-term limb salvage and AFS rates after EVT in HD patients with critical limb ischemia.

P5967 | BENCH
Initial experience with idarucizumab in dabigatran-treated patients requiring emergency surgery or interventon: interim results from the RE-VERSE AD study

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Background: Dabigatran, an oral thrombin inhibitor, is widely used for stroke prevention in non-valvular atrial fibrillation. Although its half-life of 12–17 hours allows for a timely interruption of dabigatran prior to elective surgery, rapid reversal is desirable to restore hemostasis in those who require urgent surgery or intervention. Idarucizumab, a humanized Fab fragment directed against dabigatran, has demonstrated immediate, complete, and sustained reversal of the anticoagulant effects of dabigatran in healthy volunteers, and attenuated bleeding in various animal models. Therefore, idarucizumab has the potential to streamline management of dabigatran-treated patients who require reversal of anticoagulation prior to urgent surgery.
Methods: The phase III RE-VERSE-AD study is the first clinical trial to test a specific reversal agent to a novel oral anticoagulant in patients with life threatening or uncontrolled bleeding or in those requiring urgent surgery. In this ongoing study, dabigatran-treated patients requiring emergency surgery or intervention are given intravenous idarucizumab as two 2.5 g bolus infusions administered 15 min apart. The primary endpoint is the maximum reversal of the anticoagulant effect of dabigatran, based on central laboratory determination of the dilute thrombin time or ecarin clotting time. A secondary endpoint for surgical/procedural patients is the clinical classification of periprocedural bleeding as normal hemostasis during the procedure; mildly abnormal intraprocedural hemostasis as judged by quantity or quality of blood loss (e.g. slight oozing); moderately abnormal (e.g. controllable bleeding); or severely abnormal (e.g. severe refractory hemorrhage).
Results: Of the first 22 patients given idarucizumab prior to emergency surgery, periprocedural bleeding was assessed as normal in 20 and mildly abnormal in 2. Cases included 7 major abdominal procedures and 5 emergent orthopedic procedures. The effect of idarucizumab on coagulation parameters and the clinical outcomes of the patients will be presented.
Conclusions: Idarucizumab is a rapidly acting, specific reversal agent for dabigatran. Preliminary results from the RE-VERSE AD study suggest that idarucizumab administration to dabigatran-treated patients requiring urgent surgery enables timely intervention with little or no excessive bleeding. Therefore, idarucizumab has the potential to streamline the management of dabigatran-treated patients who require rapid reversal of anticoagulation.

P5968 | BEDSIDE
Long-term safety and efficacy of evolocumab in patients with statin intolerance

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Purpose: In two previously reported trials of statin intolerant patients (GAUSS-1 & -2) evolocumab, a fully human monoclonal antibody against PCSK9, reduced LDL-C 41–63%. We report the safety and tolerability of evolocumab+standard of care (SoC) vs SoC alone in an open label long term extension (OLE) trial.
Methods: We conducted a pooled analysis of patients who completed GAUSS-1 & -2 – and were enrolled into OLE studies, OSLER-1 & -2. For the OLE, patients were re-randomised 2:1 to evolocumab + SoC or SoC.
Results: 382 patients from GAUSS-1 and -2 (N=102 and 280, respectively) were randomised to evolocumab+SoC, N=251 or SoC, N=131: Demographics, discontinuations, adverse events (AE), laboratory AEs, and LDL-C are shown in the Table. Muscle AEs were reported in 35 (13.9%) patients on evolocumab + SoC and 20 (15.3%) SoC patients with myalgia being the most common: 21 (8.4%) and 11 (8.4%), respectively. The mean percent change in LDL-C from baseline to 1 year was –56.1% and –12.4% in the evolocumab+SoC and SoC groups, respectively.

Table 1. Safety and efficacy summary

Open-label extension randomised group	SoC (n=131)	Evolocumab + SoC (n=251)
Open-label extension study exposure in months, median (IQR)	11.0 (9.2, 12.9)	11.0 (9.0, 12.9)
Patients who discontinued the study, n (%)	8 (3.2)	16 (4.2)
AEs, n (%)		
Any AE	99 (75.6)	191 (76.1)
AE leading to study drug discontinuation	5 (3.8)	9 (3.6)
Potential muscle events, n (%)	20 (15.3)	35 (13.9)
Myalgia	11 (8.4)	21 (8.4)
Muscular weakness	1 (0.8)	1 (0.4)
Musculoskeletal pain	7 (5.3)	4 (1.6)
*LDL-C (calculated)		
Phase 2 study baseline, mg/dL, mean (sd), [n]	193.5 (57.5), [131]	192.3 (57.2), [251]
52 weeks, percentage change from baseline, mean (se), [n]	–12.4 (3.1), [42]	–56.1 (1.9), [74]

*OSLER-2 values are from week 48.

Conclusions: In 382 patients with history of statin-associated muscle-related side effects, long-term treatment with evolocumab was well-tolerated, no new safety signals emerged, and efficacy was maintained with 56% reduction in LDL-C.

P5969 | BEDSIDE
The effects of optimal medical therapy on coronary plaque

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Background: The results of the COURAGE trial which is a well-known study had a considerable impact on us as interventionists in the circulatory organ area.
Purpose: We evaluated the effects of optimal madical therapy (OMT) on coronary plaque using intravascular ultrasound (IVUS).
Methods: We simultaneously performed IVUS and VH-IVUS on 82 coronary plaque lesions, which were mild stenotic lesions not requiring PCI, in 65 stable angina patients who required PCI and performed qualitative and quantitative assessments. Ten months later, we divided the patients into an OMT group (30 cases, 33 lesions) and a standard treatment group (non-OMT group; 35 cases, 49 lesions) to re-evaluate the therapies using IVUS and VH-IVUS of the target lesions for each of the groups. Plaque regression and compositional change rates were compared between the groups. The OMT group was defined as follows: 1) no smoking was allowed (including non-smokers); 2) systolic pressure of 140 or below and diastolic pressure of 90 or below measured both at home and physician's office were met at least 80% of the time; 3) HbA1c levels were consistently below 7 during follow-up; and (4) LDL cholesterol levels were consistently below 100 during follow-up. Patients who did not meet any of these criteria were included into the non-OMT group.
Results: No significant differences were observed between the two groups at baseline. Other results were as follows, respectively: mean plaque volume of the target lesions was 80±5 mm^3 and 72±7 mm^3, and mean %plaque volume was 55±9% and 52±9%; after 10 months, plaque volume was 72±8 mm^3 and 75±10 mm^3, and %plaque volume was 54±7% and 54±8%; rates of change over the period of 10 months were –8.7±5 mm^3 and 3±6 mm^3 for plaque volume (p=0.001), and –1±0.8% and 2±0.5% for %plaque volume (p=0.01). Thus, both plaque volume and %plaque volume were significantly decreased in the OMT group. VH-IVUS was also used to further subdivide coronary plaque into four types of composition. Consequently, results for % necrotic core volume (%NCV), which is a marker for necrotic lesions of coronary plaque, indicated that necrotic lesions decreased significantly over the period of 10 months in the OMT group compared to those in the non-OMT group (–5±2 vs 1±3%, p=0.01).
Conclusions: Coronary plaque volume decreased significantly over the 10-month period of follow-up in the OMT group compared to that in the non-OMT group. These results, therefore, suggest that strict control of lifestyle-related diseases is important in the secondary prevention of ischemic heart disease and that medical treatment may improve unstable coronary plaque.

P5970 | BEDSIDE
Medical compliance after acute myocardial infarction in the Netherlands

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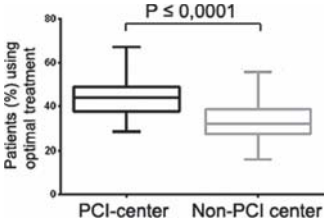
Purpose: Optimal medical treatment is associated with increased survival and lower rate of new cardiovascular incidents. Current study assess medical compliance one year after acute myocardial infarction between 89 Dutch hospitals.
Methods: In 2008 and 2009, national diagnose-codings of 89 Dutch hospitals of ST-Elevation myocardial infarction (STEMI) and Non-ST-Elevation myocardial infarction (NSTEMI) patients from the Dutch Information System Hospital Care (IZiZ) were acquired. Furthermore, one year after myocardial infarction, data on medication in these patients was extracted from the Dutch Pharmacy Information System (FIS). Optimal medical treatment was defined if patients used at least 300 minimum doses of antiplatelet agents (aspirin or thienopyridine), statins, beta-blockers and ACE-inhibitors in the year following myocardial infarction. Additionally, medical compliance was compared between PCI-centers and non-PCI-centers.
Results: In total 42.020 patients were analysed. After one year, 85% of the patients used platelet inhibitors, 89% statins, 69% beta-blockers and 62% ACE-inhibitors. Overall, 40% of patients was on optimal medical treatment one year after acute myocardial. Significant hospital differences in medical compliance were observed. Patients in a PCI-center more often received optimal medical treatment than patients in a non-PCI-center (45% ± 7.8 vs 32% ± 7.7; P≤0,0001)



Difference in medical compliance.

Conclusion: In 2008 and 2009, 40% of patients received optimal medical treatment one year after myocardial infarction in the Netherlands. Patients in a PCI-center more often received optimal medical treatment (45% PCI vs 32% non-PCI).

P5971 | BEDSIDE
Fixed-dose (10 mg and 5 mg) versus phenotype-based prasugrel dose to match therapeutic zone with acute coronary syndrome: the A-MATCH trial

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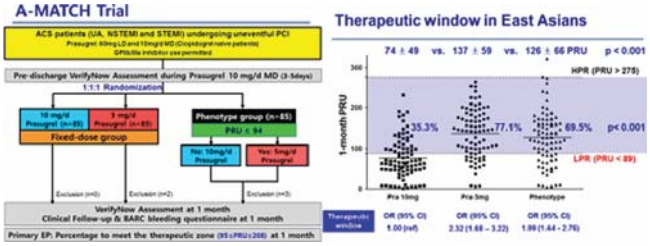
Background: Patients have shown low thrombophilia and increased risk of bleeding during antithrombotic therapy. Compared with others, they have enhanced response to potent P2Y12 inhibitors.
Purpose: To determine proper dose/strategy of P2Y12 inhibitor and develop "therapeutic window" in patients.
Methods: After standard prasugrel therapy, PCI-treated ACS patients were randomized to prasugrel 10mg/d (PRA10), prasugrel 5mg/d (PRA5) or LPR-based dosing (Phenotype) (Figure: left). Pharmacodynamic effects were assessed with VerifyNow (PRU), and prevalence of bleeding events at 1-month was monitored using BARC questionnaires. Primary endpoint was percentage to match "therapeutic window in population" (95≤PRU≤208).
Results: During follow-up, ischemic events rarely occurred (n=1), but BARC bleeding events were frequently observed (n=69; 24.4%, 7.2% and 0.4% of type 1, 2 and 3 events). At 1-month FU, PRA5 and Phenotype showed the higher level of platelet reactivity compared with PRA10 (p values<0.001). Prevalence to match "therapeutic window" was greater in PRA5 and Phenotype than in PRA10 (p values<0.001). Compared with PRA10, bleeding risk was reduced in PRA5 (HR, 0.75; 95% CI, 0.51 to 1.09) and Phenotype (HR, 0.73; 95% CI, 0.49 to 1.07). In ROC curve analysis, optimal cutoffs for BARC type 1 and BARC type ≥2 events were ≤145 PRU (AUC, 0.608; 95% CI, 0.533 to 0.683; p=0.011) and ≤88 PRU (AUC, 0.645; 95% CI, 0.510 to 0.780; p=0.041) (Figure: right).



AMATCH_Therapeutic zone in East Asians

Conclusions: Among ACS patients, compared with prasugrel 10 mg/d, prasugrel 5 mg/d and VerifyNow-based dosing were associated with increase in matching therapeutic window and decrease in bleeding risk. Proposed LPR criteria should be taken into consideration to develop tailored antiplatelet strategy for patients.

P5972 | BEDSIDE
Management of oral anticoagulation in patients undergoing cardiac catheterization

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Background: The optimal peri-procedural management of anticoagulation with Vitamin K antagonists (VKA) and the newer direct acting anticoagulants (DOAC) in patients undergoing cardiac catheterization is still matter of debate. The purpose of this study was to evaluate the current treatment strategies in a large cohort of patients undergoing cardiac catheterization and to assess the risk of bleeding and/or embolism.
Methods and results: 499 consecutive episodes were collected in the German BNK online bridging registry (BORDER 2)of which 89% of patients had atrial fibrillation (CHA2DS2VASc 2.8±1.6), 3.2% received OAC after mechanical heart valve implantation, 6% after venous thromboembolism, and 1.8% due to other reasons. 70.6% of patients were treated with DOACs and 29.5% with VKA. Overall, bridging therapy with was more common in VKA- patients than in patients under DOAC (67%, 28%; p<0.0001), and the duration [days] of OAC interruption took longer in the VKA group (VKA, 8.1±5.8; DOAC, 1.9±3.4; p<0.0001). No embolism (0%) and19 bleeding events (3.9%) occurred during 30 days of follow up, including one major bleed (0.2%) and three clinical relevant bleeds (0.6%). Independent risk factors for bleedings were the use of bridging anticoagulants (odds ratio [OR] 3.6, 95% confidence interval [CI] 1.3–9.5; p=0.01), history of bleeding (OR 4.2, 95% CI 1.0–20.1; p=0.05) and if patients underwent pulmonary vein isolation (OR 3.1,

95% CI 1.2–8.0; p=0.02); all other factors (DOAC pretreatment, HASBLED, antiplatelet therapy, procedural details) were not associated with the occurrence of bleeding events (p>0.05).
Conclusions: Peri-procedural complications are rare and bridging therapy is uncommon in patients with direct acting oral anticoagulants undergoing cardiac catheterization. Independent risk factors for bleedings are the use of heparins during OAC interruption, a history of bleeding and procedural details.

MANAGEMENT IN HEART FAILURE: NEW PERSPECTIVES

P5973 | BEDSIDE
A long-term prognosis of adaptive servo ventilation therapy for patients with heart failure regardless of the severity of sleep-disordered breathing

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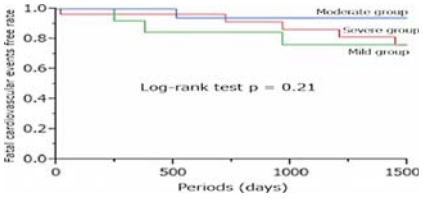
Introduction: Adaptive servo-ventilation (ASV) is used for treating heart failure (HF). Previously, we reported that ASV therapy for patients with mild sleep-disordered breathing (SDB) resulted in almost equal improvements in BNP and LVEF compared to for the levels in patients with moderate and severe SDB, demonstrating ASV therapy to be effective for all patients with HF. It is unclear whether ASV improves long-term prognosis for all patients with HF, regardless of severity of SDB.
Purpose: The purpose of this study is to estimate the long-term prognosis of ASV therapy for patients with HF regardless of the severity of SDB.
Methods: Sixty-one consecutive HF patients (70±10 years) were initiated ASV therapy for HF treatment after estimating polysomnography. The patients were classified into 3 groups based on the apnea hypopnea index (AHI). A group of 28 patients with an AHI of ≥40/h was designated as Severe group, 20 patients with an AHI of ≥20/h but <40/h was designated as Moderate group, and 13 patients with an AHI of <20/h was designated as Mild group. We observed 3-year follow-up data including fatal cardiovascular events (death from myocardial infarction, cardioembolic stroke, and fatal cardiac arrhythmias) to estimate long-term prognosis.
Results: There were no significant differences among the 3 groups respect to age and gender, and LVEF. The BNP and LVEF were improved almost equally in the 3 groups after ASV treatment. After 3-year follow up, no significant difference was observed with respect to the increased risk for fatal cardiovascular events (p=0.21) (Figure).



Fatal cardiovascular event-free rate

Conclusions: Our results suggest that ASV therapy shows good prognosis and revealed that ASV therapy is effective for all patients with regardless of the severity of SDB.

P5974 | BEDSIDE
Influence of angina and revascularization in patients with left ventricular systolic dysfunction and coronary artery disease: insights from the STICH trial

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Background: Patients with heart failure and coronary artery disease (CAD) who have angina are deemed to have a worse prognosis and, potentially, gain a greater benefit from coronary artery bypass surgery (CABG).
Purpose: We conducted a post-hoc analysis of the STICH (Surgical Treatment for Ischemic Heart Failure) trial in which patients with an ejection fraction ≤35% and CAD were randomised to CABG or medical therapy (MED) to investigate whether 1) angina is associated with a worse prognosis in those assigned to MED; 2) angina identified patients who had a greater benefit from CABG; 3) whether CABG relieved antianginal symptoms in this population.
Methods: Angina was measured using the Canadian Cardiovascular Society (CCS) Grading Scale at baseline and each follow-up visit. Patients were categorized according to presence or absence of angina if CCS ≥ I. We used multivariable Cox models to assess the association between CABG vs. MED and outcomes in patients with and without angina. To ascertain relation between CABG vs. MED and presence of angina at follow-up, we modeled a multivariable logistic regression using ≥1 CCS grade improvement as dependant predictor.
Results: At baseline, 770 patients (64%) reported angina and 442 patients (36%) reported no angina. Among patients assigned to MED, mortality rates were similar in patients with and without angina (HR=1.05; 95% CI [0.79–1.38]). All-cause mortality was similar in patients assigned to CABG compared to MED whether they had angina (HR=0.89; 95% CI [0.71–1.13]) or not (HR=0.68; 95% CI [0.50–0.94]) (p interaction=0.14). When cross-overs were considered, CABG reduced mortality in patients with and without angina ((HR=0.67; 95% CI [0.53–0.85] and HR=0.64; 95% CI [0.47–0.88] respectively). Composite of all-cause death or rehospitalisation was lowered in patients assigned to CABG whether they had angina (HR=0.78; 95% CI [0.66–0.93]) or not (HR=0.80; 95% CI [0.64–1.00]). Patients who reported angina before CABG were more likely to improve their symptoms with CABG (odds ratio, 1.43; 95% CI, 1.11 to 1.83; p<0.01).
Conclusions: Angina does not predict death in medically treated patients, nor does it identify patients with LV dysfunction and CAD that are more or less likely to benefit from CABG. However, CABG improves anginal symptoms to a greater extent than MED alone. These findings may influence clinical practice by diminishing the relevance of angina for treatment decisions and prognostication in patients with ischemic cardiomyopathy.

P5975 | BEDSIDE
Adherence to treatment guidelines and its association with clinical outcomes in chronic heart failure patients

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Background: Heart failure is a common disease characterized by high mortality and frequent exacerbation resulting in repetitive re-hospitalization. Pharmacological treatments–indicated in the chronic heart failure (CHF) treatment guidelines published by Japan Circulation Society–are reported to be beneficial. However, no large-scale study has evaluated adherence to the guidelines and its effects on outcomes.
Purpose: We aimed to investigate adherence to the CHF guidelines for drug therapy and the association between adherence and re-hospitalization in Japanese CHF patients.
Methods: We included CHF patients with records of New York Heart Association (NYHA) class at the first hospitalization in a prescription database of Japanese acute hospitals. Adherence was evaluated using class adherence indicator (CAI)–defined as the proportion of patients prescribed at least 1 drug from each drug class recommended in the guidelines–and global adherence indicator (GAI). For each patient, we calculated the GAI-5 value, which is the proportion of indicated care (across all five therapeutic classes) that was prescribed. Patients were categorized into 3 groups based on the GAI-5 values (good, 100%; intermediate, 50–80%; poor, <40%). We performed a Cox proportional hazard analysis to identify risk factors associated with poor prognosis.
Results: In total, 6,533 CHF patients (mean age, 74.4 years; 54.6% men; NYHA class I, 9.6%; II, 30.7%; III, 31.5%; IV, 28.2%) were eligible for analysis. CAI for angiotensin-converting enzyme inhibitors or angiotensin receptor blockers was 63.8% (such patients were termed "adherers"). Of the patients, 89.7%, 61.0%, 56.1%, and 25.0% showed adherence to diuretics, beta-blockers, mineralocorticoid receptors, and digitalis, respectively. Furthermore, 20.0%, 58.4% and 21.5% showed good, intermediate, and poor adherence, respectively. Kaplan-Meier curves with the log-rank test revealed that risks for re-hospitalization due to CHF worsening or due to any other cause within 360 days of discharge were higher in those with lower GAI-5 values.
Conclusions: To our knowledge, this is the first large-scale study on adherence to the Japanese CHF guidelines for treatment and its effects on outcomes. Similar to the reports of previous studies, CHF treatment in Japanese patients remained suboptimal. Our results suggest that poorer adherence to the guidelines may result in higher re-hospitalization rates. Thus, optimal pharmacological therapies that are in accordance with the latest guidelines are necessary to improve clinical outcomes in CHF patients.

P5976 | BEDSIDE
Clinical outcomes and benefit of ambulatory pulmonary artery pressure monitoring in heart failure patients according to initial pulmonary artery diastolic pressure

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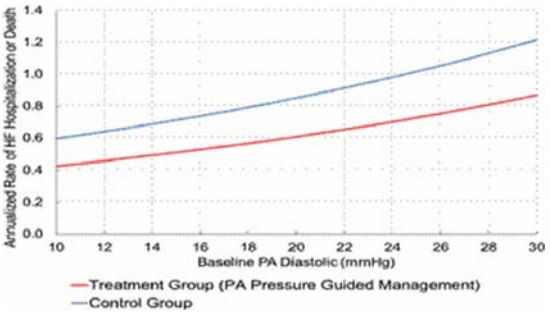
Background: Higher intracardiac filling pressures may identify heart failure (HF) patients at increased risk for hospitalization or death and represent a therapeutic target.

Purpose: Assess clinical outcomes and efficacy of pulmonary artery (PA) pressure monitoring in HF patients with reduced (HFrEF) or preserved (HFpEF) ejection fraction according to initial PA diastolic pressure (PAD).
Methods: CHAMPION randomized patients with HFrEF (<40%, n=430) or HFpEF (≥40%, n=119) to HF management with or without longitudinal guidance from a implantable PA pressure sensor. Clinicians had access to initial pressure measurements for all patients. The association between baseline PAD and risk of HF hospitalization (HFH) or death during the randomized access period and the interaction between baseline PAD and the efficacy of PA pressure-guided therapy were examined using the Andersen-Gill model.
Results: Over median follow-up of 18 months, there were 461 HF hospitalizations (373 in HFrEF, 88 in HFpEF) and 114 deaths (93 in HFrEF, 21 in HFpEF). Median baseline PAD for HFrEF was 19 mm Hg (IQR 14–25) and for HFpEF was 15 mm Hg (IQR 11–21). For the entire population, higher baseline PAD was associated with higher risk for HFH and death even after adjustment for clinical predictors (HR 1.03 per 1 mm Hg, p<0.001). Baseline PAD above the median was associated with higher risk for HFH and death in patients with HFrEF (adjusted HR 1.93, 95% CI 1.55–2.40, p<0.001) and HFpEF (adjusted HR 2.10, 95% CI 1.26–3.49, p=0.004). For any PAD at baseline, PA-pressure guided management reduced the risk of HFH and death (Figure).



Conclusions: Higher PAD at baseline enhances risk for HFH and death in both HFrEF and HFpEF. HF management guided by ongoing PA pressure monitoring reduces HFH and death at all levels of baseline PAD.

P5977 | BEDSIDE
The effect of disease management on health-related quality of life and depression symptoms in patients with heart failure: A randomized controlled trial

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Purpose: To study the effect of a disease management (DM) program on health related quality of life (HRQoL) and depression symptoms during follow-up in heart failure (HF) patients.
Methods: Patients with HF [N=1,360; 27.5% women; mean age (SD) =71 (11) years], recruited either from the community or after recent hospital admission for HF exacerbation, were randomly assigned to DM group (N=682) or usual care (UC) control group (N=678). Patients assigned to DM were cared by multidisciplinary teams of cardiologists and nurses operating in ten HF centers and a central call center. The primary composite outcome of the trial was time-to first hospital admission for HF exacerbation or death from any cause. HRQoL was measured with the short form (SF) 36-health survey and depression symptoms with the patient health questionnaire (PHQ) 9, at baseline and every 6 months during follow-up. Adjusted odds ratios (ORs) for attaining a =>2.5 points increase from baseline (minimal clinically important difference) in the physical component summary (PCS) and mental component summary (MCS) of SF-36 and having a PHQ-9 score =>10 during follow-up, were calculated.
Results: Patients were followed for a median period of 2.7 years (range: 0–5). DM was not found to be superior to UC with respect to the primary composite outcome. Compared to patients assigned to UC, patients assigned to DM were more likely to attain a =>2.5 points increases in PCS and MCS OF SF-36, and less likely to have depression symptoms (PHQ-9 score =>10) during follow-up; ORs (95% CIs): 1.53 (1.16, 2.01), 1.57 (1.25, 1.97), and 0.69 (0.53, 0.90), respectively; adjusted for baseline score, age, sex, study center and study period, year at recruitment, baseline NYHA classification and 6-minute walking distance. The odds of attaining a >2.5 points increases in PCS and MCS, and a PHQ-9 score >10 during follow-up was positively associated with greater baseline 6-minute walking distance. Female sex was associated with lower HRQoL scores compared to men.
Conclusions: DM program improved significantly HRQoL and depression symptoms in HF patients.

P5978 | BEDSIDE
Obesity is associated with increased risk of heart failure in patients with coronary artery disease

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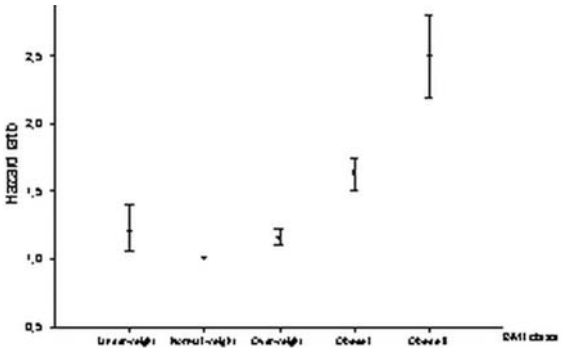
Background: Obesity is a known risk factor for development and progression of heart failure (HF). Only a few studies have examined the risk of developing HF in patients with obesity and coronary artery disease.
Purpose: We investigated the relationship between body mass index (BMI) and the risk of HF among patients with newly diagnosed coronary artery disease in Danish registers.
Methods: In a register-based retrospective cohort, a total of 34,430 patients with angiographically proven coronary artery disease were categorized according to their body mass index (BMI) into five groups. Normal weight (i.e. BMI 20–25 kg/m^2) was used as the reference group. HF was defined as diagnosis for HF or use of loop diuretics. Hazard ratios (HRs) with 95% confidence interval (CI) were estimated using multivariable Cox regression models.
Results: During the study (12 years of follow-up), 8,015 patients developed HF. Compared with the normal weight patients, the multivariable-adjusted hazard ratios (HRs) for HF were 1.19 (CI 1.1 to 1.3), 1.15 (CI: 1.1 to 1.2), 1.62 (CI: 1.5 to 1.7), and 2.5 (CI: 2.2 to 2.8) in underweight (BMI <20), overweight (BMI 25–30), obese class I (BMI 30–35), and obese class II (BMI >35) patients, respectively (Fig.1).



Association between BMI and risk of HF

Conclusions: We found a 2-fold increased risk of HF in obese patients with coronary artery disease compared to the patients with normal weight. Effective weight reduction strategies in this patient group may reduce the risk of developing HF.

P5979 | BEDSIDE
Heart failure disease management program and the six months readmission rate

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Background: HF is a chronic syndrome associated with frequent hospitalizations. It represents a considerable burden to the healthcare system with high rates of readmissions. Optimizing medical care through a special DMP may improve outcome and decrease readmission rates.
Purpose: To assess the effect of heart failure (HF) disease management program (DMP) on the six months all cause readmission rate for patients with HF as compared to regular care.
Methods: This is a prospective non-randomized clinical trial that was conducted during 2012 - 2013. Patients presenting with acute HF with EF ≤40% were recruited. We enrolled 151 patients of whom 71 were in DMP and 80 in the control group. Patients were enrolled in the control group when they elected to receive only regular care by their physicians. The DMP consists of 2 phases. Phase I started during the index hospitalization where education about HF symptoms, medications, diet and exercise was delivered. Phase II consisted of close outpatient follow-up after discharge. The first visit was at 7 days, then at 1 month and every 3 months for a total of 6 months. During follow-up augmentation of HF medications, education on disease management, diet and exercise were done. The primary outcome was all cause readmission rate at 6 months. The secondary outcome was all cause mortality at 6 months.
Results: The two groups were comparable at baseline. The majority were males, with 58% had ischemic heart disease and 40% were diabetics. The average EF in both groups was 30%. Patients enrolled in the DMP had a shorter length of stay in days (9.5±7.1 DMP group vs. 12.7±10.5 control group), (P=0.03).

However, the cost of each hospitalization was not significantly different (DMP: $3320.00±2785.00) vs. (control: $4218.00±$4519.00), (P=0.14). The primary outcome of all cause readmissions at 6 months was significantly lower in the DMP (28.2% DMP group vs. 57.5% control group) (P<0.001). The secondary outcome of all cause mortality tends to be lower at 6 months in the DMP vs. control (9.9% vs. 20.0% repectively) (P=0.08). A multivariate analysis for the predictors of the readmissions at 6 months was only significant for the DMP vs. the control group (Adjusted OR (95% CI); 0.26 (0.12–0.56); (P=0.001). The use of digoxin and dobutamine was associated with higher mortality (P=0.009).
Conclusion: A HF DMP that entails close follow-up after discharge with education, diet and exercise will decrease all cause readmission rates at 6 months and tends to lower mortality when compared to regular care.

TREATMENT OF HYPERCHOLESTEROLEMIA. A VISION TO THE FUTURE

P5980 | BEDSIDE
Sustained treatment effect of alirocumab on Lp(a): pooled analyses from 4,915 patients in ten phase 3 trials in the ODYSSEY program

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Background: Lipoprotein (a) [Lp(a)] is an independent risk factor for cardiovascular (CV) disease. Current treatment options for elevated Lp(a) levels are limited. Statins have not shown any effect on Lp(a).
Purpose: To evaluate the treatment effect of alirocumab on serum Lp(a) using data from 10 Phase 3 trials of 24–78 week duration, conducted in patients with heterozygous familial hypercholesterolemia, high CV risk, and/or statin intolerance, as monotherapy or on a variety of background lipid-lowering therapies (LLTs).
Methods: Pooled analyses were conducted across 2 trials (LONG TERM, HIGH FH, n=2,416) that compared alirocumab 150 mg every two weeks (Q2W) versus placebo and 8 trials that evaluated alirocumab 75 mg Q2W (increasing to 150 mg Q2W at Week 12 if LDL-C goals not achieved at Week 8) versus control. In 5 trials (COMBO II, OPTIONS I and II, ALTERNATIVE and MONO, n=1,456) the comparator was ezetimibe and in 3 trials (COMBO I, FH I and II, n=1,043) the comparator was placebo.
Results: After 24 weeks, Lp(a) levels were reduced from baseline by 25% with alirocumab 150 mg Q2W (vs. control) and by up to 23.5% (Week 12, vs. control) in studies using 75 mg Q2W (p<0.0001; Table). Reductions were observed at Week 12 and sustained through the end of the observation period (either Week 24 or 52, depending on the study). Treatment-emergent adverse event (TEAE) rates were generally similar between alirocumab and control patients. Common TEAEs in alirocumab-treated patients include influenza, headache, myalgia, and mild injection site reactions. Data up to 78 weeks will be available for presentation.
Conclusions: Across the ODYSSEY program, alirocumab therapy resulted in a sustained and significant reduction in Lp(a) maintained for at least 1 year independent of statin use. The mechanism for this effect requires further investigation.

P5981 | BEDSIDE
Futility of supplementation with Coenzyme Q10 for statin-induced myopathy: an updated (2015) meta-analysis of randomized controlled trials

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Introduction: A previous meta-analysis has not suggested any benefit of CoQ10 supplementation in improving muscle pain and plasma creatine kinase (CK) levels, two main measures of statin-induced myopathy (SIM). However, new studies have been published.
Purpose: To re-evaluate the efficacy of CoQ10 supplementation on SIM.
Methods: We searched the MEDLINE, Cochrane Library, Scopus, and EMBASE databases (up to 10 February 2015) to identify RCTs investigating the impact of CoQ10 on muscle pain and plasma CK activity.
Results: We included 10 RCTs with 446 participants. The results of the meta-analysis did not provide compelling evidence as to a significant effect of CoQ10 supplementation in reducing either the severity of myopathic pain (SMD: –0.36, 95% CI: –0.82–0.09, p=0.117) (figure) or plasma CK activity (WMD: 3.47 U/L, 95% CI: –2.32–9.26, p=0.240). These findings were robust in the leave-one-out analysis, and the calculated effect sizes were not sensitive to any single study included in the meta-analysis. A subgroup analysis was performed to assess the impact of dose (<200 vs ≥200 mg/day) and duration (<12 weeks vs ≥12 weeks) of supplementation with CoQ10 on the calculated effect sizes. The results suggest that changes in both efficacy measures were independent of dose and duration of supplementation. Likewise, large doses of CoQ10 - <400 and ≥400 mg - had also no significant effect both on myalgia and plasma CK activity (SMD –0.45, 95% CI: –1.02–0.13; p=0.13 and –0.08; 95% CI: –0.52–0.36; p=0.721, and WMD 5.06 U/L, 95% CI: –5.34–15.46; p=0.34, and –3.52 U/L –72.04–65.00; p=0.92, respectively).

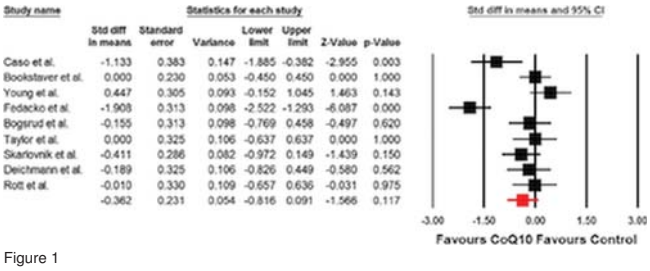

Figure 1

Conclusion: The results of this meta-analysis support the lack of any significant benefit of CoQ10 supplementation in improving statin-induced myopathy, even using higher CoQ10 doses.

P5982 | BEDSIDE
Effect of K-877, a potent and selective PPAR alpha modulator (SPPARM alpha), on cholesterol efflux from macrophages in dyslipidemic patients

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Introduction: Plasma concentration of high-density lipoprotein cholesterol (HDL-C) is inversely associated with the risk of atherosclerotic cardiovascular disease (ASCVD). The protection against atherosclerosis is largely mediated by stimulating the removal of cholesterol from macrophages by HDL and its component, ApoA1. K-877 is a potent and selective peroxisome proliferator-activated receptor alpha (PPARa) modulator, which improves lipid profiles including HDL-C, ApoA1 and ApoC3. Here, we hypothesized that K-877 increases cholesterol efflux capacity (CEC), which could be translated into ASCVD risk reduction.
Purpose: To investigate whether CEC is increased by K-877 in dyslipidemic patients.
Methods: This was a double-blinded, randomized cross-over study. A total of 33 dyslipidemic patients with fasting hypertriglyceridemia (≥150, <400 mg/dL) and low HDL-C (<50 mg/dL for males, <55 mg/dL for females) were randomized to twice-daily, K-877 0.4 mg/day or placebo groups for 4 weeks. After 4 weeks, each group was switched to the other treatment group and treated for another 4 weeks. Plasma lipids, lipoproteins, apolipoproteins and preß1-HDL were measured. CEC was measured by validated method; after pre-labeling with [3H] cholesterol, J774 cells were incubated with a media containing HDL fraction isolated by ultracen-

Abstract P5980 – Table 1

Alirocumab (n) and Control (n)	Pool of alirocumab 75/150 mg[a] vs ezetimibe (on background statins)[b] Alirocumab (669) vs Control (436)	Pool of alirocumab 75/150 mg[a] vs placebo (on background statins)[c] Alirocumab (693) vs Control (350)	Pool of alirocumab 75/150 mg[a] vs ezetimibe (without statins)[d] Alirocumab (178) vs Control (173)	Pool of alirocumab 150 mg vs placebo (on background statins)[e] Alirocumab (1601) vs Control (815)
Lp(a), % change to W12 vs control (ITT)[†]	–23.5 (1.7)*	–18.5 (1.6)*	–12.9 (2.8)*	–25.0 (1.2)*
Lp(a), % change to W24 vs control (ITT)[†]	–21.8 (1.9)*	–17.4 (1.7)*	–14.4 (2.9)*	–25.1 (1.2)*
Lp(a), % change to W52 vs control (ITT)[†]	–	–19.4 (1.8)*	–	–23.9 (1.3)*

W, week. All patients in pool of alirocumab vs placebo and ODYSSEY COMBO II were receiving background of maximally tolerated statin ± other LLT; patients in ODYSSEY OPTIONS studies were on commonly used statin doses. Intent-to-treat analysis. [a]Dose was increased from 75 to 150 mg at W12 if W8 LDL-C was ≥1.8 or ≥2.6 mmol/L (depending on CV risk); [b]Pool of ODYSSEY COMBO II + OPTIONS I + OPTIONS II (NCT01644188, 01730040, 01730053); [c]Pool of ODYSSEY COMBO I + FH I + FH II (NCT01644175, 01623115, 01709500); [d]Pool of ODYSSEY ALTERNATIVE + MONO (NCT01709513, 01644474); [e]Pool of ODYSSEY LONG TERM and HIGH FH (NCT01507831, 01617655). [†]Combined estimate for adjusted mean difference (SE) vs control; *p<0.0001 vs control.

trifugation from the patients. CEC was calculated from the ratio of [3H] cholesterol quantity in the HDL fraction.
Results: Treatment with K-877 increased HDL-C and ApoA1 and decreased ApoC3 from the baseline (16.1, 8.34 and –31.35%, respectively; $p<0.01$), but placebo did not. Treatment with K-877 also increased HDL3-C and preß1-HDL from the baseline (28.3 and 57.36%, respectively; $p<0.01$), but placebo did not. HPLC analysis showed that K-877 increased medium, small and very small HDL-C (22.34, 37.90 and 23.69%, respectively) and reduced large and very large HDL-C (–47.58 and –11.45%, respectively). HDL from patients treated with K-877 stimulated CEC more than that with placebo (2.97%, p=0.049). Positive correlation with CEC was observed in HDL-C and ApoA1.
Conclusions: This study revealed that K-877 exerted a positive influence on HDL-C in both quantity and quality based on the assessment on ApoA1, ApoC3 and CEC. These findings suggest that K-877 could reduce the risk of ASCVD by increasing CEC along with an increase of ApoA1, preß1-HDL and HDL3-C. Thus K-877 may inhibit the progression and even promote the regression of atherosclerosis.

P5983 | BEDSIDE
K-877, a selective PPAR alpha modulator (SPPARM alpha), ameliorates dyslipidaemia in patients with well-controlled LDL Cholesterol levels on statin therapy, without increases in serum creatinine

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Background: Patients treated with statins, particularly those with elevated TG and reduced HDL-C, are still at risk of cardiovascular disease (CVD) even when LDL-C are controlled. Additonal therapy to benefically alter the lipid profile is therefore warranted. K-877 is a SPPARMα, designed to be highly selective for PPARα, co-administerable with statins, and to modulate PPAR activity without undesirable effects.
Purpose: To assess the efficacy and safety of K-877 in dyslipidaemia patients whose LDL-C levels are adequately controlled with statins.
Methods: This was a multi-country, placebo-controlled, randomised, double-blind, parallel-group study in patients on atorvastatin, rosuvastatin or simvastatin with significant residual dyslipidaemia. Principal efficacy endpoints were % changes in TG and non-HDL-C, and principal safety endpoints were changes in serum creatinine and homocysteine. Male and female patients with controlled LDL-C were eligible for inclusion if concentrations of TG were 175–500 mg/dL (1.9–5.7 mmol/L) and HDL-C were 50 mg/dL (1.3 mmol/L) or 55 mg/dL (1.4 mmol/L) or less in men and women, respectively. The study was conducted in compliance with the principles of the Declaration of Helsinki.
Results: 408 patients were randomised to 7 treatment groups (placebo, 0.05 mg BID, 0.1 mg BID, 0.2 mg BID, 0.1 mg QD, 0.2 mg QD and 0.4 mg QD) and 91.9% completed 12-weeks treatment. Baseline TG, HDL-C and LDL-C levels were 245.3 mg/dL (median), 39.2 mg/dL (mean) and 88.4 mg/dL (mean), respectively. Compared to placebo, K-877 significantly reduced TG by 34.0–54.4% in all the treatment groups and non-HDL-C by 7.8–9.1% at 0.2 mg BID, 0.2 mg QD and 0.4 mg QD. K-877 also significantly reduced remnant cholesterol (TC - LDL-C - HDL-C) and apo CIII in all the treatment groups by 35.6–58.0% and 15.5–36.0%, respectively. In addition, K-877 significantly increased HDL-C by 7.4–12.9% in all the treatment groups except 0.1 mg QD and LDL-C by 9.2–20.5% in all the treatment groups except 0.05 mg BID. Serum creatinine was not changed significantly in any of the treatment groups. Homocysteine were significantly elevated at 0.2 mg BID and 0.4 mg QD by 2.3 and 2.4 μmol/L, respectively. Adverse events occurred in 56.7% of patients on placebo, but 46.4% of those in the K-877 groups. No other safety concerns were found during this 12-week study.
Conclusion: K-877 was well tolerated by statin-treated subjects with well-controlled LDL-C levels over 12 weeks. K-877 significantly reduced TG, non-HDL-C, remnant cholesterol and Apo CIII without significant increases in serum creatinine.

P5984 | BEDSIDE
Relationship of body weight and dosing of Evolocumab (EVO) for the treatment of hypercholesterolemia

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Background: Recent clinical trials have evaluated monoclonal antibodies (MABs) directed against proprotein convertase subtilisin kexin-9 (PCSK-9) as a novel treatment for hypercholesterolemia. Optimal dosing remains a subject of investigation. In particular, the effect of body weight (BW) has been incompletely analyzed.
Purpose: To evaluate whether BW leads to differences in the effects of evolocumab (EVO), an investigational MAB directed against PCSK-9.
Methods: Data from eleven Phase 2 and 3 clinical trials were analyzed by quartiles of BW. This data included unpublished information correlating EVO concentrations, free PCSK-9 levels, LDL-cholesterol response, and adverse events (AEs) by baseline BW. Biweekly versus monthly dosing regimens were separately analyzed.
Results: Circulating concentrations of EVO were highest in patients with the lowest BW and lowest in the heaviest patients. However, this difference resulted in only minor differences in free PCSK-9 levels and no discernible effects on LDL reduction. In all groups, EVO led to robust LDL reductions between 58.0% and 69.1% on top of that achieved by baseline therapy. AEs occurred at similar rates across quartiles of BW.

PK/PD data by quartile of body weight

Dose	Body weight (kg)	EVO conc. (μg/mL)	PCSK9 (% change)	LDL-C (% change)
140 mg biweekly	N	1055	1103	1131
41 to 69	11.2 (1.8 to 32)	–79.4 (–95.2 to –39.5)	–69.1 (–92.3 to –33.7)	
70 to 81	6.0 (1.3 to 20.9)	–74.4 (–92.6 to –38.7)	–69.1 (–89.3 to –26.8)	
82 to 93	4.6 (1.0 to 15.1)	–63.3 (–93.3 to –24.2)	–65.2 (–88.0 to –24.7)	
94 to 160	2.7 (1.0 to 10.7)	–56.7 (–89.2 to –30.2)	–62.9 (–87.0 to –16.6)	
420 mg monthly	N	1756	1795	1836
39 to 69	15.9 (3.0 to 45.8)	–52.6 (–86.8 to –22.7)	–63.1 (–85.5 to –28.2)	
70 to 81	8.9 (1.8 to 28.1)	–50.4 (–80.2 to –17.3)	–62.3 (–86.0 to –31.7)	
82 to 93	5.9 (1.2 to 21.6)	–41.4 (–74,9 to –5.0)	–60.7 (–84.9 to –24.4)	
94 to 175	4.5 (1.2 to 17.2)	–42.3 (–63.6 to –9.7)	–58.0 (–79.9 to –19.4)	

Median (90% CI) EVO concentration, PCSK9, and LDL-C at week 12.

Conclusion: EVO is a highly efficacious therapy for hypercholesterolemia across patients with different BW. Nonetheless, the lower levels of EVO found in the heaviest patients suggest that these individuals may experience a more rapid increase in LDL-C during delays in dosing or when discontinuing therapy. Therefore, heavier patients may have a narrower time window for optimal dosing.

P5985 | BEDSIDE
K-877, a selective PPAR alpha modulator (SPPARM alpha), improves dyslipidaemia in statin-treated patients with type 2 diabetes mellitus

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Background: Diabetic dyslipidaemia, characterised by elevated levels of TG and remnant cholesterol together with reduced concentrations of HDL-C is common in patients with type 2 diabetes mellitus (T2DM), even on statin therapy, and poses residual risk of cardiovascular disease (CVD). K-877 is a SPPARMα, designed to be highly selective for PPARα, co-administrable with statins, and to modulate PPAR activity without undesirable effects.
Purpose: To assess the efficacy and safety of K-877 in patients with T2DM who were adequately treated with statins.
Methods: We conducted a post-hoc, subgroup analysis of patients with a pre-existing diagnosis of T2DM who participated in a larger multi-country, placebo-controlled, randomised, double-blind, parallel group study in patients with statin (atorvastatin, rosuvastatin or simvastatin) controlled LDL-C but concentrations of TG 175–500 mg/dL (1.9–5.7 mmol/L), and of HDL-C 50 mg/dL (1.3 mmol/L) or 55 mg/dL (1.4 mmol/L) or less in men and women, respectively. The clinical study was conducted in compliance with the principles of the Declaration of Helsinki.
Results: 161 (39%) of 408 patients randomised to the main study had T2DM and received one of 7 treatments (placebo, 0.05 mg BID, 0.1 mg BID, 0.2 mg BID, 0.1 mg QD, 0.2 mg QD and 0.4 mg QD) for 12 weeks. 95.6% of the patients completed treatment. Baseline TG, HDL-C and LDL-C levels were 230.8 mg/dL (median), 38.4 mg/dL (mean) and 79.5 mg/dL (mean), respectively. Compared with placebo, which worsened most parameters, K-877 significantly reduced TG by 44.7–67.4%, Apo CIII by 23.8–39.7% and remnant cholesterol (TC – HDL-C – LDL-C) by 55.6–81.8% in all active treatment groups. Decreases in non-HDL-C by 5.4–17.3% compared to placebo were less consistent across groups, whereas significant increases in LDL-C were seen at 0.2 mg BID and 0.1 mg QD by 17.2% and 15.5%, respectively. Serum creatinine were not increased in any of the active treatment groups. Homocysteine concentrations were significantly increased by 1.7–3.2 μmol/L in all the active treatment groups except 0.2 mg QD. 57.7% of placebo patients reported an adverse event, as did 25.0–71.4% of K-877 patients, with no relationship to dose.
Conclusion: K-877, administered for 12 weeks in patients with significant dyslipidaemia despite statin-controlled LDL-C, was well tolerated by patients with T2DM and significantly reduced atherogenic lipids including TG, Apo CIII, remnant cholesterol and non-HDL-C, with no increase in serum creatinine.

P5986 | BEDSIDE
Impaired acetylsalicylic acid antiplatelet effects caused by dipyrone (metamizole) comedication can be prevented by order of intake

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Background: Acetylsalicylic acid (ASA) is the backbone of primary and sec-

ondary prevention of cardiovascular events. Impaired ASA antiplatelet effects are associated with increased incidence of events. Acute and chronic pain is frequent in patients with coronary artery disease (CAD). The majority of these patients rely on drugs for pain control. It is known, that non-steroidal anti-inflammatory drugs interact with ASA resulting in inhibition of ASA antiplatelet effects. Dipyrone (metamizole) is a non-opioid analgesic with favorable analgesic and antipyretic effects. We have recently shown that dipyrone interacts with ASA antiplatelet effects.

Purpose: We investigated the ASA and dipyrone interaction in patients with CAD and analyzed the drug-drug interaction to develop strategies to prevent the interaction.

Methods: We conducted an observatory study in 56 CAD patients on permanent ASA medication. 36 of these patients had additional dipyrone medication because of various forms of pain. Furthermore a parallel group trial in twelve healthy individuals was performed to investigate if order of intake influences the incidence of ASA and dipyrone interaction. In-vitro analyses in seven healthy individuals were conducted to investigate the drug-drug interaction. Antiplatelet effects were measured by light-transmission aggregometry and thromboxane formation. Dipyrone plasma levels by high-performance-liquid-chromatography.

Results: ASA antiplatelet effects were sufficient in all ASA treated CAD patients without dipyrone comedication. However residual platelet reactivity despite ASA medication occurred in 50% of ASA and dipyrone comedicated CAD patients. Dipyrone plasma levels coincide with the ASA induced inhibition of thromboxane formation. In-vitro increasement of ASA concentrations restores the inhibited antiplatelet effects of ASA. In healthy individuals, ASA medication 30 minutes prior to dipyrone medication prevents the inhibition of ASA antiplatelet effects by dipyrone whereas dipyrone medication prior to ASA blunts ASA antiplatelet effects.

Conclusion: Dipyrone medication inhibits ASA antiplatelet effects in CAD patients. This pharmacodynamic drug-drug interaction can be prevented by a strict order of intake with ASA medication prior to dipyrone intake.

PERCUTANEOUS VERSUS SURGICAL MANAGEMENT OF VALVULAR AORTIC STENOSIS: BOUNDARIES VERSUS OPPORTUNITIES

6016 | BEDSIDE
Improved outcomes following TAVI for aortic stenosis in low and intermediate risk vs. high risk patients: results from a multi-center Israeli TAVI registry

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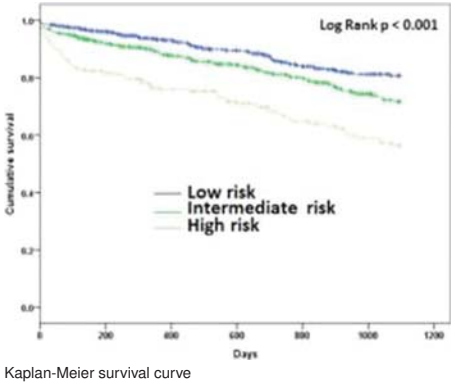
Background: Transcatheter aortic valve implantation (TAVI) for high risk aortic stenosis patients is comparable to surgical replacement. Despite a lack of data regarding the safety and efficacy of TAVI in lower risk patients they are already being treated by TAVI in many countries.

Aim: To assess safety and efficacy of TAVI in low risk patients.

Methods: Patients undergoing TAVI during 2008–2014 were enrolled (n=1349). Procedural outcomes were adjudicated according to VARC-2 definitions. Patients were stratified according to their STS score into 3 groups: High (STS ≥8, n=279, 21%), Intermediate (STS 4–8; n=494, 37%) or Low risk (STS <4; n=576, 42%).

Results: Low risk patients were younger and more likely to be males compared to intermediate/high risk patients. Baseline characteristics differed significantly between the groups with gradual increase in rates of prior CABG, stroke, PVD, renal failure, COPD and frailty, from low to high risk groups. Low risk patients were more likely to undergo TAVI via transfemoral route (72% vs. 88% vs. 95%, p<0.0001) and under conscious sedation (59% vs. 72% vs. 81%, <0.0001). Interestingly, there were no significant differences in the rates of procedural complications apart from bleeding. Short- and long-term mortality (Figure) were significantly lower for intermediate- and even more, for low-risk patients as compared to high-risk patients (p<0.001). Lower mortality for intermediate (HR 0.44, 95% CI 0.29–0.67) and low risk patients (HR 0.27, 95% CI 0.17–0.43) was maintained also after multivariable adjustment.



Kaplan-Meier survival curve

Conclusions: TAVI for intermediate or low risk patients is safe and associated with improved outcome compared to high risk patients. These data support the hypothesis that TAVI may achieve results comparable to surgical AVR also in lower risk patients.

6017 | BEDSIDE
The longterm outcome of patients after TAVI remains uninfluenced by pacemaker implantation in case of AV-block third degree

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Introduction: The transfemoral aortic valve implantation (TAVI) has established as a common therapy in patients with severe aortic stenosis and high surgical risk. Currently, different prosthesis types are available. A typical complication is AV block third degree with need for pacemaker implantation (PM). Our aim is to investigate whether the choice of the prosthesis type has an impact on the long-term outcome of patients.

Methods: From July 2008 to February 2014 560 TAVIs have been implanted at our Heart Center. 48.0% (n=269) received a Medtronic CoreValve (CV), 44.3% (n=248) an Edwards Sapien XT (SA), 4.8% (n=27) a Direct Flow, 2, 3% (n=13) a Portico and 0.5% (n=3) an Edwards Sapien S3. In 15.4% (n=86) of the patients the implantation of a pacemaker was indicated due to intracardiac conduction disturbances. The patients were examined during regular follow-up visits and received a pacemaker inspection with regard to the existence of an intrinsic rhythm (Ventricular pacing (VP) <50%). Additionally, a Kaplan-Meier survival analysis was performed.

Results: The 1-year mortality rate for patients with CV and SA is up to 15.0%. The mortality in the group of SA with PM, containing a small-sized number of cases, is slightly higher but not significantly different after 1 year and is balanced after 2 years. In 53% of the patients the intrinsic AV conduction recovered. There was no significant difference in the valve type between patients with or without recovering intrinsic AV conduction. The prosthesis diameter showed significant difference between these two groups. The smaller the valve diameter of the used valve prosthesis, the higher was the amount of patients with an intrinsic activity in the follow-up (p=0.046).

Conclusions: The long-term outcome seems to be independent of the type of prosthesis (SA vs. CV) and the presence of a pacemaker. The recovery of the AV node function due to periinterventional AV block applies to more than half of the patients and appears to be mainly dependent on the prosthesis diameter but not the valve type.

6018 | BEDSIDE
Outcomes from surgical para-valvular leak repair versus percutaneous closure

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Background: Para-valvular leak (PVL) is a complication after valve replacement surgery due to incomplete apposition from the suture ring to the native tissue. It has an incidence of 2–10% and 7–17% in the aortic and mitral position respectively. Although the great majority of cases has a benign course, 1–5% can have serious clinical consequences such as heart failure and hemolytic anemia. Redo-surgery mortality is high (10–15%), and rises even more with the number of previous sternotomies. Percutaneous treatment of PVL has emerged during last years as an alternative to surgery.

Purpose: To compare the in-hospital and one-year outcomes between surgical and percutaneous treatment of isolated PVL.

Methods: Patients who underwent either surgery or percutaneous treatment for PVL were included in the study. Those with additional surgical or percutaneous treatment other than isolated PVL were excluded from the analysis.

Results: Between 2006 and 2014 a total of 35 patients (mean age of 69.5±8.2 years and 43% of males) were included in the study. Of those, 18 (52%) and 17 (48%) underwent percutaneous and surgical techniques respectively. Among them, 10 (28.5%) were located in the aortic and 25 (71.5%) in the mitral valve without differences between groups. Similarly, no differences in age, gender, cardiovascular risk factors, left ventricular ejection fraction, renal function and pulmonary pressure were observed among groups. Euro-score 2 was 20,1±18,9 and 14,7±25 in the percutaneous and surgical group respectively, p=0.124. Successful treatment was achieved in all percutaneous patients and 94.1% of those with surgical techniques. In-hospital mortality was 5.5% in the percutaneous branch and 29.4% in the surgical group; p=0.061. Patients with percutaneous techniques had a shorter in-hospital admission than those surgically treated (6.0±6.5 vs. 32.5±33.0 days; p=0.004). At one year follow-up, cardiovascular mortality was lower in the percutaneous group (5.5% versus 31.2%;p=0.05). In addition, re-intervention rates were 5.8% and 27.3% in the percutaneous and surgical groups respectively, p=0.114.

Conclusions: In this series of patients, percutaneous treatment of isolated PVL

seems to be associated with a lower length of stay and one-year mortality than cardiac surgery. Larger series of patients will be necessary to confirm the results of this analysis.

6019 | BEDSIDE
An adapted ACEF score improves prediction of mid- and long-term mortality in patients undergoing TAVI

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Background: There are a several scoring systems available for risk stratification in cardiac surgery, the most important of which are the EuroSCORE-II, the STS and the ACEF score. However, in patients undergoing TAVI these scores have shown only a low accuracy for predicting both mid- and long term all-cause mortality. Postoperative acute kidney injury significantly worsens prognosis after TAVI. We aimed to assess the prognostic value of ACEF-7, a new score which includes the highest creatinine level detected within 7 days after the procedure, in predicting 6-month and 1-year mortality after TAVI.
Methods: 253 consecutive patients undergoing trans-aortic valve replacement (transfemoral n=210; transapical n=43) were enrolled. ACEF score, EuroSCORE II, STS score were calculated pre TAVI for all enrolled patients. ACEF-7 was calculated for all 1-week survivors (n=245, 97%) based on peak creatinine values post TAVI. The first analysis compared established scores (EuroSCORE-II, STS, ACEF) for all-cause mortality at 6-month and 1 year. In a second analysis we compared the predictive value of ACEF-7 to all the other scores for the same outcome. Patients were further stratified according to tertiles of ACEF-7.
Results: Overall mortality at 6 months and 1-year was 6.7% and 19% accordingly. The Euro-SCORE II, STS Score, and ACEF showed similar low accuracy for prediction of 6-month (AUC: 0.638 p=0.07; 0.632 p=0.01 and 0.664 p=0.001 respectively] and 1 year mortality (AUC: 0.635 p=0.01; 0.624 p=0.02 and 0.672 p=0.001 respectively).
In survivors at 1 week post TAVI (n=245) only ACEF scores showed significant accuracy in prediction of 6-month (AUC: 0.648, p=0.009) and 1-year mortality (AUC: 0.655, p=0.007). Most importantly the ACEF-7 score further improved this predictability for all-cause mortality at 6 month (AUC: 0.742 $p<0.001$) and 1 year (AUC: 0.750 $p<0.001$) as compared to the ACEF score. Multivariate analysis demonstrated that ACEF-7 was an independent predictor of both 6-month (HR 1.70 CI: 1.052–2.75; p=0.03) and 1-year mortality (HR 2.28 CI: 1.55–3.36;$p<0.001$).
Finally the predefined tertiles of ACEF-7 allowed an accurate risk stratification with a predicted 6-month survival of 91.1% in the ACEF-7mid tertile and of 65.7% in the ACEF-7high tertile (both $p<0.001$). Predicted 1-year survival was 88% for patients in the ACEF-7mid tertile and 52% for those in the ACEF-7high tertile.
Conclusions: The ACEF-7 score improves accuracy of mid and long term predictability of all-cause mortality beyond the currently used scores in patients undergoing TAVI.

6020 | BEDSIDE
Impact of right ventricular dysfunction on short- and long-term mortality following transcatheter aortic valve implantation

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Introduction: Impaired right ventricular (RV) function is an established predictor of adverse events after open-heart surgery for treatment of left-sided heart valve disease. The relevance of RV dysfunction on clinical outcomes following transcatheter aortic valve implantation (TAVI) is unknown.
Methods: Before undergoing TAVI for treatment of symptomatic severe aortic stenosis, 273 unselected patients had quantitative assessment of RV function by transthoracic echocardiography using tricuspid annular plane systolic excursion (TAPSE) and/or tricuspid annular velocity by Doppler tissue imaging (DTItv). The patients were divided into two groups: normal RV function (TAPSE$\geq$16mm and/or DTItv$\geq$10cm/s; n=190) and RV dysfunction (TAPSE$<$16mm and/or DTItv$<$10cm/s; n=83). Primary endpoints were all-cause and cardiovascular mortality at 30 days and 1 year.
Results: RV dysfunction was detected in 83/273 patients (30%). At baseline, patients with RV dysfunction were at higher surgical risk (mean STS score 9.7±5.5 vs. 6.9±4.6; $p<0.001$), had lower LVEF (42% vs. 54%; $p<0.001$) and had more often undergone coronary artery bypass grafting (18% vs. 6%; p=0.008). Concomitant moderate or severe mitral regurgitation was detected in 43% of patients with impaired RV function as compared to 20% of patients with normal RV function ($p<0.001$). Right heart catheterization revealed significantly higher pulmonary artery pressures in the RV dysfunction group (mean PA pressure 39 vs. 32mmHg; $p<0.001$). After multivariable adjustment, higher rates of all-cause (4% vs. 13%; HR 3.44, 95% CI 1.25–9.45; p=0.017) and cardiovascular mortality (3% vs. 12%; HR 4.27, 95% CI 1.40–13.04; p=0.011) were observed at 30 days among patients with RV dysfunction. However, this difference was no longer significant at 1 year of follow-up.
Conclusion: Patients with RV dysfunction as determined by transthoracic echocardiography at baseline have higher short-term, but not long-term mortality after TAVI. This observation may have important implications for patient selection and peri-procedural management.

6021 | BEDSIDE
Which is the optimal strategy for patients with severe aortic stenosis and intermediate-high risk profile? A multicenter propensity-score analysis in 991 consecutive patients

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Background: Despite the use of transcatheter aortic valve implantation (TAVI) has been proved as an effective strategy in patients at extremely high-risk or contraindicated to conventional cardiac surgery, the possibility to extend the use of TAVI also in patients with intermediate-high risk profile has been widely debated.
Purpose: Aim of this multicenter, European study was to investigate the clinical outcomes of patients with severe aortic stenosis and intermediate-high risk profile treated either by means of conventional surgery (sAVR), sutureless valves (SV) implantation or TAVI. Primary end-points were hospital (30 days) mortality as well as overall survival at 24 months follow-up; secondary end-points were cardiac related mortality, freedom from a composite end-point of MACCEs (defined as cardiac-related mortality, myocardial infarction, cerebrovascular accidents and major haemorrhagic events) and periprosthetic regurgitation$>$2.
Methods: Among 991 consecutive patients with intermediate-high risk profile (defined as STS-PROM$>$4 and Logistic Euroscore I $>$10), a propensity-score analysis was performed based on the strategy adopted: sAVR (Group 1, G1, n=204), SV (Group 2, G2, n=204) and TAVI (Group 3, G3, n=204). The criteria adopted for the propensity match were: STS-PROM, Logistic Euroscore I, age, LVEF, BMI, gender, diabetes, COPD, peripheral vascular disease, chronic renal failure, previous cerebrovascular accidents.
Results: Short-term mortality was significantly higher in patients undergoing TAVI (G1 = 3.4% vs G2 = 5.8% vs G3 = 9.8%; p=0.005) as well as peripheral vascular complications (G1 = 0% vs G2 = 0% vs G3 = 9.8%, $p<0.001$) and post-procedural PM implantation (G1=3.9% vs G2=9.8% vs G3 = 14.7%, $p<0.001$). At 24 months follow-up, overall survival (G1 = 91.3±2.4% vs G2 = 94.9±2.1% vs G3 = 79.5%±4.3%; p=0.001), and the survival free from the composite end-point of MACCEs and significant prosthetic regurgitation (G1 = 92.6±2.3% vs G2 = 96±1.8% vs G3 = 77.1±4.2%; $p<0.001$) were significantly higher in patients undergoing sAVR and sutureless valves than those receiving TAVI. Moreover, TAVI was identified as independent risk factor for overall mortality (OR=2.5, CI: 1.1–4-2, p=0.018) at multivariate Cox regression analysis.
Conclusions: TAVI was associated with a significantly higher incidence of perioperative complications (as postoperative PM implantation and peripheral vessels complications) and reduced survival at follow-up compared to sAVR and SV in patients with intermediate-high risk profile. The use of TAVI in this specific subset of patients should be investigated by further prospective randomized trials.

6022 | BEDSIDE
Matched comparison of surgical aortic valve replacement versus transcatheter valve implantation in intermediate to low risk aortic stenosis patients

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Background: Although results of transcatheter aortic valve implantation (TAVI) in intermediate-to-low risk patients have not been evaluated in randomized trials, the truth is that this therapy has been employed in this scenario with underreported results as compared to surgical aortic valve replacement (SAVR).
Methods: We enrolled 362 consecutive patients with severe symptomatic aortic stenosis and intermediate-to-low surgical risk (logEuroScore $<$20%) treated in our center with TAVI (103 pts) or single SAVR (259 pts) between 2009 and 2014. Patients were matched according to age, gender, logEuroSCORE, and left ventricular ejection fraction (LVEF).
Results: Mean age was 73±10.4 years, and 40.3% were women. LogEuroScore was 7.0±4.4% with mean LVEF of 52±9%. There were no differences regarding other comorbidities. The length-of-hospitalization was 11±8 days after TAVI vs. 17±7 days after SAVR (p=0.003), with n-hospital mortality rate of 7.8% in the TAVI group vs. 3.5% after SAVR, P=0.097. At one year follow-up, 4.9% of the TAVI pts and 7.3% of the SAVR group had suffered stroke (p=0.392), while mortality was 14.7% in the first group and 4.2% after SAVR, p=0.001.
Predictors of 1-year mortality in our entire study population included use of TAVI (14.7% vs. 4.2 after SAVR, p=0.001), a higher logEuroSCORE (9.3±4.3 vs. 6.9±4.3, p=0.006), and $\geq$2 residual aortic regurgitation (AR) (27.7% vs. 4.9%,

p<0.001). However, the last was the only independent predictor of mortality in multivariate analysis with OR=4.8, 95% CI (1.76–13.17), p=0.02.
Stratified risk analysis showed that among lower risk patients (log EuroSCORE <10%) both, the use of TAVI and ≥2AR were associated to higher mortality, with a rate of 13% in TAVI patients and 23.8% in those with ≥2AR as opposed to 4.3% of SAVR patients and 4.2% of patients with <2AR, p=0.032 and p=0.004, respectively. On the contrary, the use of TAVI was not related to higher mortality in the higher risk group (log EuroSCORE ≥10%) with 16.1% vs. 3.7% mortality rate, p=0.155 but, again, ≥2AR predicted higher risk of death (33.3% vs. 7.5%, p=0.016). In both risk subgroups only ≥2AR remained as predictor of mortality after multivariate analysis (OR=5.13 95% CI (1.3–20.2), p=0.019, and OR=4.62% 95% CI (1.04–20.5), p=0.044, respectively).
Conclusions: Mortality was higher after TAVI than after SAVR at 1-year follow-up but only in the lower risk subgroup of patients (LogEuroSCORE<10%). These poorer outcomes seems more related to a higher rate of residual aortic regurgitation than to the type of procedure chosen and, therefore, could be potentially improved with new-generation devices.

6023 | BEDSIDE
Prognostic effect of permanent pacemaker implantation on mortality after transcatheter aortic valve replacement

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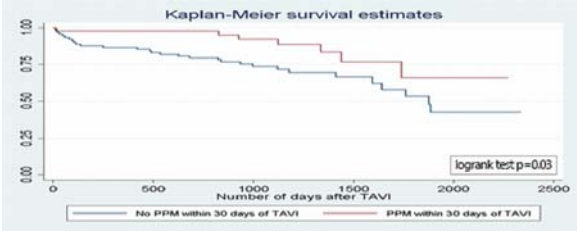
Background: Transcatheter aortic valve implantation (TAVI) is now an established treatment for high-grade aortic valve stenosis in patients found unfit for open heart surgery, but has been shown to cause cardiac conduction disorders requiring permanent pacemaker (PPM) implantation. Long-term effect of PPM implantation in this setting remains ambiguous.
Purpose: To investigate the association between post-TAVI PPM implantation and long-term all-cause mortality.
Methods: In this single-center study, we included 168 consecutive patients who underwent TAVI from 2008 to 2012 and were followed until mid-2014. Patient characteristics, ECGs (prior to and within 4 days of TAVI) and PM data were collected retrospectively through electronic medical records. Kaplan-Meier plots and Cox regression analysis were performed.
Results: 40 subjects were excluded due to PPM prior to TAVI or missing ECGs, leaving 128 patients for final inclusion. 41 (32%) patients received a PPM (mean age 82 vs. 80 in patients without PPM, p=0.06) within 30d of the TAVI procedure. The PQ- and QRS-interval increased significantly from 182±37 and 107±27 pre-TAVI to 200±55 and 132±41 ms post-TAVI. Median follow-up time was 1387d (691–2335) and 37 (29%) patients died. One- year mortality was 14% for non-PPM patients vs. 2% in PPM patients, and mortality at 5 yrs 70% vs. 54% (Figure). Independent mortality predictors were: not receiving a PPM (HR 3.4, p=0.01), post-procedural atrial fibrillation (HR 8.7, p=0.01) and a prior diagnosis of chronic obstructive pulmonary disease (HR 3.3, p=0.003). Left bundle branch block was not statistically significant (HR 1.9, p=0.11).



Survival curves by PPM-status

Conclusion: In this study TAVI-patients with a PPM implanted had better long-term survival than patients in whom a PPM was not implanted.

6024 | BEDSIDE
Impact of small annulus on reverse remodeling of left ventricular hypertrophy and mid-term outcome following transcatheter aortic valve implantation compared with surgical aortic valve replacement

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Background: The extent and effect of Left ventricular (LV) reverse remodeling in aortic stenosis (AS) patients with small annulus remains unclear. And the impact of small annulus on those outcome after transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement (SAVR) also remains equivocal.
Purpose: The aim of this study was to investigate the impact of small annulus on reverse remodeling of LV hypertrophy and mid-term outcome in patients with severe AS following TAVI compared with SAVR.
Methods: From Jan. 2013 to Aug. 2014, a total of 206 consecutive patients underwent aortic valve replacement were retrospectively enrolled. We defined annulus with 20mm or less as small annulus and the ratio between the measured LV mass index (LVMi) to the pre-procedural LVMi as LVMi ratio.
Results: The age of the 75 severe AS patients with small annulus ranged from 63 to 95 years (mean±SD, 80.7±7.0 years). In the analysis of small annulus, aortic valve intervention reduced LVMi immediate after the procedure and kept decreasing to 6months follow-up. In comparison with each procedure, post-procedural LVMi, LVMi ratio were significantly lower in the SAVR group than in the TAVI group, and these difference remained to 6months follow up. However, clinical efficacy endpoint 30 days after procedure was similar between the two groups (P=0.40).

Change of LV mass index

	All	SAVR	TAVI	P value
Post-procedure				
LV mass index (g/m^2)	128.5±32.2	123.5±29.4	139.9±35.8	0.03
LV mass index ratio	0.95±0.16	0.92±0.17	1.03±0.10	<0.0001
3 months follow up				
LV mass index (g/m^2)	122.8±30.9	116.1±27.6	138.9±33.1	0.003
LV mass index ratio	0.90±0.14	0.85±0.11	1.01±0.12	<0.0001
6 months follow up				
LV mass index (g/m^2)	120.3±31.9	112.4±27.0	138.1±35.6	0.001
LV mass index ratio	0.88±0.15	0.82±0.09	1.02±0.16	<0.0001

Conclusion: In the severe AS patients with small annulus, aortic valve intervention reduced LVMi. And SAVR significantly decreased LVMi compared with TAVI. Though mid-term clinical efficacy outcome was similar, further investigation was considered to be needed in order to confirm long-term outcome.

6025 | BEDSIDE
High-sensitivity troponin and diagnosis of myocardial infarction after combined aortic valve replacement and coronary artery bypass grafting

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Background: The Universal Definition for type 5 myocardial infarction (MI) applies to coronary artery bypass grafting (CABG), while perioperative MIs for other cardiac surgeries are rarely studied and not specifically defined. Our previous studies found isolated aortic valve replacement (AVR) to have higher troponin rises than CABG.
Purpose: We assessed whether post-operative high-sensitivity troponin (hs-TnT) at pre-specified thresholds, with or without concurrent ischaemic changes on ECG or echocardiogram, predicted mortality and morbidity after AVR+CABG.
Methods: Patients undergoing AVR+CABG during July 2010-December 2012 were identified (n=167), and hs-TnT routinely measured 12–24 hours post-operatively were collected. We pre-specified 140ng/L (10 times 99th percentile upper reference limit (URL)), 500ng/L (10 times coefficient of variation of 10% for 4th generation troponin T applied to hs-TnT as cutpoints for analyses and excluded patients with unstable elevated pre-operative troponins (n=26).
Results: Amongst 141 patients, median hs-TnT was 690ng/L, with 141 (100%) having post-operative hs-TnT>140ng/L and 95 (67.4%) >500ng/L, while 27 (19.1%) had new ECG or echocardiographic changes. C-statistics and 95% confidence interval for operative mortality were hs-TnT alone 0.711 (0.576–0.845), ECG and/or echocardiographic changes alone 0.730 (0.527–0.932) and combination with hs-TnT>500ng/L threshold 0.764 (0.559–0.968). In multivariate analyses, the MI criteria to independently and most strongly predicting operative mortality was hs-TnT>500ng/L+ECG and/or echocardiographic changes odds ratio 15.9 (95% confidence interval 2.33–109); and for mortality during follow-up the same criteria hazards ratio 7.05 (2.40–20.7).
Conclusion: Hs-TnT>500ng/L+ECG and/or echocardiographic criteria was strongly prognostic of short and long-term mortality after AVR+CABG. Our findings suggest higher hs-TnT thresholds for defining MI after AVR+CABG than isolated CABG to be more appropriate.

NOVEL INSIGHTS IS PATHOPHYSIOLOGY

6037 | BEDSIDE
Hypotension in patients with acute heart failure: Insights from RELAX-AHF

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Background: Hypotension during treatment of acute heart failure (AHF) is an important adverse event linked to worse outcomes. The clinical variables associated with in-hospital hypotension, and whether its outcomes differ with serelaxin are unknown.

Methods: RELAX-AHF was a randomized trial of serelaxin vs. placebo in 1161 AHF patients (pts) with systolic blood pressure (SBP)>125 mmHg. We assessed the baseline (BL) clinical characteristics associated with in-hospital confirmed BP decrease events (CBPDE). The protocol definition for CBPDE was either a decrease in SBP to <100 mmHg or a >40 decrease from BL or both. Study drug dose was reduced by 50% in those who dropped by 40 vs BL and were still >100. Pts with SBP decrease <100 had to discontinue study drug. In post-hoc multivariate analysis, we evaluated biologic correlates and outcomes of pts with and without CBPDE, as well as the impact of serelaxin. Outcomes included in-hospital worsening heart failure (WHF), cardiovascular (CV) death or HF/renal rehospitalization (60-day), and CV mortality (180-day).
Results: Of 1150 AHF pts with complete CBPDE data, 272 (24%) had a CBPDE of which 93% were asymptomatic. Clinical variables associated with CBPDE were older age, increased BL respiratory rate, worse BL dyspnea, lower hemoglobin and sodium, and increased bilirubin and alkaline phosphatase. Event rates for in-hospital WHF and 180-day CV mortality were lower in serelaxin-treated pts compared with placebo-treated pts regardless of whether a CBPDE occurred (Table).

Table 1. Unadjusted and adjusted association of CBPDE with and without treatment with subsequent outcomes

Outcomes	No CBPDE (N=878)		CBPDE (N=272)		Adjusted interaction p-value
	Serelaxin (N=405)	Placebo (N=473)	Serelaxin (N=168)	Placebo (N=104)	
Worsening heart failure	27 (6.7%)	51 (10.8%)	12 (7.1%)	20 (19.2%)	0.14
HF/RF rehospitalization through day 60	39 (9.8%)	41 (9.0%)	20 (12.4%)	9 (9.2%)	0.59
CV mortality through day 180	24 (6.0%)	44 (9.4%)	10 (6.1%)	10 (9.8%)	0.88

Data presented as n (K-M %).

Conclusion: Blood pressure decrease events occurred in nearly a quarter of AHF pts during hospitalization and were associated with older age, baseline dyspnea severity, and abnormal laboratory values. WHF and 180-day CV mortality were lower in serelaxin-treated pts compared with placebo-treated pts regardless of whether a blood pressure decrease event occurred.

6038 | BENCH
Neutrophil-dependent cardiac post-infarct remodeling in mice is mainly mediated by myeloperoxidase

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Background: Polymorphonuclear neutrophils (PMNs) play a pivotal role within the orchestra of inflammation, oxidative stress and structural remodeling in response to cardiac injury following myocardial infarction (MI). Neutrophil depletion reduces post-MI infarct size and the extent of cardiac injury. However, the mechanisms by which PMNs mediate MI-induced LV remodeling remains to be fully elucidated. Myeloperoxidase (MPO) is primarily released by activated PMNs and influences structural remodeling in a redox-sensitive manner. In order to improve our understanding on how PMNs influence post-MI LV remodeling and cardiac function, we compared the effect of PMN-depletion and MPO-knockout on LV remodeling and cardiac function in a murine model of MI.
Purpose: Understanding how PMNs influence post-MI LV remodeling and cardiac function might give rise to new therapeutic options for post-MI patients.
Methods and results: PMN-depleted mice, MPO-knockout (MPO–/–) mice and wild type (WT) mice were subjected to left ventricular infarction by ligation of the left anterior descending artery. Depletion of PMNs was performed two days before LAD ligation by Ly6G antibody injection. FACS analysis revealed complete absence of Ly-6G positive plasma cells for at least 14 days. Functional and structural analyses were performed on day 7 and 8 after MI. Echocardiography revealed a significantly improved ejection fraction (EF) in PMN-depleted and MPO–/– mice compared to WT mice (8.58±1.12% in WT vs 18.01±0.98% in MPO–/–, $p<0.001$; vs 13.59±1.85% in PMN-depl., $p<0.05$). Histological analysis demonstrated attenuated structural remodeling, indicated by significantly reduced LV fibrosis (78±2% in WT vs 65±2% in MPO–/–, $p<0.001$; vs 61±5% in PMN-depl., $p<0.05$) and augmented LV wall thickness in PMN-depleted and MPO–/– mice compared to WT mice (470.2±14.51 μm in WT vs 651.7±38.69 μm in MPO–/–, $p<0.01$; vs 680.1±41.76 μm in PMN-depl., $p<0.01$). Interestingly, there was no significant difference in regards to cardiac dysfunction and structural remodeling between MPO–/– and PMN-depleted mice.
Conclusion: Myeloperoxidase-deficiency was as effective as PMN-depletion in the attenuation of post-MI LV dysfunction and structural LV remodeling. Thus, MPO appears to be an important mediator of PMN-induced LV remodeling and cardiac dysfunction after myocardial infarction in mice.
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6039 | BENCH
Circulating microRNAs in experimental model of heart failure with preserved ejection fraction: effects of high-intensity exercise training

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Background: Although the incidence of heart failure with preserved ejection fraction (HFpEF) is increasing, current diagnostic methods are not precise and treatment remains a major challenge. Therefore, the need for better predictive methods and therapies is obvious.
Purpose: To investigate the diagnostic utility of plasma circulating miRNAs and the effects of high intensity interval training (HIT) on miRNA profile in an animal model of HFpEF.
Methods: Female Dahl salt-sensitive rats were randomized in three groups: sedentary low-salt diet (LS, N=15: 0.3% NaCl), sedentary high-salt diet (HS, N=11: 8% NaCl) or high-salt diet submitted to HIT (N=10: 8% NaCl + HIT, 3×38 min/wk; 4 intervals of 4 min at 90% peakVO2). Cardiac function was evaluated by echocardiography, while circulating miRNA profile was assessed in the plasma by qPCR, followed by construction of ROC curve analysis.
Results: We found two miRNAs (rno-miR-21–5p and rno-let-7b-5p) differently expressed in the plasma of HS compared to LS rats. Both miRNAs correlated modestly with most of the echocardiographic parameters for HFpEF (miR-21: R2=0.3913 and p=0.0016 for E/e' ratio; R2=0.5746 and p=0.0040 for E/A ratio; let-7b: R2=0.3807 and p=0.0019 for E/e' ratio; R2=0.3487 and p=0.0031 for E/A ratio). ROC curve analyses revealed that both miRNAs presented superior sensitivity and specificity as compared to NT-proBNP (AUC: 0.9273 vs. 0.8667 vs. 0.7879) for distinguishing HS from LS rats. MiR-21 was 1.5 fold reduced and let-7b level was 1.7 fold increased in HS when compared to LS rats. In addition, HIT prevented deregulation of both miR levels in HFpEF rats.
Conclusion: Taken together, our data suggest miRNA plasma profiling is a useful diagnostic tool for HFpEF. We also show that HIT prevented miRNA deregulation in an animal model of HFpEF, and therefore might serve as a potential new therapeutic strategy.
Acknowledgement/Funding: European Commission (FP7 - Health - 2013; OPTIMEX - 602405)

6040 | BEDSIDE
The association between platelet/lymphocyte ratio (PLR) and coronary artery disease severity in asymptomatic low ejection fraction patients

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Background and aim: Performing a coronary angiography in patients with heart failure of unknown etiology is often justified by the diagnostic assessment of ischemic heart disease. However, the clinical benefit of this strategy is not known. The platelet-lymphocyte ratio (PLR) is a novel inflammatory marker, which may be used in many diseases for predicting inflammation and mortality The aim of this study was to investigate whether PLR levels before coronary angiography predict CAD severity.
Methods: We examined 156 Heart Failure (HF) patients with no symptoms of refractory heart failure or angina, who underwent coronary angiography. Coronary artery disease severity was calculated by using Gensini score after coronary angiography. Score 0 was control group, score 0–20 was mild atherosclerosis group and score >20 was severe atherosclerosis group. Mean PLR values of the three study groups were compared.
Results: The mean PLR of the severe atherosclerosis group was significantly higher than that of the mild atherosclerosis and controls groups ($p<0.001$). Pre-procedural PLR level was found to be independently associated with Gensini score, together with age and high LDL levels in the multivariate analysis

Table 1. Comparison of baseline demographic characteristics and cardiovascular risk factors of the study population

	Control Group n=60	Mild atherosclerosis n=64	Severe atherosclerosis n=32	P
Age, years	54.3±13.1	61.8±11.6	60.8±10.2	0,002
Male, n (%)	43 (71)	46 (71)	22 (68)	0,94
Hypertension, n (%)	18 (30)	23 (35)	15 (46)	0,27
Diabetes, n (%)	10 (16)	10 (15)	9 (28)	0,29
LVEF	30±6,3	32±6,9	32±5,6	0,06
LDL, mg/dL	139±54	168±55	176±57	0,03
HDL, mg/dL	42±10	46±13	46±12	0,108
WBC, $x10^9$/L	7,8±2,1	7,8±2,0	7,6±2,0	0,90
Platelet, $x10^9$/L	213±66	233±69	305±80	0,001
Lymphocyte, $x10^9$/L	1,91±0,63	1,84±0,76	1,78±0,70	0,70
PLR	118,4±40,4	145,2±96,5	183,5±61,6	0,001

Conclusions: Our study suggests that high PLR appears to be additive to conventional risk factors and commonly used biomarkers in predicting severe atherosclerosis of asymptomatic low ejection fraction patients.

6041 | BEDSIDE

Gremlin-1 expression correlates with cardiac fibrosis and left ventricular dysfunction visualized by cardiac magnet resonance imaging in non-ischemic heart failure

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Background: Gremlin-1 (Grem1), an antagonist of bone morphogenetic proteins, is involved in fibrotic tissue formation in kidney and lung. Recently, it was shown that Grem1 correlates with the degree of myocardial fibrosis on endomyocardial biopsy and adverse prognosis. However, the correlation of endomyocardial Grem1 expression and late gadolinium enhancement (LGE) in cardiac magnet resonance imaging (MRI) is unknown.
Methods: 211 patients with non-ischemic heart failure underwent endomyocardial biopsy with Grem1 staining and contrast-enhanced cardiac MRI (1.5 Tesla scanner; Siemens Medical Systems, Germany). Grem1 staining was classified as "negative" (score 1 or 2) or "positive" (score 3 or 4). Scores for Grem1 were obtained in a blinded manner from 1–2 sections per staining by 2 investigators. For LGE imaging a two-dimensional inversion-recovery segmented k-space gradient-echo MR sequence was performed. MRI images were acquired in short- and long-axis views 10–15 minutes after intravenous injection of 0.15 mmol per kilogram body weight gadobutrol (Gadovist, Bayer Healthcare, Germany). End-diastolic volumes and end-systolic volumes were used to determine left ventricular ejection fraction.
Results: 140 out of 211 patients (66.4%) had Grem1 positive endomyocardial biopsies. Grem1 positive patients had a significantly higher rate of LGE-positive cardiac MRIs (65% vs. 51% in Grem1 negative patients, respectively, p=0.045). Further, Grem1 positive patients were in higher NYHA-class (mean 2.2±0.8 vs. 1.9±0.7; p=0.010), had a lower LVEF (39.1±14.6 vs. 46.1±15.3%, p=0.002), a higher LVEDD (55.1±9.4 vs. 51.9±9.5, p=0.013) and higher serum levels of BNP (2462±3356 mg/dl vs. 936±1508 mg/dl, p=0.003).
Conclusions: Patients with a higher expression of Grem1 in their endomyocardial biopsy demonstrate a higher amount of cardiac fibrosis visualized by contrast-enhanced cardiac MRI. Grem1 positive patients show more severe clinical signs of heart failure.

6042 | BEDSIDE

Biomarkers of heart failure in exhaled breath

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Purpose: Heart failure (HF) is widely prevalent disease that have multiple causes. Patients with HF often present with signs and symptoms that are often nonspecific. The purpose if this study was to find out novel biomarkers of HF in exhaled breath.
Methods: From October 2013 to February 2015, we included 46 patients with LV EF less than 45% in heart failure group and 15 patients without HF in control group. We collected fasting exhaled breath samples of all patients in 1L Tedlar bags. Exhaled breath was analyzed using PTR-MS (Compact PTR-MS, Ionicon, Austria).
Results: The baseline characteristics were similar in both groups. The mean EF in HF group was 34±8%. In compare with control group several biomarkers were significantly higher in HF group. They are acetone, acetic acid, ethanol, propylene and xylol (Table 1). The greatest difference was observed in the concentrations of acetone ($p<0,0001$) and propylelne (p=0,002). Receiver operator characteristic (ROC) analyses were performed to assess optimal cutoff points for these biomarkers and to calculate sensitivity and specificity. The areas under the ROC curve for acetone and propylene were 0,809 and 0,77, respectively. The optimal cutoff concentration for acetone was 268,2 ppb, corresponding to sensitivity of 86,7% and specificity of 46,7%. The optimal cutoff concentration for propylene was 119 ppb, corresponding to sensitivity of 71,1% and specificity of 46,7%.

Biomarkers in exhaled breath

	HF group (n=46)	Control group (n=15)	p
Acetone, ppb	800 (352 - 2986)	316,8 (230–376)	<0,0001
Propylene, ppb	207,5 (103–568)	106 (74–138)	0,002
Acetic acid, ppb	31,7 (21–48)	23,5 (20–25)	0,012
Ethanol, ppb	18,9 (13–32)	10,4 (9–21)	0,021
Xylol, ppb	1,1 (0,8–2,7)	0,64 (0,6–1,2)	0,027

Conclusion: There is significant difference in exhaled breath between patients with and without heart failure. The concentrations of several biomarkers in exhaled breath are higher in patients with heart failure with reduced EF. We estimated cutoff concentrations of acetone and propylene for heart failure. These biomarkers possessed tolerable sensitivity and low specificity.
Acknowledgement/Funding: This study was supported by Russian Academy of Science

6043 | BEDSIDE

The novel cardiovascular biomarker secretoneurin predicts mortality and shock in critical ill patients with infections

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Background: Secretoneurin (SN) has a direct effect on cardiomyocyte Ca2+ handling and provides independent prognostic information in patients with cardiovascular disease, but whether SN may predict mortality and shock in critically ill patients with infections is not known.
Methods: We measured circulating SN levels in 232 patients with severe sepsis (FINNSEPSIS Study) and validated the results in 94 patients with acute respiratory failure and infections (FINNALI substudy). SN was compared to established risk factors and biomarkers, including high-sensitivity troponin T (hs-TnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP).
Results: SN levels measured on intensive care unit (ICU) admission in both cohorts were correlated with established risk indices in patients with critical illness, including SOFA and SAPS II scores, and with hospital mortality (Fig). In patients with severe sepsis, admission SN levels (logarithmically transformed) were associated with hospital mortality (OR 3.17 [95% CI 1.12–9.00], p=0.030) and shock during the hospitalization (OR 2.17 [1.06–4.46], p=0.034) in analyses that adjusted for the other risk factors, including cardiovascular biomarkers. SN levels were also associated with hospital mortality after adjusting for other risk factors in the validation cohort, while neither hs-TnT nor NT-proBNP were associated with mortality or shock in multivariate analyses in the two cohorts. In both cohorts the optimal cutoff for SN levels on ICU admission to predict hospital mortality was ~175 pmol/L and higher levels were associated with mortality also when adjusting for SAPS II and SOFA scores.

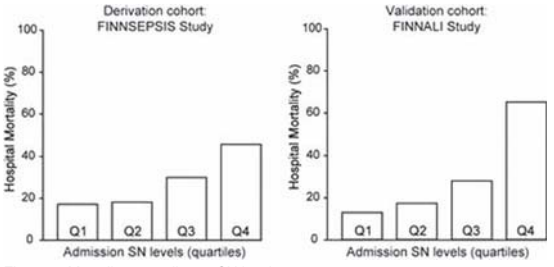

Figure 1. Mortality according to SN levels

Conclusion: SN levels provide incremental information to established risk indices for the prediction of mortality and shock in critically ill patients with severe infections.
Acknowledgement/Funding: This study was funded by Akershus University Hospital.

6044 | BEDSIDE

Myocardial fibrosis at cardiovascular magnetic resonance predicts left ventricular reverse remodelling

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Purpose: In nonischaemic dilated cardiomyopathy (NICM), myocardial fibrosis at cardiovascular magnetic resonance (CMR) is associated with worse prognosis. Aim of the study was to investigate whether myocardial fibrosis progresses during follow-up and whether its absence is associated with left ventricular reverse remodelling (LV-RR).
Methods: One-hundred-and-twenty-five NICM patients (age 51±16 years, 82 male) were enrolled and underwent baseline CMR; patients with ischaemic, valvular, congenital heart disease, other cardiomyopathies or contraindications to CMR were excluded from study entry. After a 24-month follow-up on optimal medical therapy, all patients underwent a second CMR; patients who died, underwent device implantation or declined a second CMR, were also excluded from the study. Late gadolinium enhancement (LGE), an index of myocardial fibrosis, was quantified on post-contrast CMR images. LV-RR was defined as an increase in LV ejection fraction ≥10 U or decrease in LV end-diastolic volume ≥10% at follow-up.
Results: Mean LV ejection fraction was 41±11% at baseline, 47±12% at follow-up: LV-RR was observed in 59 patients (47%), with no age or gender difference (p=NS). LGE was present in 48 (38%) patients at baseline (mean extent 5±6% of LV mass), in 76 (61%) patients at follow-up (mean extent 7±7%, $p<0.01$ vs. baseline). Patients experiencing LV-RR during follow-up presented a baseline worse LV ejection fraction (36±12%) than no-LV-RR patients (45±9%, $p<0.01$), greater

LV volumes (123±38 vs. 110±22 ml/m^2, p=0.02) and worse right ventricular ejection fraction (54±12% vs. 59±10%, p=0.02). Nevertheless, only 17 (29%) LV-RR patients presented LGE compared to 31 (47%, p=0.04) no-LV-RR patients. Moreover, among LGE-positive patients (n=48), only 17 (35%) developed LV-RR, while among LGE-negative patients (n=77), 42 (55%) developed LV-RR (p=0.04). Multivariate regression analysis showed that the absence of LGE at baseline CMR was a strong predictor of LV-RR (p=0.02), even after correction for age, New York Heart Association class, LV volumes and systolic function.

Conclusions: In patients with idiopathic dilated cardiomyopathy, LGE tended to increase during follow-up; the absence of LGE at baseline was a strong independent predictor of LV-RR at 2-year follow-up, irrespective of the initial clinical status and the severity of ventricular dilatation and dysfunction.

6045 | BEDSIDE
Determinants of long-term outcomes in the extremely aged patients hospitalized for acute heart failure

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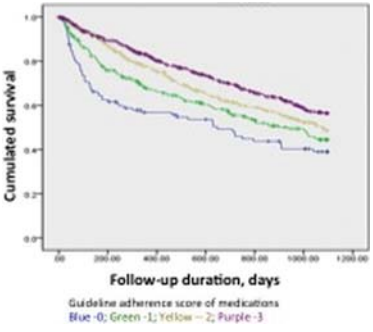
Background: The clinical characteristics and prognostic factors of patients with acute heart failure (AHF) might be different between the elderly and the general population. We attempt to explore the determinants of outcomes in the extremely aged patients.

Methods and results: Based on the data of an intramural registry, patients aged ≥80 years and hospitalized for AHF were eligible for this analysis. A guideline adherence score of medications (GASM) was calculated by the prescriptions of β-blocker, spironolactone, and ACEI/ARB, each medicine was count 1 point, 3 points was considered as the best medical adherence. National Death Registry was linked for the outcomes. A total of 1295 extremely aged subjects (86±4 years, 34.1% systolic HF) were enrolled. During a mean follow-up duration of 26.7±24.3 months, 532 subjects (41.1%) died. The dead were even older, had lower hemoglobin, sodium level and eGFR, and higher LVEF, RVSP, uric acid (UA) and NT-proBNP levels. With adjustments of age, gender and eGFR, Hgb [0.90 (0.86–0.95)], sodium [0.97 (0.96–0.99)], LVEF [0.54 (0.39–0.75)], RVSP [1.01 (1.003–1.01)], UA [1.07 (1.03–1.12)], and NT-proBNP [2.01 (1.53–2.65)] remained associated with mortality. The Kaplan-Meier survival analysis clearly demonstrated a trend toward better survival along with the increase of GASM in subjects with systolic HF and in the total population.(Figure)



Conclusions: The proposed prognostic factors remained associated with mortality in the extremely aged patients hospitalized for AHF. Adherence to the guideline still was essential to improve their clinical outcomes.

6046 | BEDSIDE
Predictors of insulin resistance in chronic systolic heart failure

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Background: Insulin resistance (IR) is a common finding in symptomatic systolic chronic heart failure (CHF). Nevertheless, there is lack of data about clinical and pathophysiological features of patients (pts) of this group.

Objective: To establish clinical factors associated with presence of IR in systolic CHF.

Methods: 107 stable CHF pts (NYHA class II-IV, left ventricular ejection fraction ≤40%) were examined (vital signs, routine laboratory tests, echocardiography, flow-mediated vasodilation (FMD) of brachial artery, fasting insulin and glucose levels). The HOMA index was calculated by standard formula. Plasma levels of tumor-necrotic factor (TNF-α), interleukin 6, leptin (L) and adiponectin (A) were detected by immunoassay method; FMD of brachial artery was calculated by the standard cuff test. The L/A ratio was determined too.

Results: IR (defined as HOMA ≥2.77) was observed in 45 (42%) pts, the HOMA index median (Me) in IR group was 3.58 [2.96; 5.74] vs 1.85 [0.95; 2.31] in non-IR group. No significant differences between IR and non-IR groups were observed by age, sex distribution, CHF etiology, NYHA class, body mass index, heart rate, blood pressure, echo parameters and the A level. Simultaneously, pts with IR demonstrated higher levels of L (Me=8.30 [3.69;22.01] ng/ml vs 5.53 [1.36;16.97] ng/ml, respectively, p=0.044); TNF-α (Me=3.40 [1.35;19.25, pg/ml] vs Me=2.80 [0.82;5.38], pg/ml, respectively, p=0.041); plasma uric acid (549.37±155.23, vs 463.55±131.15, mmol/l, respectively, p=0.003), and poorer FMD (Me=5.40 [4.63;7.95] vs Me=7.99 [5.21;11.50], %; respectively, p=0.033) in comparison with pts of non-IR group.

By cluster analysis, the cut-off values of corresponding variables strongly associated with IR, were established (table 1).

Table 1. Predictors of IR in systolic CHF

Variable	Cut-off value	OR (95% CI)	p-value
TNF-α, pg/ml	>16.48	3.900 (1.257–12.102)	0.028
Uric acid, mmol/l	>584.00	3.200 (1.276–8.027)	0.021
Leptin, ng/ml	>2.265	3.117 (1.196–8.126)	0.030
L/A ratio	>0.16	3.030 (1.106–8.302)	0.047
FMD, %	<6.27	2.884 (1.160–7.171)	0.037

Conclusion: IR is present in 42% pts with stable systolic CHF and is associated with higher plasma levels of leptin, TNF-alpha, uric acid and poor FMD of brachial artery.

MODULATING CARDIAC HYPERTROPHY

6056 | BENCH
PMCA4 ablation in cardiac fibroblasts protects the heart from pathological hypertrophy

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The plasma membrane calcium ATPase 4 (PMCA4) is a ubiquitously expressed calcium pump that is important in mediating molecular signalling in the heart. Here we investigated a novel role of PMCA4 in cardiac fibroblasts that is important in controlling myocardial hypertrophy.

We generated three PMCA4 conditional knockout mouse strains: i) PMCA4 systemic knockout (PMCA4–/–); ii) PMCA4 cardiomyocyte-specific knockout (PMCA4cko); iii) PMCA4 fibroblast-specific knockout (PMCA4fko). Following transverse aortic constriction (TAC) for 5 weeks PMCA4–/– and PMCA4fko mice displayed a significantly reduced hypertrophy compared with control mice. This was accompanied by less fibrosis and a lower expression of hypertrophic marker ANP. However, PMCA4cko mice did not show any protective effect following TAC prompting us to hypothesise that the protective effect might be due to PMCA4 ablation in fibroblasts. Microarray analysis revealed a ~100 folds up-regulation of the secreted frizzled-related protein 2 (sFRP2) in PMCA4–/– fibroblasts, which was confirmed by qRT-PCR and Western blot. sFRP2 is a potent inhibitor of the Wnt/β-catenin pathway. We then cultured isolated wild type (WT) cardiomyocytes with conditioned medium from either PMCA4–/– or WT fibroblasts. In response to phenylephrine stimulation cardiomyocytes cultured in PMCA4–/– fibroblasts conditioned medium displayed 88% less hypertrophy than those cultured in WT fibroblasts conditioned medium ($P<0.01$). Mechanistically, PMCA4–/– fibroblasts showed a significant elevation in NFκB activity, a transcription factor regulating sFRP2 expression. Inhibition of NFκB activity significantly reduced the expression of sFRP2 in PMCA4–/– fibroblasts to the level comparable with WT expression. A chemical library screen identified a novel PMCA4 inhibitor, aurintricarboxylic acid (ATA). ATA treatment enhanced sFRP2 expression in mouse heart. Importantly, ATA inhibited and reversed TAC-induced cardiac hypertrophy in mice showing its efficacy in both preventive and therapeutic strategies.

In conclusion, our data shows that PMCA4-mediated signaling in cardiac fibroblast plays a key role in controlling hypertrophy. Thus, PMCA4 might be a target for the treatment of cardiac hypertrophy in the future.

6057 | BENCH
Genetic ablation of the G-protein coupled receptor 99 (GPR99) increases pressure overload-induced hypertrophy in mice

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The G-protein-coupled receptors (GPCRs) family of proteins play essential roles in the heart, including in the regulation of cardiac hypertrophy. One member of this family, the GPR99, may have a crucial role in the heart because it acts as a receptor for α-ketoglutarate, a metabolite that is elevated in heart failure patients. GPR99 is expressed in the heart but its precise function during cardiac patophysiological process is unknown. Here we used both in vivo and in vitro approaches to investigate the role of GPR99 during cardiac hypertrophy.

Genetic ablation of GPR99 in mice (GPR99–/–) resulted in a significant increase in hypertrophy following two weeks transverse aortic constriction (TAC), as indicated by heart weight/tibia length ratio (HW/TL: GPR99–/– TAC: 7.9±0.31mg/mm; WT-TAC: 7.1±0.24 mg/mm; n=6–7; $P<0.05$). GPR99–/– mice displayed an increased cardiomyocyte cross-sectional area and expressions of hypertrophic markers ANP and BNP. Moreover, interstitial fibrosis was increased by 11.8% and fractional shortening was reduced by 11.3% in GPR99–/– TAC mice compared to wild type (WT) controls following TAC. Using yeast two hybrid screening analysis we identified novel interacting partner and downstream signalling pathways that are regulated by the GPR99. First, we found that GPR99 forms a

molecular complex with TYK2, an upstream regulator of pro-hypertrophic factors, STAT1 and STAT3. Adenoviral mediated overexpression of GPR99 in neonatal rat cardiomyocytes significantly reduced TYK2 and STAT1/3 phosphorylation. Conversely, this pathways was over-activated in GPR99–/– mice following TAC. Secondly, we found that through interaction with CSN5, GPR99 regulates the ubiquitination of Interferon Regulatory Factor 5 (IRF5) and IRF8, which are known as pro-hypertrophic factors. Overexpression of GPR99 enhanced ubiquitination of both IRF5 and IRF8 whereas deletion of this receptor reduced IRF5/8 ubiquitination.
In conclusion, our study has identified GPR99 as a novel regulator of pathological hypertrophy via the regulation of the STAT pathway and the ubiquitination of IRF5/8. Identification of molecules that can specifically activate or inhibit this receptor may be very useful in the development of new therapeutical approach for cardiac hypertrophy.

6058 | BENCH
Urocortin-2 improves right ventricular function in pulmonary arterial hypertension

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Urocortin (UCN)-2 has shown promising therapeutic effects in humans and animal models with heart failure (HF). This study analyzed the effects of UCN-2 treatment in an animal model of right ventricle (RV) HF, secondary to pulmonary arterial hypertension (PAH).
Male Wistar rats received monocrotaline (MCT, 60mg/kg) or vehicle. After 2 weeks, animals were randomly assigned to receive UCN-2 (5μg/kg/day) or vehicle. The study resulted in 4 groups: CTRL (n=9),CTRL+UCN-2 (n=9), MCT (n=7) and MCT+UCN-2 (n=10). Hemodynamic studies and sample collection were performed 4 weeks after MCT injection. Only significant results (mean±SEM,$p<0.05$) are given.
Hemodynamic studies revealed that MCT group developed PAH, as shown by increased RV end-systolic pressure (MCT vs CTRL: 60±3 vs 22±1mmHg), end-diastolic pressure (6.0±0.7 vs 3.7±0.3mmHg), RV dilation (end-diastolic volume) (280±14 vs 222±11μL) and decreased cardiac output (35±6 vs 64±3mL/min) and ejection fraction (32±4 vs 75±3%). UCN-2 treatment resulted in attenuation of these changes (48±4mmHg; 4.3±0.3mmHg; 213±12μL; 47±2mL/min and 60±3%, respectively). Moreover, the survival rate for UCN-2 treated rats was higher (76%) than for MCT rats (44%). PAH rats presented RV hypertrophy as shown by the morphometrical analysis (RV weight/tibia length ratio, MCT vs CTRL: 0.08±0.00 vs 0.04±0.00g/cm) and by histology (cardiomyocyte cross-sectional area: 366±25 vs 255±27μm^2). UCN-2 treatment attenuated RV remodeling (0.06±0.00g/cm and 288±26μm^2,respectively). The MCT group presented increased UCN-2 expression (MCT vs CTRL: 2.5±0.9 vs 1.0±0.3AU) and decreased CRHR2 expression (0.5±0.1 vs 1.0±0.1AU) in the RV, that were reversed by UCN-2 treatment (0.2±0.1 and 0.9±0.1AU, respectively). The increased expression of pathology markers in MCT animals, such as BNP (15.3±2.5 vs 1.0±0.1AU), ET-1 (3.4±0.4 vs 1.0±0.2AU) and HIF-1α(1.6±0.3 vs 1.0±0.2AU), as well as markers of apoptosis including caspase-3 (3.9±0.6 vs 1.0±0.1AU) and caspase-8 (2.8±0.3 vs 1.0±0.2AU) were attenuated by UCN-2 (6.9±2.1, 1.8±0.6, 1.0±0.1, 2.0±0.4 and 1.3±0.2AU,respectively). The protein expression of both ERK and p38 kinases was decreased in MCT animals (MCT vs CTRL: 0.5±0.1 vs 1.0±0.1 and 0.5±0.04 vs 1.0±0.1,respectively) and was reversed by UCN-2 (0.9±0.1 and 1.1±0.2,respectively).
UCN-2 treatment reduced the severity of PAH and RV hypertrophy, as well as the expression of genes associated with overload, hypertrophy, hypoxia and survival. These findings suggest that the UCN-2/CRHR2 pathway has a relevant role on the pathophysiology of PAH and RV failure, representing a potential therapeutic target in these conditions.

RENAL SYMPATHETIC DENERVATION

6065 | BEDSIDE
Long-term verification of functional and structural renal damage after renal sympathetic denervation

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Background: Previous studies on renal sympathetic denervation (RSD) excluded patients with impaired renal function to avoid potential RSD-related renal damage. A recent study of our working group showed that RSD does not aggravate functional or structural renal damage during the early post-procedural period, as reflected by the highly sensitive biomarkers neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1). The aim of the present study was to examine the effect of RSD on blood pressure (BP) and renal function after a long-term follow-up.
Methods: A total of 62 consecutive patients undergoing RSD were included in this study. Venous blood samples for analysis of serum NGAL and KIM-1 were collected prior to RSD and at 24 hours, 48 hours, and 3 months after RSD. BP measurements, antihypertensive medication use, and safety events were followed over a three-year period.
Results: Follow-up data were available over 36.9 [±3.4] months in 47 of 64 (73.4%) of the initially included patients. Serum levels of the conventional creatinine (BL: 0.9 [0.8;1.2] mg/dL, vs. 48h: 1.07 [0.8;1.4] mg/dL; p=0.9), the estimated GFR (eGFR) (BL: 76.71 [±24.9] ml/min/1.73m^2 vs. 48h: 58.7 [±28.9] ml/min/1.73m^2; p=0.22), and blood urea nitrogen (BUN) (baseline: 40 [31.3;54.8] mg/dL vs. 48h: 53 [30;60] mg/dL; p=0.6) showed no significant increase during the early period after RSD. In addition, there were no significant differences in NGAL levels (BL.14.5 [7.0;33.1] ng/dL vs. 48h: 13.4 [4.6;37.0] ng/dL, p=0.24) and also no significant changes in KIM-1 levels (BL: 0.64 [0.28;0.96] ng/mL vs. 48h: 0,61 [0,32;0.89] ng/mL; p=0.78) during the early post-procedural period. After a 3 years follow-up a significant SBP reduction of 23 mmHg ($p>0.001$) was documented, and there were also no significant changes in serum creatinine (0.96 [0.8;1.3] ng/dL; p=0.14), BUN (41 [32;61] mg/dL; p=0.33), or eGFR (79.5 [±20.9] ml/min/1.73m^2; p=0.2) values. There were also no significant changes documented in patients with impaired renal function (eGFR<45 ml/min) during the early post-procedural period or the long-term follow-up, respectively (p=0.34).
Conclusion: The results of the present study show a sustained effect of RSD on BP reduction after a long-term follow-up of 3 years. In addition, there is no evidence of renal failure during the early post-procedural period or after a long-term follow-up. The results of the present study provide additional verification of the long-term safety and effectiveness of RSD, even in patients with impaired renal function.

6066 | BEDSIDE
24 months follow up of the Luebeck and Erlangen RDN registry: RDN improves 24 h peripheral and central blood pressure as well as 24h-arterial stiffness

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Background: Percutaneous renal denervation (RDN) became a controversially discussed treatment option for resistant arterial hypertension, especially after publication of the Symplicity HTN-3 trial. Despite information about effects on peripheral office blood pressure, hard cardiovascular endpoints are still lacking. Parameters of arterial stiffness, central blood pressures and hemodynamics can be used as much better and well-established surrogate markers for cardiovascular outcome. We therefore aimed to evaluate the effects of RDN on these parameters in ambulatory 24h measurements.
Methods: 90 patients (31–82 years, mean age 65±10 years, 5±1 antihypertensive drugs) suffering from resistant arterial hypertension were included in two centers following the Symplicity HTN-3 criteria. Secondary arterial hypertension, including obstructive sleep apnea, was excluded. The 1st generation of the Ardian/Medtronic RDN radiofrequency ablation catheter system was used for treatment. An I.E.M. device was used for 24h blood pressure and stiffness measurements. For pulse wave velocities (PWV) a multivariate analysis of variance (f-test) was performed.
Results: RDN was successfully performed in all patients without complications. Office systolic blood pressure (SBP) showed a significant decrease over 24 months. Response rate, defined as a reduction of 10 mmHg SBP, was 66% after 12 months and 65% after 24 months, respectively. SBP improved significantly from 170±24 mmHg to 147±21 mmHg [$p<0.001$] after 6 months, 149±16 mmHg after 12 months [$p<0.001$] and 150±21 mmHg after 24 months [p=0.002]. Central SBP was lowered significantly from 138±14 mmHg to 130±13 mmHg [$p<0.001$] after 6 months, to 129±12 mmHg after 12 months [$p<0.001$] and to 129±12 mmHg after 24 months [$p<0.001$]. PWV improved at daytime by 0.24 m/s after 12 months [p=0.017] and by 0.36 m/s after 24 months [p=0.007], respectively, whereas no significant effects were observed during night-time.
Conclusions: This study proved for the first time a sustained effect of RDN on established cardiovascular surrogate endpoints. An extensively exclusion of a secondary arterial hypertension is crucial for RDN patient selection and might, at least in part, explain some differences as compared to Symplicity HTN-3.

6067 | BEDSIDE
Neuropeptide Y as an indicator of successful alterations in sympathetic nervous activity after renal sympathetic denervation

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Background: The persistence of resistant arterial hypertension (HT) is partially regulated by the renal sympathetic nervous system (SNS). Renal sympathetic denervation (RSD) represents a save and effective treatment option for certain patients with HT, and has been shown to decrease sympathetic activity. Neuropeptide Y (NPY) is a neurotransmitter that is co-released with norepinephrine and is upregulated during increased sympathetic activity. The primary aim of the present study was to examine the effect of RSD on NPY, which is regarded as

a specific biomarker of sympathetic activity. Further, the association between changes in NPY levels and blood pressure reduction after RSD was analyzed.
Methods: A total of 150 consecutive patients (age: 64.9±10.2 y) from 3 clinical centers undergoing RSD were included in this study. Response to RSD was defined as an office systolic blood pressure (SBP) reduction of >10 mmHg 6 months after RSD. Venous blood samples for measurement of NPY in serum were collected prior to and 6 months after RSD.
Results: A significant reduction in the office SBP of 23.0 mmHg (SBP baseline: 168.6 mmHg [SD: 20.8], p<0.001) was observed 6 months after RSD. In addition NPY serum levels were significantly reduced by 0.24 ng/mL after 6 months follow up, when compared to baseline values (NPY baseline: 1.71 [IQR: 0.84; 2.67], p=0.01). There was a significant correlation between baseline SBP and RSD-related systolic BP reduction (r=–0.43, p<0.001) and between serum NPY baseline values and NPY level changes (r=–0.52, p<0.001) after the 6-month follow-up. Successful SBP reduction after RSD (responders) was associated with a significantly greater NPY level reduction when compared with BP non-responders (p=0.002).
Conclusion: In addition to the blood pressure reduction in response to RSD, this study demonstrates an effect of RSD on serum NPY levels, as a specific marker for sympathetic activity. The association between RSD-related changes in SBP and NPY levels provide further evidence of the effect of RSD on the SNS.

TRANSLATIONAL ELECTROPHYSIOLOGY OF ATRIAL FIBRILLATION

6074 | BEDSIDE
Serum YKL-40 as a novel marker of left atrial fibrosis assessed by delayed enhancement MRI in lone atrial fibrillation

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Background: Assessment of the presence and extent of left atrial (LA) fibrosis by using delayed-enhanced magnetic resonance imaging (DE-MRI) in AF patients is a pioneering non-invasive method. Serum YKL-40 is a novel marker for inflammation and known to be play a role in ongoing tissue fibrosis. However, its role in LA fibrosis is unclear.
Objective: We aimed to investigate the association of serum YKL-40 level with both the presence and extent of LA fibrosis by using DE-MRI.
Methods: A total of 50 patients with lone paroxysmal AF (62% male; age:47.2±7.0) underwent cardiac DE-MRI as a study protocol. Cardiac DE-MRI at 1.5T scanner to quantify LA fibrosis, serum YKL-40 levels, clinical and echocardiographic data were recorded. Fibrosis degree was categorized according to Utah class defined in the DECAAF study.
Results: DE-MRI revealed any degree of LA fibrosis in 31 (62%) patients with a median enhancement of 15% of the LA surface area. Median serum YKL-40 was significantly higher (p=0.008) and LVEF was lower (p=0.047) in patients with LA fibrosis as compared to patients without LA fibrosis. Extent of LA fibrosis was significantly correlated with age, duration of AF history, serum CRP and serum YKL-40 levels. Only log (YKL-40) level was found as independent predictor for the presence of LA fibrosis (OR: 1.626, p=0.022). Multivariate linear regression analysis pointed out that duration of AF history (β=0.330, p=0.003) and serum log (YKL-40) levels (β=0.546, p<0.001) were significantly and independently associated with the extent of LA fibrosis.

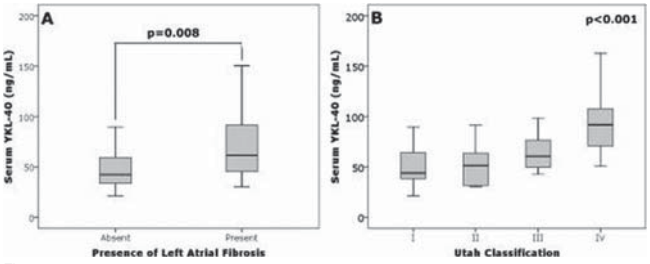

Figure 1

Conclusion: Higher levels of serum YKL-40 are associated with both the presence and more extensive LA fibrosis in patients with lone AF. As a novel marker of inflammation, serum YKL-40 may also be used as an indicator for the degree of LA fibrosis.

6075 | BEDSIDE
Exercise-induced left atrial hypertension in patients with non-valvular atrial fibrillation: prevalence and impact on clinical outcome of cathter ablation

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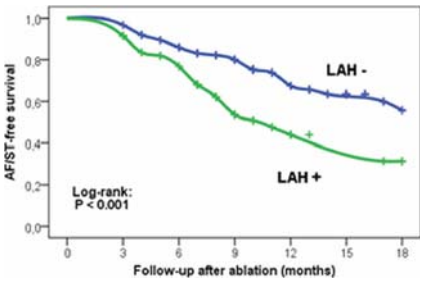
Purpose: We investigated whether static handgrip exercise would induce left atrial hypertension (LAH) in the patients with non-valvular atrial fibrillation (AF) and whether the exercise-induced LAH would project worse outcome of catheter ablation for the AF.
Methods: LA pressure was measured directly after transeptal puncture at rest and during static handgrip exercise (40% maximal voluntary contraction) in 225 patients undergoing radiofrequency ablation for non-valvular AF (paroxysmal/persistent AF, 66/33%). Functional limitation was assessed at baseline and at 3 months after the ablation by the SF-36 questionnaire. Patients were followed for AF recurrence for 10±6 months.
Results: Mean LA pressure increased during the handgrip by 3±4 mmHg (range 0–25 mmHg). LAH, defined as mean LA pressure >15 mmHg was present at rest and during the handgrip in 14% and 30% of the patients. The strongest risk factors (p<0.001) for the exercise-induced LAH were older age, increased afterload, increased LA volume, decreased LA appendage doppler flow and lower LA bipolar voltage. AF recurred in 46% of the patients with LAH compared to 24% of the patients without LAH (p=0.002). The patients with LAH were more limited during physical activity before and also after the ablation, even after adjusting for the heart rhythm and heart rate (p<0.001 by the SF-36). However, the LAH patients who maintained sinus rhythm after the ablation improved their physical functioning by 24% (p=0.02).



AF recurence with regard to LAH

Conclusions: Exercise-induced LAH is common in the patients with non-valvular AF. Presence of the LAH doubles the risk of AF recurrence and impedes complete functional recovery after ablation. On the other hand, managing AF by ablation in the patients with LAH may substantially improve their physical functioning.

6076 | BEDSIDE
Both low and high resting heart rate is associated with an increased risk of incident atrial fibrillation

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Background: A recent meta-analysis of randomized clinical trials investigating the heart rate-reducing agent ivabradine in patients with cardiovascular disease has shown an increased risk of atrial fibrillation (AF) when treated with ivabradine compared to placebo. However, whether the increased risk of AF observed is due to ivabradine per se or due to ivabradine-induced bradycardia remains to be established.
Purpose: We aimed to describe the association between resting heart rate and the risk of AF in an observational setting of primary care patients referred for electrocardiogram (ECG) recording. Moreover, as secondary endpoints, we aimed to describe the association between resting heart rate and the risk of death from all causes as well as stroke.
Methods: Using computerized ECG analysis, resting heart rate was obtained from 282,015 individuals referred for ECG recording at a general practitioner's core facility from 2001 to 2011. Data on drug use, comorbidity, and outcomes were collected from administrative healthcare registries. Among several things, we were able to adjust for treatment with heart rate-modulating medication.
Results: During a median follow-up time of 5.6 years, 7,607 developed AF, of which 875 developed lone AF. Having a resting heart rate below the 5th percentile (≤51 beats/min) was associated with a multivariable-adjusted hazard ratio of 1.15 (95% CI 1.01–1.30; P=0.031) for developing AF compared with the reference group (40th to <60th percentile, 66–72 beats/min). From the reference group and upward, the risk of AF increased with increasing heart rate, reaching a multivariable-adjusted hazard ratio 1.31 (95% CI 1.19–1.45; P<0.001) for those with a heart rate above the 95th percentile (≥95 beats/min). The association was accentuated when looking only at lone AF, as evidenced by a hazard ratio of 1.49 (95% CI 1.08–2.07; P=0.017) and 1.97 (95% CI 1.46–2.66; P<0.001) for those with a heart rate below the 5th percentile (≤51 beats/min) and above the 95th percentile (≥93 beats/min), respectively. Regarding secondary end-points, the multivariable-adjusted analysis revealed that the risk of death and stroke increased almost linearly with increasing heart rate.
Conclusions: In this large ECG study, we found that both low and high resting heart rate is associated with an increased risk of AF independently of treatment with heart rate-modulating medication. This association was even stronger for the

outcome of lone AF. For death and stroke, we found almost linear increased risks for increasing resting heart rate.

ADVANCES IN SCIENCES: PERIPHERAL CIRCULATION

6084 | BEDSIDE
Defining the value of the toe-brachial index for normal, mild, moderate and severe PAD

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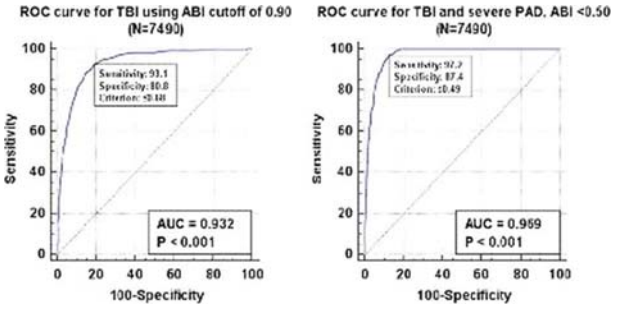
Background: The ankle-brachial index (ABI) has been used to define peripheral arterial disease (PAD) as either mild (ABI, <0.90), moderate (ABI, <0.80) or severe (ABI, <0.50). The toe-brachial index (TBI) has traditionally been reserved for those patients with a high ABI (>1.30) where it is felt that incompressibility due to peripheral arterial calcification impairs the reliability of the ABI for the diagnosis of obstructive PAD. While there has been data to categorize a TBI as either normal or abnormal, to our knowledge there has never been a similar categorization of PAD as mild, moderate or severe using the TBI. The purpose of our investigation was to define the cutoffs for PAD severity for the TBI using the ABI cutoffs of severity.
Methods: Our database was searched for all patients who had both ABI and TBI measured. There were 7,490 legs where both ABI and TBI were recorded. ROC curves were constructed using the ABI cutoffs for mild, moderate and severe as described above. All ROC graphs and statistical calculations were performed using the MedCalc statistics program.
Results: The TBI that best separated those without PAD and those with mild PAD was ≤0.68 (sensitivity 93.1%, specificity 80.8%, AUC, 0.932 [95% CI, 0.926–0.938], P value <0.001). The TBI that best separated those with moderate PAD was ≤0.61 (sensitivity 92.2%, specificity 84.2%, AUC, 0.941 [95% CI, 0.936–0.947], P value <0.001). The TBI that best separated those severe PAD was ≤0.49 (sensitivity 97.2%, specificity 87.4%, AUC, 0.969 [95% CI, 0.965–0.973], P value <0.001). The ROC curves for mild and severe PAD are shown in the figure below.



ROC curves for mild and severe PAD.

Conclusions: We can now categorize the severity of PAD based on the TBI alone. A normal TBI is >0.68, mild disease is 0.62–0.68, moderate disease 0.50–0.61 and severe disease ≤0.49.

6085 | BEDSIDE
Burden of subclinical atherosclerosis assessed by carotid and femoral 3D vascular ultrasound: the PESA (Progression of Early Subclinical Atherosclerosis) study

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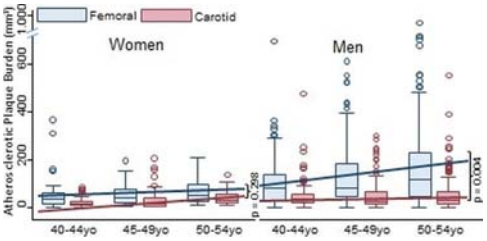
Introduction: Plaque volume assessment with real 3D vascular ultrasound (r3D-US) is a novel approach to detecting and quantifying atherosclerosis. Here we characterize, for the first time, carotid and femoral plaque burden in an asymptomatic middle-aged population.
Methods: PESA is an observational, prospective, cohort study of bank employees aged 40 to 54 that evaluates the presence and progression of subclinical atherosclerosis. We report data from the first 1970 participants screened with r3D-US. Atherosclerotic burden was defined as the sum of all plaque volumes in the carotid and femoral arteries. Linear regression models were used to explore the association between burden and age.
Results: Atherosclerosis was detected in 47% of the participants (46±4yo, 35%female). Atherosclerotic burden was greater in men (median (IQR) 79mm^3 (179–31) vs 32mm^3 (72–13) in women) and in the femoral arteries (median (IQR) 78mm^3 (170–36) vs 28mm^3 (58–14) in carotids). Stratifying by age (Figure) revealed a significant increase in femoral burden (FB) in men (ß coef 5.59; p<0.001), whereas carotid burden (CB) showed no age association (ß coef 0.16; p=0.852). In contrast, women showed a significant age-related increase in CB (ß coef 2.59; p=0.002) but no association for FB (ß coef 0.86; p=0.579). Age-related differences between the development of FB and CB were significant in men (p=0.004) but not in women (p=0.298).



Conclusions: In this first report on carotid and femoral plaque volume with r3D-US we detected higher atherosclerotic burden in men and in the femoral arteries. Interestingly, men showed rapid development of femoral burden over the studied age rage. Assessment of plaque burden by r3D-US is a valuable tool for screening subclinical atherosclerosis in the carotid and femoral arteries.

6086 | BEDSIDE
Association of ankle brachial index, protein-energy wasting and inflammation status with cardiovascular mortality in patients on chronic hemodialysis

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Background: Abnormal ankle brachial index (ABI) reflects atherosclerosis in various population including hemodialysis (HD) patients. Protein-energy wasting (PEW), considered to be due to inflammatory process rather than poor nutritional intake, is also associated with increasing risk of cardiovascular (CV) mortality. We investigated the association of ABI, PEW and chronic inflammation status with clinical prognosis in HD patients.
Methods: A total of 973 outer patients stably treated with maintenance HD therapy were enrolled in this study. ABI was measured using standard technique. As a marker of the PEW, geriatric nutritional risk index (GNRI) was calculated as follows; GNRI = (14.89 × albumin) + [41.7 × (body weight/body weight at BMI of 22)]. Serum C-reactive protein (CRP) levels were also measured using a latex-enhanced high-sensitive CRP immunoassay. Cut-off levels were 91.2 for GNRI defined from previous studies and 1.9 mg/l for CRP as median value, respectively. They were followed-up for 8 years.
Results: Abnormal ABI (<0.9 or ≥1.3) was seen in 332 (34.1%) patients. Declined GNRI and elevated CRP levels were independently associated with abnormal ABI [odds ratio (OR) 0.97, 95% confidence interval (CI) 0.96–0.99, p=0.0009 and OR 1.40, 95% CI 1.07–1.83, p=0.013, respectively]. The GNRI levels were also independently correlated with the CRP levels (β=–0.126, p<0.0001). During follow-up period (median 46 months), 283 (29.1%) patients died including 163 (16.8%) CV cause. Abnormal ABI [adjusted hazard ratio (HR) 1.61, 95% CI 1.18–2.21, p=0.0029], GNRI<91.2 (adjusted HR 1.71, 95% CI 1.22–2.39, p=0.0018) and CRP>1.9 mg/l (adjusted HR 1.76, 95% CI 1.28–2.44, p=0.0005) were independent predictors for CV mortality, respectively. Furthermore, when patients were divided into groups according to number of these three risk factors, 8-year freedom from CV mortality was 85.9%, 72.4%, 57.2% and 32.1% among groups with no risk factor, any 1 risk factor, any 2 risk factors and all risk factors, respectively. Patients with all risk factors had 5.68-fold (95% CI 2.84–11.7, p<0.0001) higher risk for CV mortality compared to those without any risk factor after adjustment for other confounders. Similar results were obtained in all-cause mortality (adjusted HR 7.98, 95% CI 4.90–13.3, p<0.0001).
Conclusion: ABI, GNRI and CRP levels were closely associated with each other, and the combination of these variables could strongly stratified CV- and all-cause mortality in HD patients. These results may manifest a so-called malnutrition, inflammation and atherosclerosis syndrome in this population.

IMAGING MODALITIES FOR PULMONARY HYPERTENSION

6103 | BEDSIDE
A feasible method for non-invasive measurement of pulmonary vascular resistance in pulmonary arterial hypertension: combined use of transthoracic Doppler-echocardiography and cardiac magnetic resonanc

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Background: Transthoracic Doppler-echocardiography (TTE) can estimate mean pulmonary arterial pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) reliably, and cardiac magnetic resonance (CMR) is the best modality for non-invasive measurement of cardiac output (CO). Therefore, TTE and CMR

can complement each other in the evaluation of pulmonary vascular resistance (PVR).
Purpose: The study was performed to investigate whether combined use of TTE and CMR provided a feasible method for non-invasive measurement of PVR in pulmonary arterial hypertension (PAH).
Methods: Right heart catheterization (RHC) was undertaken in 77 patients (17M/60F) with PAH, and simultaneous TTE was carried out to evaluate MPAP, PCWP and CO. Within 2 days, CO was measured again with CMR in similar physiological status. Then, PVR was calculated with the integrated non-invasive method: TTE-derived (MPAP-PCWP)/CMR-derived CO and the isolated TTE method: TTE-derived (MPAP-PCWP)/ TTE-derived CO, respectively. The results were compared with RHC-calculated PVR using the Bland-Altman analysis.
Results: The PVR calculated with integrated non-invasive method correlated well with RHC-calculated PVR (r=0.931, 95% confidence interval 0.893 to 0.956). Between the integrated non-invasive PVR and RHC-calculated PVR, the Bland-Altman analysis showed the satisfactory limits of agreement (mean value: –0.89±2.59). In comparison, the limits of agreement were less satisfactory between TTE-calculated PVR and RHC-calculated PVR (mean value: –1.80±3.33). Furthermore, there were excellent intra- and inter-observer correlations for the measurements of TTE and CMR ($P<0.001$ for all).
Conclusions: The combined use of TTE and CMR provides a clinically reliable method to determine PVR non-invasively. In comparison with RHC, the integrated method shows good accuracy and repeatability, which suggests the potential for the evaluation and serial follow-up in patients with PAH.

6104 | BEDSIDE
Atrial volume and function during exercise in chronic thromboembolic pulmonary hypertension

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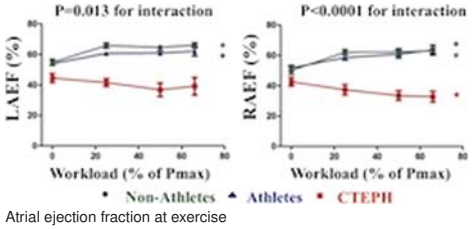
Background: Although atrial volume and function have prognostic significance in many cardiovascular conditions, their changes with exercise are not well known.
Purpose: The aim of this study was to evaluate left and right atrial (LA and RA) volume and function during incremental exercise, both in normal individuals, after athletic remodelling, and in patients with chronic thromboembolic pulmonary hypertension (CTEPH).
Methods: Fifteen healthy non-athletes, 15 athletes and 15 CTEPH patients underwent exercise cardiac magnetic resonance imaging with simultaneous invasive hemodynamic measurements.
Results: At rest, athletes had larger indexed maximal RA and LA volumes (iRAVmax, iLAVmax) than CTEPH patients and non-athletes, the latter two groups having similar values. CTEPH patients had lower RA and LA ejection fraction (EF) at rest. During exercise, RA volumes (maximum and minimum) increased in CTEPH patients, whilst decreasing in athletes and non-athletes ($P<0.0001$). The exercise-induced change in iLAVmax was similar between groups, but iLAVmin did not decreased in CTEPH patients. Thus exercise-induced increases in RAEF and LAEF, as seen in normal physiology, were significantly impaired in CTEPH patients. At peak exercise, RA volumes (maximum and minimum) and EF correlated highly with RA pressure (R=0.70; P=0.005; R=0.83; $P<0.0001$; R=–0.87; $P<0.0001$). On multivariate analysis, peak exercise RAEF and iLAVmin were independent predictors of VO2peak in CTEPH patients and together explained 72% of the variance in VO2peak (ß =0.581 and ß=–0.515, respectively).



Atrial ejection fraction at exercise

Conclusions: In normal physiology, RA and LA function increase with exercise; whereas CTEPH patients have significantly impaired LA and RA function, which becomes more apparent during exercise.
Acknowledgement/Funding: FS was funded by a grant of the French Federation of Cardiology

6105 | BENCH
Association between endothelial function and micro-vascular remodeling measured by synchrotron radiation pulmonary micro-angiography in pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is a progressive disease with increased vascular constriction and resistance. Previously, we established a method for synchrotron radiation pulmonary micro-angiography (SRPA) in an in-vivo rat model and succeeded to visualize micro-vasculature in the PAH rats. In this study, we aimed to quantified micro-vascular remodeling in monocrotaline induced PAH rats. In addition, to determine the association of endothelial function to the vascular remodeling, local expression of endothelin-1 (ET-1), endothelial nitric oxide synthetase (eNOS) and vascular endothelial growth factor (VEGF) was evaluated by immunohistochemical staining.
Methods: A monocrotaline induced PAH rats were made by a single subcutaneous injection of 60 mg/kg monocrotaline to 4 week-old male Sprague-Dawley rat. After 2 weeks, SRPA was performed at the Photon Factory of the High Energy Accelerator Research Organization (Tsukuba, Japan). Rat lung was extracted after SRPA. To analyze microvascular density of the PAH lung, the internal diameter of the pulmonary arterioles was measured using SRPA pictures by ImageJ software. Semi-quantified analysis of ET-1, eNOS and VEGF expression on pulmonary arterioles was performed by immunohistochemical staining. All data are presented as mean ± SD.
Results: SRPA visualized decreased pulmonary micro-vasculature in the PAH rats compared with the control. Microvascular density in the PAH rats was significantly decreased and the internal diameter of pulmonary arterioles the PAH rats was 77±12 μm compared with 149±16 μm of control. eNOS expression was significantly decreased the PAH rats compared with control (2.12±0.59 vs 2.91±0.66, $p<0.05$). ET-1 expression was significantly increased in the PAH rats compared with control (1.53±0.45 vs 0.8±0.14, $p<0.05$), although, VEGF expression was not different in the PAH rats and control.
Conclusion: SRPA was useful to visualize decreased and narrowed pulmonary micro-vasculature in the PAH rats. Increased ET-1 expression may contribute to a proliferation and remodeling of pulmonary arterioles. Also decreased eNOS expression may associate with vasospasm of pulmonary arterioles induced by endothelial dysfunction due to increased shear stress in PAH. Further study for detailed endothelial function would be necessary to investigate the mechanism of vascular remodeling associated with PAH. This newly developed SRPA technology makes it possible to visualize the micro-vasculature remodeling and could provide insights regarding the correlation between endothelial function and vascular remodeling in PAH.
Acknowledgement/Funding: JSPS KAKENHI Grant Number 23791560

BEST POSTERS SESSION 7

BEST POSTERS IN CATHETER ABLATION

P6112 | BEDSIDE
The utility, efficacy and safety of a new rapid high-resolution mapping system in the catheter ablation of atrial and ventricular arrhythmias in humans

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Background: A novel 3D electroanatomical mapping system, capable of rapidly acquiring detailed maps based on automatic annotation of thousands of points was recently released for clinical use. We present our initial clinical experience.
Methods: The first 20 catheter ablation procedures (7 atrial tachycardia, 8 atrial fibrillation, 3 ventricular tachycardia and 2 ventricular ectopic beat ablation) based on standard indications are described. The system uses a bidirectional deflectable basket catheter with 64 closely spaced mini-electrodes (A). It automatically accepts and annotates electrograms when a number of predefined criteria that filter out the non-relevant signals are met.
Results: Thirty right atrial maps were acquired in median 11 (4–15) min consisting of 7220 (3467–10947) points, 22 left atrial maps in 11 (14–43) min consisting of 7818 (4379–12262) points and 10 left ventricular maps in 37 (14–43) min consisting of 8709 (2605–15514) points. The mini-basket catheter could reach all areas of interest without deflectable sheaths. No embolic events, bleeding complications or endocardial structure damage was observed. Correction of the automatic annotation was performed in 0.02% of points in 4/62 maps. The system revealed re-entry circuits of atrial tachyarrhythmias (B), identified gaps on linear

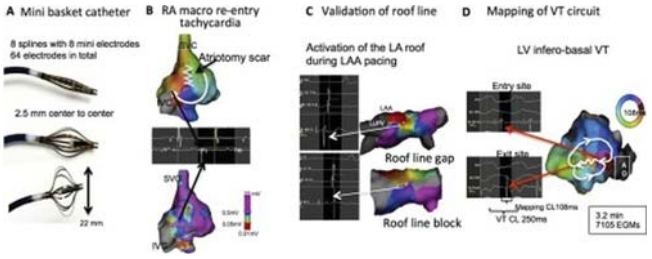

Figure 1

lesions (C) and correctly identified and annotated the clinical ventricular ectopic beats and channels of slow conduction within ventricular scar (D).
Conclusions: The novel automatic mapping system was rapid, safe and efficacious in mapping a variety of cardiac arrhythmias in humans. Further clinical research is needed to optimise its use in the ablation of complex arrhythmias.

P6113 | BEDSIDE
Ablation of hemodynamically unstable VT with support of a microaxial pump, early experience

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Introduction: Besides progress in the ablation of ventricular arrhythmias with precise definition of the arrhythmic substrate, with its precise localization by three dimensional mapping and additional LAVA ablation there are still patients that cannot be treated successful by these means alone. In these cases the induction of the clinical VT is essential. In patients with severely depressed LV function or with immediate syncope the poor tolerability of these VT can be overcome by using a hemodynamic support by a microaxial pump. With this support an ablation is possible even under light sedation with a high success rate. We here report the results our first 11 procedures.
Methods and results: Retrospective analysis of consecutive patients admitted for VT ablation with an ejection fraction well below 25% or with immediate syncope. All patients were treated by RF-Ablation under hemodynamic support with a microaxial pump. Since 2013 there were 12 procedures performed in 11 patients. The median age was 64 years (Range 51–71).Nine patients had CAD, one patient suffered from dilative cardiomyopathy and one patient from arrhthmogenic rightventricular dysplasia. The maximum hemodynamic support was achieved in 9 of 11 patients. Time spent in ongoing VT until all morphologies were successfully ablated took more than 30 minutes in 9/11 patients. Median follow-up is now 9 month (range 1–15). Recurrence of VT occurred in 2 patients (1 DCM, 1 CAD). One heavy hemolysis occurred. One death occurred. In one patient another VT occurred and a repeat procedure was performed.
Conclusion: In patients with severely depressed LV function or with immediate syncope with beginning of VT an ablation under hemodynamic support with a microaxial pump expands therapeutic possibilities with an acceptable safety profile.

P6114 | BEDSIDE
The impact of NavX in pediatric arrhythmia ablation on safety, procedure duration and number of RF lesions. Is it a time to change approach?

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Non-fluoroscopic approach to pediatric ablation gets broad acceptance as it reduces the x-ray exposition. The only limitation is that it in most reports increases the duration of procedure.
Our objective is to compare the standard x-ray ablation (X) with nearly-0 fluoroscopy ablation with NavX (NavX) in pediatric population undergoing ablation. From the cohort of 538 consecutive patients we excluded 16 patients with complex congenital heart disease after surgical correction.
In the NavX group the procedure was started from RA reconstruction, followed by CS, tricuspid valve and His bundle. Left sided WPW ablation was performed retrogradely or transseptally. Short fluoroscopy was used during transseptal puncture, when VT originated close to aortic valve or when CS diverticulum was suspected.
We analyzed the procedural (duration of GA and procedure), x-ray (fluoroscopy, dose) and ablation parameters (time to 1st and the last application, the number of applications and the cumulative duration of energy delivered as well and procedural success rate).
We included 522 patients (age 13,4±6,2 years, 238F) with SVT (202), WPW+AVRT/PAF (183), asympotomatic WPW (41), AT (26) and VEs/VT (48) or nondocumented palpitations. Finally AVNRT ablation was performed in 131 patients, WPW in 287 patients, AT in 22 and VEs/VT in 44 cases. The NavX was used in 278 patients. In patients with AVNRT the "0" fluoroscopy was possible in 82%, in WPW: 47%, in AT: 50% and for VEs/VT: 41%. Generally, the majority of ablations were completed with "0" fluoroscopy (162, 58%). For the NavX in comparison to X, the procedural parameters were significantly shorter (procedural time 66±33 vs 76±39 min., GA time 89±36 min., DAP 10±24 vs 59±95mGy, and fluoro time 2±5 vs 17±14 min.). Ablation parameters were also in favour of NavX (time to 1st application 23±15 vs 27±18 min., time to last application 47±31 vs 52±33 min, as well as the number of applications 7,7±7,8 vs 8,7±9 and total RF time 253±274 vs 264±271 sec) however this not reached statistical significance. Procedural success rate was 90% for NavX and 91% for RTG ablation.
We conclude that nonfluoroscopic approach with NavX is safe and successful method for pediatric ablation. If the method is used systematically it leads not only to reduced radiation burden but also to shorter procedural and GA time and the application lesions.

P6115 | BEDSIDE
Initial international multicenter human experience of a novel epicardial access tuohy needle embedded with a real time pressure/frequency monitoring to facilitate epicardial access

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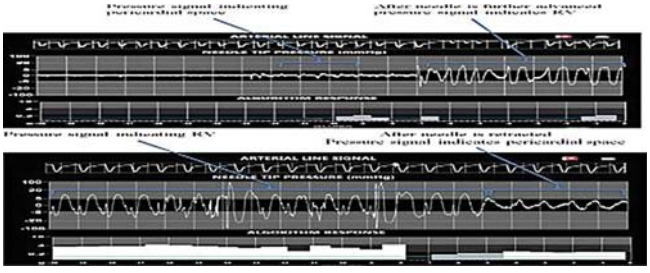
Introduction: Epicardial (epi) ablation is often necessary for the treatment of challenging arrhythmias refractory to endocardial ablation. The subxiphoid approach is the most used method for epi access. However, major and minor complications may occur even in experienced centers with reported rates of 4–7%. We evaluated the feasibility and safety of the EpiAccess™ Needle by EpiEP, Inc., a novel "tuohy" epi access needle in a multicenter study.
Methods: 25 patients with a clinical need for epi access were enrolled.
Epi access was obtained with the EpiAccess Needle whose tip is embedded with a pressure sensor able to report the pressure waveform in real time. Successful epi access was assessed through the device and confirmed by fluoro and contrast injection.
Results: Patients were male (92%) with a mean age of 65.6±13.9. Epi access due to VT ablation occurred in 84% of the patients. Successful epi access was obtained in all cases. Mean access time was 280 secs ± 98.9 secs. Mean pericardial pressure/pulsation was 4.72±1.7 mmHg. Pressure monitoring identified pericardial wire access in 100% of the cases. In 2 cases (8%) the needle sensor suggested tenting of the pericardial space but not access to pericardial space as evidenced by an increased pressure to 11 mmhg. Unintended RV perforation occurred in 1 pts (4%) and was detected by the device (figure). No drainable hemopericardium was reported. No acute or late complications were observed.



Conclusion: Epicardial access with the novel EpiAccess™ tuohy needle and real time pressure monitoring is feasible and safe. The pressure monitoring identifies successful epi access and minimizes complications. This has relevant clinical implications.

BEST POSTERS IN MEDICAL THERAPY OF STABLE CORONARY ARTERY DISEASE

P6117 | BEDSIDE
Impact of long-acting nifedipine on coronary vascular function after drug-eluting stent implantation - The NOVEL study

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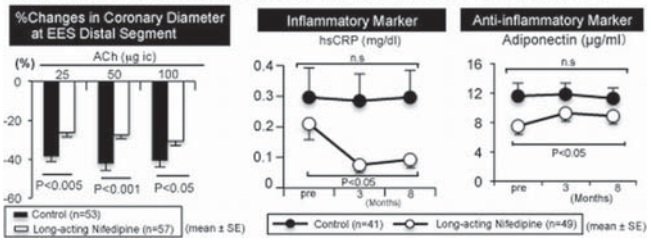
Background: It is widely known that drug-eluting stents (DES) induce coronary vasomotion abnormalities. We have recently demonstrated that chronic treatment with long-acting nifedipine, which exerts cardiovascular protective effects through inhibition of vascular inflammation, suppresses DES-induced abnormal coronary vasoconstriction in pigs.
Purpose: In order to test whether this is also the case in humans, we performed a prospective, randomized, multicenter trial, termed as the NOVEL Study.
Methods: We enrolled 146 patients with stable angina pectoris who underwent scheduled implantation of everolimus-eluting stents (EES) in the left coronary arteries. They were randomly assigned to receive either conventional treatments alone (aspirin, clopidogrel, RAS inhibitor and statin) or additionally long-acting nifedipine (20–40mg/day) (n=73 each). After 8–10 months, they were evaluated for coronary reactivity to intracoronary acetylcholine (ACh) by quantitative coronary angiography after 48-hour withdrawal of nifedipine.
Results: Finally, ACh-induced coronary reactivity at the EES edges was examined in 53 patients in the control and 57 in the nifedipine group. Baseline pa-

tient characteristics and procedural profiles were comparable between the two groups. Coronary vasoconstricting responses to ACh were most enhanced at the distal edge of EES as compared with non-stented vessel, and were significantly inhibited in the nifedipine group (Figure). Furthermore, the inflammatory profiles, including serum levels of hsCRP and adiponectin, were also improved in the nifedipine group (Figure).

Figure. Effects of Long-acting Nifedipine on Coronary Vasomotion and Inflammatory Markers



Conclusions: These results indicate that long-acting nifedipine suppresses DES-induced coronary hyperconstricting responses in humans.

P6118 | BENCH

Atorvastatin downregulates in vivo the immediate-early response gene EGR1 in patients with acute coronary syndromes

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Background: Statins have anti-inflammatory and immune-regulatory effects besides lowering lipids that may, at least partially, account for their beneficial effects. In a previous ex vivo study, atorvastatin improves the functional profile of CD4+T-cells isolated from statin-naïve acute coronary syndrome (ACS) patients and, among the other genes, markedly down-regulates early growth response 1 (EGR1) gene expression, as assessed by PCR array analysis. EGR-1 is an immediate-early response gene, based on rapid kinetics of its expression and induction. EGR1 up-regulation alters a wide array of EGR1 target downstream genes such pro-inflammatory cytokines, and also negatively regulates the expression of the anti-inflammatory interleukin-10 at post-transcriptional level. Thus, we hypothesized that EGR1 might mediate the immune-regulatory effects of atorvastatin in ACS.
Purpose: To verify the in vivo effects of atorvastatin on EGR1, we analyzed EGR1 gene expression and protein levels in CD4+T-cells isolated from 10 statin-free ACS patients at baseline (before atorvastin therapy, T0), and after 24h (T24) and 48h (T48) of atorvastatin therapy (80 mg/daily).
Results: qRT-PCR results show that EGR1 expression in vivo was reduced after 24h of atorvastin therapy, from a mean value of 26.7±5.7 (mean ± SEM) at T0 to 8.5±1.9 (mean ± SEM) at T24 (P=0.01) and to 5.9±2.1 (mean ± SEM) at 48h (P=0.005). Moreover, EGR1 protein levels were significantly downregulated 48h after 80 mg statin assumption (T0 vs T48 P=0.03) (Fig. 1).

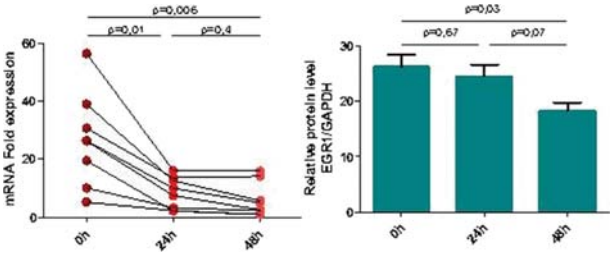

Figure 1. In vivo EGR1 expression

Conclusion: The anti-inflammatory effects of atorvastatin in patients with ACS might be related, at least partially, to direct inhibition of the master regulator EGR1. Our finding might offer a causal explanation on why statins have early beneficial effects in ACS.

P6119 | BEDSIDE

Differential benefit of statin in secondary prevention of acute myocardial infarction according to the level of triglyceride and high-density lipoprotein cholesterol

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Background: Although substantial portion of patients with myocardial infarction (MI) were diagnosed as dyslipidemia, the differential benefit of statin according to the state of dyslipidemia was sparsely investigated. We sought to address the efficacy of statin in secondary prevention of MI according to the level of triglyceride and high-density lipoprotein (HDL) cholesterol on admission.
Methods: The 24653 acute MI patients were enrolled and total patients were divided according to level of triglyceride and HDL cholesterol on admission; Group A (HDL ≥40mg/dL & triglyceride <150mg/dL; n=11819), Group B (HDL ≥40mg/dL & triglyceride ≥150mg/dL; n=3329), Group C (HDL <40mg/dL & triglyceride <150mg/dL; n=6062) and Group D (HDL <40mg/dL & triglyceride ≥150mg/dL; n=3443). We evaluated differential efficacy of statin according to the presence or absence of component of dyslipidemia. The primary end point was major adverse cardiac event (MACE) s and MACE was defined as composite of cardiac death, non-fatal MI, target-vessel revascularization and coronary artery bypass surgery for 2 years.
Results: Statin therapy significantly reduced the risk of MACEs in Group A (HR=0.676; 95% CI: 0.582–0.785; p<0.001). However, the efficacy of statin was not prominent in Group B, C or D. In propensity-matched population, the result was similar. Especially, the benefit of statin in Group A was different compared with Group D (Interaction p=0.042)
Conclusion: The benefit of statin in patients with MI was different according to the presence or absence of dyslipidemia. Especially, because of insufficient benefit of statin in patients with MI and dyslipidemia, different lipid-lowering strategy is necessary in these patients.

P6120 | BEDSIDE

Achievement of dual LDL-C (<70 mg/dL) and hs-CRP (<2 mg/L) goals more frequent with addition of ezetimibe and associated with better outcomes in IMPROVE-IT

E.A. Bohula May[1], R.P. Giugliano[1], C.P. Cannon[1], S.A. Murphy[1], J. Zhou[1], M.A. Blazing[2], J.A. White[2], A.M. Tershakovec[3], T.A. Musliner[3], E. Braunwald[1] on behalf of TIMI Study Group & DCRI. *[1]Brigham and Women's Hospital, TIMI Study Group, Boston, United States of America; [2]Duke Clinical Research Institute, Durham, United States of America; [3]Merck & Co., Inc., Kenilworth, NJ, United States of America*

Background: Statins lower LDL-C and hs-CRP and the addition of ezetimibe (EZ) to simvastatin (S) results in a further reduction in LDL-C and hs-CRP.
Purpose: An analysis of the relationship between achieved LDL-C and hs-CRP goals and outcomes for the combination of EZ and S was pre-specified.
Methods: The IMPROVE-IT trial randomized 18,144 patients stabilized after ACS to EZ/S or S alone. LDL-C and hs-CRP were measured 1 month after randomization. Outcomes were assessed in those achieving the pre-specified goals of LDL-C <70mg/dL and hs-CRP <2mg/L compared to those achieving only 1 or neither goal. Patients meeting both goals at baseline, with no 1 month values, or with endpoints prior to 1 month were excluded.
Results: Of the 15,179 included in this analysis, 39% achieved the dual LDL-C and hs-CRP goals at 1 month. The comparator group included patients meeting neither goal (14%), only hs-CRP <2mg/L (14%) or only LDL <70mg/dL (33%). Overall, those achieving the dual goals had lower rates of the primary and individual endpoints (Table 1). More patients treated with EZ/S met the goals compared to treatment with S alone (50% vs 29%, p<0.001). The clinical benefit of achieving the dual LDL-C and hs-CRP goals was similar irrespective of treatment assignment (all p-interaction NS). Data for efficacy outcomes with multivariate adjustment will be presented.

Table 1. Primary and individual endpoints by LDL-C and hs-CRP goals

	Dual goals met (N=5995) n (7 yr KM %)	No or one goal met (N=9184) (7 yr KM %)	HR* (95% CI)	p-value
CVD/MCE/stroke	1508 (28.0)	2819 (34.8)	0.79 (0.74–0.84)	<0.001
CVD	241 (4.6)	585 (7.4)	0.61 (0.52–0.71)	<0.001
MI	552 (10.8)	1093 (14.2)	0.77 (0.69–0.85)	<0.001
Coronary revasc ≥30 d	1059 (19.7)	1904 (23.9)	0.83 (0.76–0.89)	<0.001
Stroke	190 (3.8)	344 (4.6)	0.84 (0.70–1.01)	0.0606
Hospitalization for UA	76 (1.5)	141 (1.8)	0.80 (0.60–1.06)	0.125

CVD, cardiovascular death; MCE, major coronary event (myocardial infarction, coronary revascularization ≥30 days after randomization or hospitalization for unstable angina); *Adjusted for randomized treatment allocation (EZ/S vs S) and stratification criteria.

Conclusions: Significantly more patients treated with EZ/S met the dual goals of an LDL-C <70mg/dL and hs-CRP <2mg/L. Reaching both LDL-C and hs-CRP goals was associated with improved clinical outcomes.

BEST POSTERS IN ADVANCES IN ECHOCARDIOGRAPHY

P6122 | BEDSIDE

Quantification of longitudinal and radial motion of the right ventricle using 3D echocardiography: technical aspects and clinical relevance in heart transplant patients

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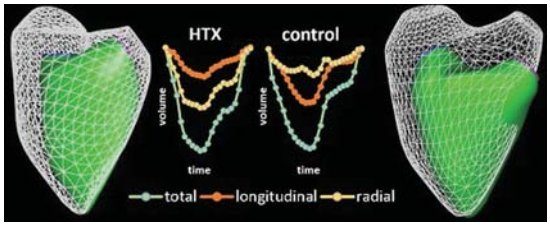
Longitudinal shortening is considered to be the most important motion determining right ventricular (RV) function. However, the radial direction ("bellows" effect) can gain particular importance in certain conditions. Our aim was to quantify the longitudinal and the radial components of RV performance using three-dimensional (3D) echocardiography and assess their relative contribution in normal subjects versus patients after heart transplantation (HTX).

Thirty HTX patients and 30 healthy volunteers were enrolled. Using dedicated software for RV 3D and speckle tracking analysis (4D RV-Function 2), beutel model was created and exported volume-by-volume throughout the cardiac cycle. Beside end-diastolic (EDV) volume and total ejection fraction (TEF), we quantified longitudinal (LEF) and radial ejection fraction (REF) by decomposing the motion of each vertex of the reconstructed 3D beutel model along three orthogonal axes and omitting the other two directions.

EDV did not differ between the groups (HTX vs control; 87±22 vs 80±26mL). In HTX patients TEF was lower, but tricuspid annular plane systolic excursion (TAPSE) was decreased to a greater extent (TEF: 45±7 vs 51±4% [–12%], TAPSE: 15±4 vs 22±3mm [–32%], $p<0.01$). LEF correlated robustly with TAPSE ($r=0.75$) and free wall longitudinal strain ($r=-0.69$, $p<0.001$). In healthy subjects, TEF correlated with LEF ($r=0.50$) and REF ($r=0.37$, $p<0.05$). In HTX patients, TEF correlated with REF ($r=0.80$, $p<0.001$), but not with LEF. REF/TEF ratio was significantly higher in HTX patients (56±12 vs 46±9%, $p<0.001$).



Our software allows to quantify longitudinal and radial motion of the RV separately using 3D analysis. Current results confirm the empirical phenomenon on the superiority of radial motion in determining RV function in HTX patients.

P6123 | BEDSIDE

Right ventricular post systolic shortening using speckle-tracking echocardiography associated with prognosis in patients with pulmonary artery hypertension

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Purpose: Right Ventricular (RV) free-wall longitudinal peak systolic strain is a predictor of the clinical outcome of patients with pulmonary artery hypertension (PAH). RV dyssynchrony including post systolic shortning (PSS) in RV free-wall appeared and associated with RV systolic function in patients with RV pressure overload. We sought to investigate the association between the degree of PSS in RV free-wall using speckle-tracking echocardiography (STE) and prognosis in patients with PAH.

Methods: We performed speckle-tracking echocardiography and right heart catheterization in 91 PAH patients (age: 42±13 years). We measured RV free-wall peak longitudinal systolic strain (PLSS) and PSS index (=RV peak longitudinal strain- peak longitudinal systolic strain)/peak strain) by STE. Mean right atrial pressure (mRAP), pulmonary vascular resistance (PVR), and cardiac index (CI) by right heart catheterization, and serum BNP were measured.

Results: Sixteen patients (17.6%) died within three years. PSS appeared in all sixteen non-survivors patients. PSS index was higher in non-survivors patients compared with survivors patients (16.7% vs. 3.7%; $p<0.001$). There were significant correlations between CI and PLSS ($r=0.71$, $p<0.01$), PSS index ($r=0.69$, $p<0.01$). There were significant correlations between mRAP and PLSS ($r=0.72$, $p<0.01$), and PSS index ($r=0.70$, $p<0.01$). There were significant correlations between PVR and PLSS ($r=0.70$, $p<0.01$), PSS index ($r=0.67$, $p<0.01$). BNP level was correlated with PLSS ($r=0.72$, $p<0.01$), PSS index ($r=0.68$, <0.01). PLSS $\geq$-10 ($p<0.01$) and PSS index $\geq$13.5% ($p<0.01$) was independent predictor to evaluate the long-term prognosis by Kaplan–Meier survival curves.

Conclusions: PSS in RV free-wall using STE was important factor for noninvasive evaluation of severity and prognosis in patients with PAH as well as PLSS.

P6124 | BEDSIDE

The contribution of pressure recovery and three-dimensional imaging on echocardiographic evaluation of severe aortic stenosis for TAVI

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Aim: In patients with aortic stenosis (AS), echocardiographic assessment of stenosis severity is of primary importance, especially for transcatheter aortic valve implantation (TAVI). Our hypothesis is that three-dimensional (3D) echocardiography and correction for pressure recovery (PR) by energy loss index (ELI) may improve aortic valve area (AVA) calculation.

Methods and results: 40 patients with severe AS evaluated for TAVI were included in the study. Left ventricular outflow tract (LVOT) and ascending aorta (AA) cross-sectional area was determined in two-dimensional transthoracic echocardiography (2DTTE), 2D transesophageal echocardiography (TEE), 3DTEE, and multislice computed tomography (MSCT). AVA was calculated by the continuity equation and corrected for PR. ELI was determined as [(AVA $\times$ AA)/(AA - AVA)]/body surface area. LVOT area was 2.39±0.20 cm^2 calculated using 2DTTE, 2.72±0.15 cm^2 calculated using 2DTEE, 3.80±0.14 cm^2 by planimetry in 3DTEE, and 4.30±0.18 cm^2 by planimetry in MSCT ($P<0.001$). AA area was 4.52±0.33 cm^2 calculated using 2DTTE, 4.44±0.23 cm^2 calculated using 2DTEE, 5.25±0.25 cm^2 by planimetry in 3DTEE, and 6.66±0.31 cm^2 by planimetry in MSCT ($P<0.001$). Indexed aortic valve area (AVAI) calculated by 2DTTE and 2DTEE was smaller (0.26±0.02 cm^2/m^2 and 0.30±0.02 cm^2/m^2) compared to 3DTEE (0.46±0.02 cm^2/m^2; $P<0.005$). When AVAI determined by 3DTEE was corrected for PR by calculation of ELI, there was a further increase (0.50±0.03 cm^2/m^2; $P<0.005$), and 10/40 (25%) patients were reclassified to moderate AS.

Conclusion: 3DTEE is more accurate than 2DTTE and 2DTEE for determining LVOT and AA dimensions. When AS severity is determined by 3DTEE and corrected for PR using the 3D values, it needs to be reclassified from severe to moderate in 25% of patients.

P6125 | BEDSIDE

Left atrial appendage thrombus in patients with atrial fibrillation before pulmonary vein isolation: discrepancy between tee and cardiac CT

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Background: Transesophageal echocardiography (TEE) is the gold standard modality for evaluating thrombus in the left atrium. Single-phase cardiac computed tomography (CCT) is commonly used in clinical practice performed prior to the pulmonary vein isolation (PVI) procedures in patients with atrial fibrillation. Here, this study aimed to evaluate the prevalence, clinical outcome, and discrepancies in thrombus formation between the two modalities.

Methods: This retrospective study included 253 consecutive patients who underwent both TEE and CCT before PVI. The evaluation of thrombus formation was performed by radiologists and echocardiography specialist, individually.

Results: All patients were diagnosed with no thrombus on TEE, and all patients were treated the oral anticoagulants; 121 patients were treated with warfarin vs. 132 patients were treated with Non-vitamin K antagonist oral anticoagulants (NAOC), whereas 21 patients (8.1% of all patients, warfarin: 12 patients, NOAC: 9 patients) were diagnosed with left atrial appendage (LAA) thrombus using CCT. PVI was achieved in all patients. We have no embolic events after PVI. Significant difference in CHADS2 score, LAA flow, and left atrial volume index was found between the patients with and without LAA thrombus detected using CCT (1.1 vs. 1.5, 47.5 vs. 22.2cm/s, and 35.3 vs. 52.9ml/m^2, all $P<0.001$, respectively). LAA flow<25.5cm/s predicted LAA thrombus identified by CCT with the sensitivity of 90% and the specificity of 87%.

Conclusions: Approximately 10% patients revealed discrepancies of thrombus formation between TEE and CCT before PVI. PVI can be performed safely and effectively in these patients whose thrombus formation was evaluated by using TEE.

BEST POSTERS IN VASCULAR SIGNAL TRANSDUCTION

P6127 | BENCH

Role of perivascular T cell dependent inflammation in the regulation of vascular dysfunction in human atherosclerosis

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Background: Atherosclerosis is an inflammatory disease. Systemic inflammation is well understood, but role and characteristics of perivascular adipose tissue (pVAT) inflammation is not clear in human atherosclerosis.

Aim and methods: We aimed to characterize using flow cytometry T cell subsets infiltrating pVAT of coronary artery (CORO) and internal mammary arteries (IMA) from total of 169 CABG patients. We also studied relationships between pVasc inflammation and vascular dysfunction assessed in IMA by isometric vasorelax-

ations to acetylcholine and ROS production by 5uM lucigenin. We tried to check the casual relationship between endothelial dysfunction and pVAT inflammation.
Results: Leukocyte (CD45+) infiltration was observed in both IMA and CORO, but was much higher in CORO pVAT (1,6±0,1 vs. 12,2±1,2%; p<0,0001). Similarly infiltration of total T cells (p<0,05) and CD8+ T cells (p<0,001) [but not CD4+] were significantly higher in CORO pVAT. Interestingly, leukocyte and T cell infiltration was correlated between these two pVAT depots [CD45+ (R=0,24; p=0,02), CD3+ (R=0,29 p=0,004), CD8+ (R=0,29 p=0,005)], suggesting systemic regulation of perivascular inflammation. Characterization of pVAT infiltrating T cells revealed that majority of T cells in pVAT were effector cells (CD45RO+CCR7-CD45RA-). Total leukocytes, T cells and CD8+ cells in pVAT inversely correlated with endothelial function (r=–0,25, r=–0,27, r=–0,31 respectively; p<0,05 for all) and positively with vascular ROS production (r=0,36, r=0,34, r=0,31; p<0,05 for all). Endothelial function was particularly strongly inversely correlated with the the presence of leukocyte activation markers such as HLA-DR, CD25, CD28 and CCR5. At the same time, T regulatory cell (CD4+/CD25+/Foxp3+) content did not correlate with endothelial function or ROS, although it was significantly higher in IMA pVAT than in CORO (8,6±6,3 vs. 3,7±2,3cells/mg p<0,05). Next, to examine the casual relationship between endothelial dysfunction and pVAT leukocyte infiltration we incubated IMA with pVAT for 24 hours and then checked relaxations to Ach. Co-incubation of IMA with high leukocyte containing pVAT resulted in exacerbation of endothelial dysfunction, while incubation with pVAT with low leukocyte content did not (ANOVA p<0,001).
Conclusion: Systemically regulated pVAT inflammation characterized by presence of activated T cell infiltration is a prominent feature of atherosclerosis and is associated with endothelial dysfunction and ROS production. We show the causative role of pVAT leukocyte infiltration in endothelial dysfunction.

P6128 | BENCH
STAT3 in vascular smooth muscle cells protects aorta from dissection

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Aortic dissection (AD) is a common and fatal disease for which pathogenesis is largely unknown. Recently we and others reported that JAK/STAT3-activating cytokines are highly expressed in human and mouse models of AD. In this study, we first examined the activation of STAT3 in human AD. We found that STAT3 was activated (phosphorylated) both in inflammatory cells and in vascular smooth muscle cells (VSMCs) in AD tissue. We used a mouse model of AD that was induced by continuous infusion of beta-aminopropionitrile, an inhibitor of lysyl oxidase that cross-links collagen and elastin, and angiotensin II (BAPN+AngII). BAPN+AngII caused thoracic and suprarenal AD starting at 7 days of the administration, and most of the mice developed AD within 14 days. To investigate into the function of STAT3 in VSMCs, we used the smooth muscle-specific knockout mice for SOCS3, a negative feedback regulator of STAT3 (smSOCS3-KO). The smSOCS3-KO mice developed less severe AD in the aortic arch (WT; 0.093±0.018 vs. smSOCS3-KO; 0.018±0.013 mm/g body weight, P=0.014), as determined by the lesion length with enlarged aortic diameter. Immunofluorescence staining of phospho-STAT3 showed activation of STAT3 by BAPN+AngII, which was more prominent in smSOCS3-KO as expected. Unexpectedly, smSOCS3-KO aorta showed more collagen fibers and non-muscle cells in adventitia, suggesting that deletion of smSOCS3 may augment the tensile strength of aorta. Indeed, direct measurement of the tensile strength of the excised rings from aortic arch indicated that smSOCS3-KO aorta had more tensile strength compared to wild type aorta before applying BAPN+AngII (WT; 0.171±0.018 vs. smSOCS3-KO; 0.234±0.011 N/mm, P=0.004). Therefore, activation of STAT3 in VSMCs reinforces the aortic wall by enhancing collagen synthesis in adventitia, thus protecting aorta from dissection. Understanding of the protection mechanism of the aortic walls from dissection would lead to better understanding of the molecular pathogenesis, which is essential for developing novel therapeutic strategy for AD.

P6129 | BENCH
High Density Lipoproteins exert pro-inflammatory effects on macrophages via passive cholesterol depletion and PKC-dependent NF-kB/STAT1 activation

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Background: Membrane cholesterol is known to modulate a variety of cell signaling pathways and functions. While cholesterol depletion by High-Density Lipoproteins (HDL) has potent anti-inflammatory effects in various cell types, its effects on inflammatory responses in macrophages remain ill defined.
Methods and results: Pre-incubation of human and murine macrophages in vitro with human reconstituted (apolipoproteinA-I/phosphatidylcholine) or native HDL significantly decreased LPS-induced anti-inflammatory IL-10 production, while the opposite was observed for the pro-inflammatory mediators IL-12 and TNF. We show that these effects are mediated by passive cholesterol depletion and lipid raft disruption, without involvement of ABCA1, ABCG1, SR-BI or CD36. These pro-inflammatory effects are confirmed in vivo in peritoneal macrophages from ApoA-I transgenic mice, which have high circulating HDL levels. Native and reconstituted HDL enhances Toll Like Receptor-induced signaling by activating protein kinase C (PKC), since inhibition of PKC ablated the observed HDL effects. Using macrophages from NF-κB luciferase mice, we observed that HDL induces NF-κB activation. Western blot analyses showed that in particular the p65 subunit was activated. Using specific knock-out mice for the upstream activation pathways, we show that the observed HDL effects are independent of the upstream kinases IKK, NIK and CKII. Furthermore, using STAT1 knock-out mice we observed that also STAT1 is involved in the pro-inflammatory HDL effects on IL-10 and IL-12 secretion. On the other hand, using pharmacological inhibitors, we show that HDL enhances ADAM protease activity, thereby mediating TNF-α release.
Conclusion: HDL exerts pro-inflammatory effects on macrophages via passive cholesterol depletion by activation of PKC, NF-kB and STAT1. These pro-inflammatory activities on macrophages could at least partly underlie the disappointing therapeutic potential of HDL raising therapy in current cardiovascular clinical trials.

P6130 | BENCH
Gp130 inhibitor reduces inflammation and reverses pulmonary arterial remodeling of monocrotaline-induced pulmonary arterial hypertension

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Background: The pathogenesis of pulmonary arterial hypertension (PAH) is characterized by three major processes including vasoconstriction, vascular remodeling and microthrombotic events. Accumulating evidences point to inflammatory cytokine interleukin (IL)-6 as a major contributor to the development of PAH. Glycoprotein130 (Gp130) is a unique signal-transducing subunit involved in the biologic activities of IL-6.
Purpose: To test the hypothesis that Gp130 inhibitor reduces inflammation and reverses pulmonary vascular remodeling of monocrotaline (MCT)-induced PAH in rats.
Methods: Sixty male Sprague-Dawley rats weighing 240 to 250 g were randomly divided into three groups: Saline-treated control, MCT-exposed and MCT-exposed plus Gp130 inhibitor. Three groups were evaluated at day 28 for haemodynamic parameters, right ventricular hypertrophy, morphometry, immunohistochemistry, IL6, phosphorylated signal transducer and activator of transcription 3 (PY-STAT3), proliferating cell nuclear antigen (PCNA), bone morphogenetic protein receptor-2 (BMPR2) expression, and proangiogenic factor, vascular endothelial growth factor (VEGF), and the proproliferative kinase extracellular signal-regulated kinase (ERK), and the antiapoptotic proteins survivin and Bcl-2 and Bax.
Results: Compared to the MCT group, the administration of Gp130 inhibitor following MCT improved haemodynamic measurements, significantly reduced the severity of inflammation measured by the levels of IL-6 and CX3CL1 (both P<0.001), and reversed pulmonary arterial remodeling assessed by the medial wall thickness (P<0.0001). The Gp130 inhibitor upregulated BMPR2 expression of MCT-exposed lungs (P<0.001).Also, it decreased the expression of PCNA, VEGF, ERK and survivin (all P<0.05).
Conclusions: Gp130 inhibitor upregulated the MCT-exposed pulmonary BMPR2 expression, restored the balance between BMPR2 and IL-6, reduced the inflammation associated with IL-6, significantly inhibited the proliferation of pulmonary arterial smooth muscle cells and reversed pulmonary vascular remodeling of MCT-induced PAH in rats.

BEST POSTERS IN RHEUMATIC HEART DISEASE

P6132 | BEDSIDE
Prevalence of rheumatic heart disease in north Madagascar: an echocardiographic screening

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Background: Rheumatic Heart Disease (RHD) is one of the major causes of morbidity and mortality all over the world. Especially in developing countries it is a significant public health concern. Historically, sub-Saharan Africa has the greatest prevalence. In epidemiologic studies, echocardiographic screening has led to increased RHD prevalence compared to clinical screening, for the higher number of asymptomatic cases diagnosed. There are no data about RHD in Madagascar and if its prevalence is similar to that of poorest nations or not is unknown. Thus,

we sought to estimate the prevalence of RHD in the North Malagasy population by an echocardiographic screening.
Methods: We screened 503 individuals (North Madagascar). According to the WHF guidelines for echocardiographic diagnosis of RHD, we studied two groups: children from 5 to 19 years old and adults more than 20 years old. Each patient underwent clinical questionnaire, cardiac examination and transthoracic echocardiogram focused on the 4 valves, by a portable ultrasound machine. In addition, children underwent oropharyngeal swab by rapid kit analysis and adults blood sample for Anti-Streptolisyn O (ASO) titer.
Results: Of the overall population 42% were children, 60% females, 64% from a rural contest. The total prevalence of RHD was 3.2% (16 cases). Of the 209 children (mean age 13.5 years), 7 (3.3%) were found having RHD disease. All had mitral disease, one patient had involvement of aortic valve too. Three cases (43%) were borderline, 4 were definite, according to WHF guidelines definition. Six of them had cardiac murmur, 3 (43%) had positive pharyngeal swab, 6 (86%) had supposed past exposition to Group A Streptococcus (GAS) infection, as derived from the clinical questionnaire. Among the 294 adults (mean age 35 years), 9 patients (3.1%) had RHD disease. Of these, 7 had mitral disease, one had both left heart valves disease, and of the 5 available ASO titer none was positive. Only 3 (33%) of the 9 RHD were positive on cardiac auscultation and 22% had past history of GAS infections.
Conclusion: This is the first study collecting epidemiologic data about RHD in North Madagascar, where RHD prevalence is similar to that of other African countries. Use of echocardiography, advanced technique in a developing country, permits to identify more subclinical cases. Moreover, we confirm the low accuracy of laboratory tests and clinical examination in RHD screening. However, new data are needed to describe the real dimension of the problem for future therapeutic and preventive strategies.

P6133 | BEDSIDE
Prevalence of clinically silent and manifest rheumatic heart disease among children in Nepal

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Background: Rheumatic heart disease continues to be a major contributor to morbidity and mortality in developing countries. Detection of clinically silent disease and timely secondary prevention may prevent progression of disease.
Objective: The objective of the study was to assess prevalence of clinically silent and manifest rheumatic heart disease, and to determine risk factors associated with diagnosis.
Methods: A multistage sampling strategy was used to randomly select public and private schools in urban and rural areas in the Sunsari district situated on the foothills of the lower Himalayan range in Nepal. All children from a selected school between the ages of 5 to 15 years underwent a standardized interview, and independent clinical and echocardiographic examination. Echocardiographic diagnosis of rheumatic heart disease was based on the World Heart Federation criteria. Clinically silent disease was recorded in the absence of a cardiac murmur.
Results: Between December 2012 and September 2014 a total of 5467 eligible children from 26 randomly selected schools were enrolled in an observational survey. After exclusion of 288 children due to incomplete documentation, 5179 children remained for the purpose of this analysis. The median age of the children was 10 years (IQR 8–13) and 48% were female. Prevalence of borderline or definite rheumatic heart disease amounted to 10.2/1000. 36 children had definite rheumatic heart disease and 17 had borderline disease. Prevalence increased across age categories from 5.5/1000 among children 5 years of age to 16.0/1000 among children aged 15 years. Silent disease (n=44) was 5 times more common than clinically manifest disease (n=9). Children with silent rheumatic heart disease were younger than children with clinically manifest disease (10.5 years QR 9–13 versus 14 (IQR 11–15) years, p=0.05). Children with rheumatic heart disease more commonly went to governmental schools (40/76% versus 2798/55%, p=0.002), were older (11 years, IQR 9–14 versus 10 years, IQR 8–13, p=0.031) and more commonly girls (female 34/64% versus 19/36%, p=0.021). In a multivariate analysis, older age, female gender, and governmental school were identified as independent predictors of RHD.
Conclusion: Prevalence of rheumatic heart disease continues to be high in Eastern Nepal. Prevalence increases with advancing age, and clinically silent disease is approximately 5 times more common than manifest disease. Older age, female gender, and governmental school were identified as independent predictors of rheumatic heart disease.

P6134 | BEDSIDE
Echocardiographic screening for rheumatic heart disease using the WHF criteria among 16,329 asymptomatic school children from 4 sites in India

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Background: Recent studies using echocardiographic screening of school children have reported a much higher prevalence of rheumatic heart disease (RHD). However, these studies have used variable criteria to diagnose RHD. Recently World Heart Federation (WHF) has published evidence based standardization criteria for echocardiographic diagnosis of RHD to enable uniformity between various studies.
Purpose: We report the prevalence of RHD using the proposed WHF echocardiographic criteria from four different sites in India to estimate the burden of the disease.
Methods: We carried out a cross sectional survey in four sites (North, North East and West) in India to diagnose RHD in asymptomatic school children aged 5–19 years using portable echocardiography. The demographic data was collected. After history and physical examination, echo-Doppler was performed, using a bedside portable echocardiography machine. Uniform methodology was used at all sites. A diagnosis of RHD was made using WHF criteria; it was divided into "definite RHD" and "borderline RHD".
Results: A total of 16,329 asymptomatic school children were screened. The mean age was 10.9±2.9 years and 54% were males. Clinical examination detected mitral regurgitation in 11 patients giving the estimated prevalence of clinical RHD as 0.67/1000 school children. Using the WHF criteria, RHD was diagnosed in 119 additional cases, giving a prevalence of 7.28/1000 school children (95% CI: 6.0–8.6/1000 children). Out of these 27 were diagnosed with definite RHD and 92 were diagnosed with borderline RHD. The prevalence of subclinical RHD in different regions is shown in the table.

Prevalence of RHD in school children

Characteristics	Manipur (n=3368)	Goa (n=2023)	Navsari (n=2490)	Ballabgarh (n=8448)
Clinical RHD	1	3	1	6
Prevalence of clinical RHD	0.29/1000	1.48/1000	0.40/1000	0.71/1000
Subclinical RHD using WHF criteria	16	20	22	61
Definite RHD	2	3	6	16
Borderline RHD	14	17	16	45
Prevalence of subclinical RHD	4.7/1000	9.9/1000	8.8/1000	7.2/1000

Conclusions: The prevalence of RHD is several folds higher using WHF echocardiographic criteria. The prevalence of RHD varies widely across India and programs to control RHD should focus on high prevalence zones.

P6135 | BEDSIDE
Echocardiographic screening among schoolchildren in Peru: prevalence of rheumatic heart disease according to different definitions and incidental findings

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Background: Rheumatic heart disease (RHD) remains a major challenge in low and middle income countries. Echocardiographic screening facilitates early detection of clinically silent valvular disease. The implications of different echocardiographic criteria for diagnosis of RHD, and the burden of incidental findings from echocardiographic screening need to be determined.
Objective: To evaluate the implications of different classifications of RHD on estimated prevalence, and to systematically assess the importance of incidental findings from echocardiographic screening among schoolchildren.
Methods: We performed a population-based observational survey using portable echocardiography among schoolchildren aged 5 to 16 years from randomly selected public and private schools in Peru. RHD was defined according to the modified World Health Organization (WHO) criteria and the World Heart Federation (WHF) criteria.
Results: Among 1395 eligible students from 40 classes and 20 schools, 1023 (73%) participated in the present survey. The median age of the children was 11 years (interquartile range 8–13 years) and 50% were female. 394 children (39%) reported a past medical history of a sore throat. Two children presented with migrating arthritis and one child had chorea; however, none of the children qualified for a diagnosis of acute rheumatic fever according to the Jones criteria. On cardiac auscultation, 44 children (4.3%) were found to have a heart murmur. Prevalence of possible, probable and definite RHD according to the modified WHO criteria amounted to 19.7/1000 children and ranged from 10.2/1000 among children 5 to 8 years of age to 39.8/1000 among children 13 to 16 years of age; the prevalence of borderline/definite RHD according to the WHF criteria was 3.9/1000 children. Reliability of echocardiographic on-site diagnosis was assessed by 5 off-site raters; prevalence-adjusted bias-adjusted kappa ranged between 0.817 and 0.975. 21 children (2.1%) were found to have congenital heart disease, 10 of which had atrial septal defects, 4 patent ductus arteriosus, 4 bicuspid aortic valves, 1 double mitral valve orifice, 1 partial anomalous pulmonary venous connection, and 1 left ventricular noncompaction.

Conclusions: Prevalence of rheumatic heart disease ranged from 3.9/1000 children to 19.7/1000 children and was paralleled by a comparable number of undetected congenital heart disease. Strategies to address collateral findings from echocardiographic screening are necessary in the setup of active surveillance programs for rheumatic heart disease.

BEST POSTERS IN CARDIOVASCULAR PREVENTION: INTERVENTIONS AND OUTCOMES

P6137 | BEDSIDE
Clinical characteristics and outcomes of dialysis patients with atrial fibrillation: The Fushimi AF Registry

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Background: Oral anticoagulants (OAC) are available for stroke prevention in patients with atrial fibrillation (AF). AF is a common arrhythmia in dialysis patients, and the use of warfarin for those patients is controversial.
Purpose: We evaluated clinical characteristics and outcomes in dialysis patients with AF in "real-world" clinical practice.
Methods: The Fushimi AF Registry is a community-based prospective survey of AF patients who visited the participating medical institutions in Fushimi-ku, Japan, which is a densely populated urban area with a total population of 283,000. Follow-up data were available for 3,304 patients by the end of July 2014 (the median follow-up of 746 days). We compared clinical characteristics and outcomes between the dialysis group (n=80, 2.4%) and others (no chronic kidney disease (CKD) group and CKD group).
Results: The dialysis group was younger (71.6 years in no CKD group, 78.2 years in CKD group, 71.1 years in the dialysis group; $p<0.01$), and had higher CHADS2 score (1.77 at no CKD group, 2.50 at CKD group, 2.64 at the dialysis group; $p<0.01$) and CHA2DS2-VASc score (3.01 at no CKD group, 4.03 at CKD group, 4.08 at the dialysis group; $p<0.01$). The dialysis group had more comorbidities such as hypertension (82.5%), diabetes mellitus (56.3%), coronary heart disease (40.0%), peripheral arterial disease (18.8%), and history of major bleeding (6.3%), compared with other groups. However, history of stroke/systemic embolism (SE) was comparable between the groups. The dialysis group was prescribed warfarin less commonly (41.3%) and anti-platelet drugs more commonly (47.5%). The incidence of stroke or systemic embolism (SE) in the dialysis group was 4.4 per 100 person-years, which was comparable with the non-dialysis group (hazard ratio (HR) 1.87; 95% confidence interval (CI), 0.73–3.87). Those of major bleeding and all-cause death in the dialysis group were significantly higher than the non-dialysis group (major bleeding: 4.6 per 100 person-years, HR 3.21; 95% CI, 1.25–6.74; all-cause death: 23.4 per 100 person-years, HR 3.78; 95% CI, 2.60–5.31). Among dialysis patients, warfarin was prescribed to those who were older and had higher CHADS2 score, but it did not significantly affect major clinical events, such as stroke/SE, major bleeding or all-cause death. [stroke/SE 1.8 vs. 6.1 (p=0.23), major bleeding 5.8 vs. 3.8 (p=0.63), all-cause death 32.4 vs. 17.6 (p=0.08)].
Conclusions: Dialysis patients with AF showed high incidence of bleeding and all-cause death, and warfarin therapy did not show significant benefit on major outcomes.

P6138 | BEDSIDE
Mortality in takotsubo syndrome is similar to mortality in myocardial infarction - a report from the SWEDEHEART registry

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Background: Takotsubo syndrome is an acute cardiovascular condition that predominantly affects women.
Purpose: In this study, we compared patients with takotsubo syndrome and those with acute myocardial infarction with respect to patient characteristics, angiographic findings, and short- and long-term mortality.
Methods: From the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA), we obtained and merged data on patients undergoing coronary angiography in Västra Götaland County in western Sweden between January 2005 and May 2013. Short- and long-term mortality in patients with takotsubo (n=302) and patients with ST-elevation myocardial infarction (STEMI, n=6595) and non-ST-elevation myocardial infarction (NSTEMI, n=8207) were compared by modeling unadjusted and propensity score–adjusted logistic and Cox proportional-hazards regression.
Results: The proportion of the patients diagnosed with takotsubo increased from 0.16% in 2005 to 2.2% in 2012 ($P<0.05$); 14% of these patients also had significant coronary artery disease. Cardiogenic shock developed more frequently in patients with takotsubo than NSTEMI (adjusted OR 3.08, 95% CI 1.80–5.28, $P<0.001$). Thirty-day mortality was 4.1% and was comparable to STEMI and NSTEMI. The long-term risk of dying in takotsubo (median follow-up 25 months) was also comparable to NSTEMI (adjusted HR 1.01, 95% CI 0.70–1.46, P=0.955) STEMI (adjusted HR 0.83, 95% CI 0.57–1.20, P=0.328).
Conclusions: The proportion of acute coronary syndromes attributed to takotsubo syndrome in Western Sweden has increased over the last decade. The prognosis of takotsubo syndrome is poor, with similar early and late mortality as STEMI and NSTEMI.

P6139 | BEDSIDE
Effect of monitoring warfarin treatment of patients by single versus multiple physicians on time in therapeutic range (TTR) and treatment associated complications: Multicenter prospective cohort study

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Background: Warfarin monitoring is a difficult problem because warfarin is affected from various conditions and has a narrow therapeutic window. In this study, we aim to evaluate the effect of single vs. multiple physicians on monitoring of warfarin treatment.
Methods: We enrolled 625 patients with nonvalvular-valvular atrial fibrillation (AF) and prosthetic valve. This is multicenter prospective cohort study including recent three years. The INR values were collected and TTR was calculated with linear interpolation method (Rosendaal method) using specialized software. The patients, whose TTR value was above 65%, were accepted as patient was on effective warfarin treatment. Minimum 6 months period of warfarin usage required and warfarin interruption with any reason was excluded. Minimum 4 INR value with maximum 2 months interval have been recorded. In hospitals with having only one cardiologist and patients warfarin treatment was monitored by the same physician, the data were grouped as "single physician". In hospitals with multiple cardiologists, patients have admitted to different physicians in each visit, the data were grouped as "multiple physicians"
Results: In this study, 24.9% of the patients (n=156) were followed by single physician. Mean age, comorbidities and indications of warfarin usage of the patients were not different between groups. Mean TTR values of the single physician group were higher than multiple physicians group (62.0±26.6 vs 54.9±27.6, p=0.009). The proportion of the effective TTR was higher in single physician group that was statistically significant (51% vs 39% p=0.026). Minor bleeding and cerebral embolism complications were lower in single doctor group ($p<0.001$). Level of confidence about warfarin usage was also higher in single doctor group ($p<0.001$).

Characteristics and complications of patient

Characteristic	Single physician (n=156)	Multiple physician (n=469)	P value
Age (year)	61.0±12.0	60.2±13.2	0.312
Cerebral embolism during warfarin use (n, %)	6 (3.8)	43 (9.2)	<0.001
Mean time in therapeutic range, TTR (%)	62.0±26.6	54.9±27.6	0.009
Patients with TTR >65% (n, %)	80 (51.2)	186 (39.7)	0.026
Level of confidence about warfarin usage (n,%)			<0.001
No	16 (10.3)	55 (11.7)	
Little	13 (8.3)	147 (31.7)	
Moderate	44 (28.2)	112 (23.9)	
Moderate to high	51 (32.7)	92 (19.6)	
High	32 (20.5)	54 (11.5)	

TTR, time in therapeutic range.

Conclusion: Mean TTR and effective TTR is higher in single physician group. Cerebral embolism and minor bleeding was also lower in this group.

P6140 | BEDSIDE
Predictive Value of the SAMe-TTR2R2 to predict quality of oral anticoagulation in atrial fibrillation: a prospective validation in the multicentre Spanish observational registry fantasiia

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The efficacy and safety of vitamin K antagonist (VKA) therapy are closely associated to the quality of oral anticoagulation (OAC) management, as reflected by the average percentage of the time in therapeutic range (TTR). A high TTR translates into a lower risk of stroke and bleeding. Thus, guidelines recommend an average individual TTR >65–70%. The SAMeTT2R2 is a clinical risk score developed to predict the quality of OAC with VKA, patients with SAME-TT2R2 score ≥2 being

at high risk of having poor quality on OAC whilst on VKAs. We explore the predictive role of the SAME-TT2R2 score for assessing poor anticoagulant control in a prospective cohort of patients on VKA treatment.
Methods: We studied VKA treated non-valvular AF patients who were prospectively recruited in the multicentre Spanish observational registry FANTASIIA. Estimated TTR was calculated from both direct and Rosendaal methods during a 6 month period. The SAME-TT2R2 score was calculated and TTR values compared for those patients with a SAME-TT2R2 score 0–1 and ≥2.
Results: We studied 948 patients (mean age 73.8±9.4 years, 57.5% male). Mean TTR was 63.8±23.8 for the direct method and 60.3±24.5 for the Rosendaal method. Prevalence of poor anticoagulation control (TTR<65%) was 54%. As expected a progressive reduction of TTR was found as SAME-TT2R2 score values increased (Table). Those patients with SAME-TT2R2 score 0–1 had better mean TTR as calculated by the Rosendaal method (62.5±24.7 vs 58.0±24.1; p<0.01).

Mean TTR for each SAMeTT2R2 value

SAMeTT2R2 score	N	TTR direct	TTR Rosendaal
0	159	65.4±22.5	63.2±24.6
1	387	64.6±23.7	61.5±24.7
2	289	63.0±25.1	58.3±24.8
3	84	61.9±23.7	58.4±23.2
4	25	57.3±18.1	52.1±19.3
5	4	54.7±21.0	61.1±20.4

Conclusions: In a multicenter prospective registry, a high SAME-TT2R2 score (≥2 points) is associated with poor quality anticoagulation in patients on VKA. Our registry demonstrates the potential role of this simple clinical risk score to predict the poor quality OAC with VKA in clinical practice, and helps decision making for additional strategies including use of the Non-VKA Oral Anticoagulants.

BEST POSTERS IN CIRCULATORY ASSIST AND OTHER

P6142 | BEDSIDE
Impact of preoperative pulmonary hypertension and right ventricular dysfunction on cardiorenal interaction after left ventricular assist device implantation

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Background: Coincidence of advanced heart and renal failure (cardiorenal syndrome (CRS)) is associated with poor outcome. Timely left ventricular assist device (LVAD) implantation may reverse renal dysfunction due to restoration of cardiac output (CO) and relief of venous congestion. Besides the mere reduction of CO, right ventricular dysfunction induced venous congestion is believed to be involved in the progression of renal failure in CRS.
Purpose: Preoperative pulmonary hypertension and right ventricular dysfunction influence the course of CRS after LVAD implantation.
Methods: We performed a retrospective analysis in patients with heart failure (HF) before and after LVAD implantation. Patients with early mortality (90 days) were excluded. Renal function was assessed by glomerular filtration rate (GFR) before, 1 month and 6 month after LVAD implantation. Right ventricular function was evaluated by preoperative echocardiography (tricuspid annular plane systolic excursion (TAPSE)) and right heart catheterization (cardiac index (CI), mean pulmonary artery pressure (mPAP)). GFR after 1 month and 6 month, respectively, were analysed versus baseline GFR by t test.
Results: 35 patients (age 53±14 years) with advanced HF were analysed. HeartWare LVAD (n=31) or HeartMate II LVAD (n=4) were implanted. Mean baseline GFR was 63±20 ml/min. After 1 month, a significant increase of GFR was observed (82±30ml/min; p=0.002) which declined after 6 month (65±21 ml/min; p=0.621). Subgroup analyses were performed regarding baseline GFR, preoperative CI, TAPSE or mPAP. Mean GFR did not change in patients with baseline GFR ≥60 ml/min. Patients with baseline GFR <60 ml/min showed a significant improvement of GFR after 1 (47±8 vs 78±33 ml/min; p=0.001) and 6 month (55±16 ml/min; p=0.036). Patients with CI above median showed a significant increase of GFR after 1 month (62±21 vs 76±17 ml/min; p=0.033; 6 month: 62±20 ml/min; p=0.926) while no change was found in patients with CI below median. Patients with TAPSE ≤14 mm showed a significant increase of GFR after 1 month (61±24 vs 85±35 ml/min; p=0.035; 6 month 59±15 ml/min; p=0.645). Also, in patients with mPAP >37.5 mmHg a significant improvement after 1 month was found (66±22 vs 85±27 ml/min; p=0.037; 6 month 71±20 ml/min; p=0.443). No changes were observed in patients with TAPSE >14 mm or mPAP <37.5 mmHg.
Conclusion: In advanced HF, LVAD implantation improves CRS. Presence of pulmonary hypertension or right ventricular dysfunction seems to be more predictive than reduction of cardiac output for potential resolution of CRS after LVAD implantation.

P6143 | BEDSIDE
Is tricuspid annuloplasty really unnecessary at pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension?

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Background: Tricuspid regurgitation (TR) is detected in most patients with chronic thromboembolic pulmonary hypertension (CTEPH). TR with a dilated annulus is supposed to be improved without tricuspid annuloplasty (TAP) after significant pulmonary artery pressure (PAP) reduction with the pulmonary endarterectomy (PEA).
Purpose: The aim of this study is to investigate the improvement of significant TR with and without TAP after PEA for CTEPH.
Methods: Since 2000, 143 patients underwent surgery for CTEPH. Of them, survived 70 patients who had preoperative TR grade 3 or 4 consist of study population. Fifty patients had TR grade 3 and 18 had grade 4. The mean PAP was 47±8 mmHg, and the mean pulmonary vascular resistance (PVR) was 1203±404 dyne.s.cm-5. PEA was performed through median sternotomy using cycles of 15–20 minute intermittent circulatory arrest at 16–20 degrees Celsius. Of them, 18 patients (25.7%) had tricuspid valve annuloplasty (TAP), due to severe annulus dilatation.
Results: Postoperative mean PAP was 25±12 mmHg, and postoperative PVR were 497±336 dyne.s.cm-5. Forty-nine patients (70.0%) showed postoperative TR grade less than grade 2 (38 pts. without TAP vs. 11 pts. with TAP, P=0.35), and 64 patients (91.4%) showed TR grade less than grade 3 (49 pts. without TAP vs.15 pts. with TAP, P=0.16). Among the 6 patients of more than postoperative TR grade 3, 3 without TAP showed TR grade 3 despite the reduction of PVR and 3 with TAP showed TR grade 3 with residual elevated PVR (Table).

Postoperative TR grade more than grade 3

TAP	Preop TR	Postop TR	Preop mean PAP	Preop PVR	Postop mean PAP	Postop PVR
Yes	4	3	33	746	29	874
Yes	4	3	59	1700	58	1428
Yes	4	3	66	1864	56	1257
No	4	3	49	1700	18	312
No	3	3	42	670	29	443
No	3	3	50	1343	11	256

TAP, tricuspid annuloplasty; TR, tricuspid regurgitation; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resisitance.

Conclusions: Most patients with more than moderate TR showed significant reduction of TR grade after PEA, however, some showed no improvement after PEA. Although TAP was not a complete solution for the TR, routine TAP for severe TR in patients with CTEPH might be an option.

P6144 | BEDSIDE
Dramatic improvements in the thrombotic burden and right heart hemodynamics with ultrasound-facilitated thrombolysis in patients with pulmonary embolism at high risk or intermediate-high risk

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EkoSonic® Endovascular System is a novel ultrasound-facilitated thrombolysis (UFT) technology which provides a high efficacy with a reduced bleeding risk in patients (pts) with pulmonary embolism (PE). In this study, we aimed to present our single-center results on this UFT technology in pts with PE at intermediate-high and high risk (IHR,HR).
Our study was based on the retrospective analysis of the 68 pts with PE (F34, M34 60,9±15,8 yrs) who underwent UFT. The routine procedures including multidetector computed tomography (MDCT), Echo, biomarkers, and PE severity index and its simplified version (PESI, sPESI) were performed in all pts. Qanadli score (QS) was used as the measure of thrombotic burden in the pulmonary arteries (PA) as assessed by MDCT. Heart rate, BP and SatO2% were 108,5±18,5 bpm,108,9±18,9 mm Hg and 88,8±4,2%,and PESI and sPESI scores were 75±25,4 and 2,5±1,0, respectively. Fifty six pts were at IHR and 12 pts were at HR status. Bilateral (n=55) and unilateral (n=13) placement of the catheters into the PAs were successful in all pts. The dosage and treatment duration of the tissue-type plasminogen activator were 34,9±17,3 mg and 22,5±7,2 hours, respectively. For unilateral and bilateral placement, both the dosage and duration were comparable (p=NS). UFT resulted in dramatic improvements in tricuspid annular planary systolic excursion (TAPSE) (mm) (3,05±3,3),PA systolic and mean pressures (mm Hg) (12,9±18,5 and 6,39±103),QS (14,5±6,02), right to left ventricle diameter ratio (RV/LV) (0,3±0,26) and right to left atrial diameter ratio (RA/LA) (0,22±0,19), and diameters of main, right and left PA regardless of the risk status (p<0.0001 for all). The significant correlations were noted among the improvements in QS, TAPSE, RV/LV and RA/LA (r=–0,39 to 0,71, p<0.001 for all). One with severe RV dysfunction due to total obstruction of right PA and other one complicated by a hemorrhagic stroke died at 12th hour of UFT. In a third octogenarian female, pneumonia was the cause of the death one week after successful UFT. In other 65 pts, UFT was not associated with major bleeding, PE-related morbidity or mortality during in-hospital period or post-discharge follow-up period of 254.8±227.5 days. In summary, this UFT technology facilitates the resolution of thrombotic burden, recovery of pulmonary hemodynamics and right heart functions with acceptable rates of procedure-related complications in the majority of the pts with PE irrespective of the risk status.

P6145 | BEDSIDE

The efficacy and safety of novel hemostasis technique: ultrasound-guided thrombin injection with ballooning

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Background: Recently percutaneous intervention via common femoral artery (CFA) has been used in not only percutaneous coronary intervention but also endovascular intervention, transcatheter aortic valve replacement (TAVR), percutaneous Impella LVAD. This technique requires use of large diameter sheath via CFA without a surgical cut-down. Complication of vascular access site has become a problem. So we has developed a novel hemostasis technique "Ultrasound-guided Thrombin Injection with Ballooning (UTIB)". Our aim was to evaluate the efficacy and safety of UTIB technique.
Methods: From April 2012 to 2013 May, 20 consecutive patients underwent to balloon aortic valvuloplasty in our institution. 12 or 14 French size sheaths was inserted via CFA without cut-down. Ultrasound-guided thrombin injection with ballooning was performed after procedure. 5 Fr. IMA catheter was introduced over a wire via the contralateral CFA to the ipsilateral common iliac artery. 0.035 inch guide wire was then introduced to the ipsilateral CFA passed the sheath. A balloon of appropriate size was deployed at the level of puncture site in the CFA. The sheath was removed and then the balloon was inflated. We detected the non-bleeding by color doppler with ultrasonography (US) from body surface. Thrombin was injected with 2.5cc syringe and 21G needle on the CFA during ultrasound guided. And then we detect stopping bleeding with US, the balloon was deflated.
Results: The mean patient age was 89.1 (range 80–95) years old and 70.0% were male. 95.0% patients were on single or dual antiplatelet therapy. The CFA diameter was 7.7±0.8mm, balloon diameter was 7.3±0.9mm. The mean bovine thrombin dose was 3133IU (range 1000–5000IU). Success cases were all cases (100%). Hemostasis time was 4.6±1.8 min. No complications were observed including thromboembolism, limb ischemia, pseudo aneurysm, infection and bleeding.
Conclusions: In percutaneous intervention that large size vascular access was needed, UTIB was useful and safety for patients under antiplatelet therapy.

BEST POSTERS IN PROGNOSIS

P6147 | BEDSIDE

Impact of non-cardiac comorbidity on mortality and morbidity in a predominantly elderly heart failure population among different heart failure phenotypes

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Background: Information on comparative prognostic impact of comorbidity across different heart failure (HF) phenotypes has not been widely known.
Objectives: The object of our study was to compare the prevalence and relative impact of a wide range of noncardiac comorbidities and multiparametric risk score (3CHF score) across different HF phenotypes (LVEF≤40% - HFrEF, LVEF 41–49% - HFbEF, LVEF ≥50% - HFpEF).
Methods: From October 2009 to December 2013 we studied all consecutive ambulatory patients with HF whose ejection fraction had been assessed. Clinical variables were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.
Results: A total of 2424 patients (mean age 78±8, 57% men) were included. Of these 1457 (60%) had HFpEF, 358 (15%) HFbEF, 597 (25%) HFrEF. The high mean age and comorbidity rates (mean 3.2±2.5; 54% patients with ≥3 non cardiac comorbidities) ran similarly across different HF phenotype, except for renal disease, which was more frequent in HFrEF group, and obesity which was more frequent in HFpEF group. At a follow-up of 28±14 months, 502 (21%) patients died. Of these 168 (28%) had HFrEF, 60 (17%) had HFbEF, and 273 (19%) had HFpEF (p<0,001). The increasing number of noncardiac comorbidities per patient was associated with higher rates of mortality (HR 1.4 [IC 1.2–1.5]; p=0.001), HF hospitalization (HR 1.5 [IC 1.3–1.7]; p<0.001) and all-cause hospitalization (HR 1.5 [IC 1.3–1.6]; p<0.001). Univariable Cox analysis, including interaction with HF phenotype, revealed a similar impact of noncardiac comorbidities on mortality across HF phenotypes, except for diabetes mellitus which contributed to a higher hazard of mortality in HFrEF vs HFpEF (HR 1.8 [IC 1.2–3.3]; p=0.05 for interaction). In addition to this, at ROC curve, multiparametric 3 C-HF score showed similar prognostic accuracy for one year mortality among different HF phenotype (AUC 0.73-HFrEF, AUC 0.76-HFbEF, AUC 0,72-HFpEF; p=0.06).
Conclusion: In an elderly real-world HF population there was a high comorbidity burden that contributed significantly to high rates of mortality and morbidity. However, individually, most comorbidities had similar prognostic impact on mortality across all HF phenotypes. Multiparametric 3 CHF score showed high prognostic accuracy, similar in all HF phenotypes. These observations may suggest that, in the setting of elderly HF patients, the management of comorbidities could have a crucial role on prognosis irrespective of HF phenotype.

P6148 | BEDSIDE

Nocturnal desaturation: a predictor of outcome in heart failure with reduced ejection fraction

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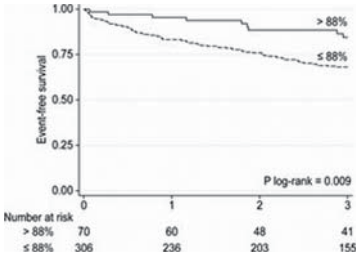
Aims: Sleep disordered breathing (SDB) is common in HF with reduced ejection fraction (HFrEF). An increased apnea-hypopnea index (AHI) is predictive of poor outcomes. Our objective was to examine whether an analysis of ND can improve the risk stratification of HFrEF patients.
Methods and results: 376 consecutive patients with stable HFrEF and LVEF≤45% were screened for SDB between 2005 and 2010 using polygraphy. SDB was defined as an AHI≥5, and sleep apnea (SA) as an AHI≥15. The mean age was 59±13y, the mean LVEF was 30±6%, and the median AHI was 18 [IQR: 9,33); 310 patients (82%) had SDB. The predefined composite primary end-points (death, heart transplantation or LV assistance) occurred in 98 patients (26%) within 3 years. Minimal oxygen saturation (MOS), the number of desaturations <90%/hour and the time spent with oxygen saturation <90% were significantly associated with adverse events (adjusted HR [95% CI]: 1.25 [1.03–1.52], 1.25 [1.03–1.53], and 1.28 [1.04–1.59], respectively) after adjustment for confounders, whereas AHI was not (1.10 [0.86–1.39]). The best MOS cut-off value for poor outcomes was ≤88%. Patients with an MOS ≤88% without SA (32/100 person-years;PY) had similar event rates to those with an MOS ≤88% with SA (31.7/100 PY). The patients with an MOS ≤88% had a significantly higher event rate (31.9/100 PY) than those with an MOS >88% (15.6/100 PY;p<0.01). The risk assessment using an MOS of ≤88% in addition to established prognostic markers yielded a net reclassification index (NRI) of nearly 6% and was particularly useful in the subgroup of patients with events (NRI: 8.4%).



Event-free survival according to MOS

Conclusions: In HFrEF patients, ND≤88% is an independent predictor of adverse events. The risk assessment in HFrEF should include ND and that SDB treatment may also focus on patients without SA who are presenting ND.

P6149 | BEDSIDE

Midregional pro-Adrenomedullin.Performance and risk stratification in patients with decompensated systolic heart failure

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Introduction and aim: Midregional pro-adrenomedullin (MR-proADM), the stable prohormone fragment of adrenomedullin, was shown to be elevated in acutely decompensated heart failure (ADHF), and proved superior to other biomarkers or risk models regarding prediction of outcomes in acute dyspnea regardless of aetiology. In the present post-hoc analysis from the Interdisciplinary Network Heart Failure (INH) Study we aimed to explore its performance as a biomarker and its predictive potential regarding short- and longer-term outcomes in patients hospitalised for ADHF.
Method and results: In 917 of 1022 study participants (72.2% male, mean age 68±12 years) MR-proADM was measured (KRYPTOR, detection limit 0.5nmol/L, sensitivity 0.25nmol/L) at discharge from hospital after best possible cardiac recompensation (BL) and (in survivors attending outpatient follow-up, n=599) after 6 months (FUP6). MR-proADM was significantly higher in patients with lower left ventricular ejection fraction (LVEF) and higher NYHA functional class and showed a high correlation (Spearman correlation coefficient 0.79) between BL and FUP6. Within the entire FUP period (18 months), 185 patients (20%) died. In a cox regression analysis, adjusted for a base model (age, sex, NYHA functional class (I/II vs. III/IV), body mass index, glomerular filtration rate (<60ml/min/1,73m^2 vs. ≥60 ml/min/1,73m^2)), left ventricular ejection fraction and anaemia), MR-proADM at BL was a strong predictor of all-cause mortality risk (hazard ratio for two-fold increase 2.0, 95% confidence interval 1.6–2.4, p<0.001) and proved significantly superior to other novel biomarkers like midregional pro-atrial natriuretic peptide (NP), N-terminal pro-brain NP (NT-proBNP), high sensitive C-reactive protein, and

copeptin ($p<0.001$ for inclusion of MR-proADM into all adjusted models). Further, in a multivariable model including the base model and both MR-proADM measurements, only the F6 value contributed significantly ($p<0.001$), whereas the BL value had no significant impact on survival during the following 12 months ($p=0.419$)
Conclusion: MR-proADM was strongly correlated with heart failure severity. It was a strong predictor for longer-term survival with a predictive power exceeding that of all other investigated novel biomarkers and NT-proBNP. Although MR-proADM values remained relatively stable over time, serial assessment after 6 months significantly improved risk stratification and helped to identify patients at highest risk.

BEST POSTERS IN HYPERTENSION TREATMENT

P6151 | BEDSIDE
Circulating endothelial progenitor cells in patients with essential hypertension

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Objective: The aim of study was to explore the quantity and properties circulating endothelial progenitor cells (CEPCs) function as well as their dynamics during antihypertensive treatment in patients (pts) of essential hypertension (EH).
Methods: 18 EH pts with LV hypertrophy (mean age 54.8±3.7 yrs, BMI 28.2±1.3 kg/m^2) were enrolled. Pts received beta blokers and hydrochlorothiazide before the study pts. During the study all pts took lisinopril up 20 mg and then were re-examined through 12 weeks therapy. 19 normotensive healthy people were examined (40.5±1.7 yrs, BMI 24.9±0.6 kg/m^2) as control group. 24-hour ABP monitoring, TTE, carotid intima-media thickness, flow-mediated dilatation (FMD) of brachial artery were done in all pts. The quantity of circulating CD34+CD133+ and CD34+CD133+VEGFR-2+-cells was assessed by flow cytometry. CEPCs function was evaluated by calculation of colony-forming units (CFU) with J.M.Hill's method. SA-beta-gal staining was used to evaluate the senescence.
Results: There were no differences in CEPCs number in EH pts and healthy control, but we revealed decreased number of CFU CEPC in EH pts. Pts with nocturnal hypertension had a lower CEPCs ($r=-0,520$, $p=0,03$) number and CFU ($r=-0,563$, $p=0,01$). Also, EPCs proliferate activity was associated with pts's age ($r=-584$, $p<0.01$) and SCORE index ($r=-0,473$, $p<0,01$). The same relations were observed between FMD of brachial artery and SCORE index ($r=-0,468$,$p<0.05$). In the end of study we found increasing CEPCs number and CFU, but the number of SA-β-gal positive cells were decreased.
Conclusion: Hypertension has a negative impact on the CEPCs functional activity. Endothelial dysfunction may be connected with impaired function of CEPCs, which may be related to CEPCs senescence. ACE inhibitors therapy improves CEPCs functional activity.

P6152 | BENCH
TAK-085 is superior to eicosapentaenoic acid in ameliorating salt-sensitive hypertension in rats

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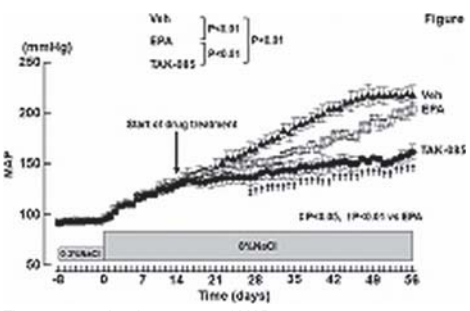
Objective: TAK-085 and eicosapentaenoic acid-ethyl ester (EPA-E) are clinically used for the treatment of hypertriglyceridemia. Unlike EPA-E products, TAK-085 contains not only EPA-E but also docosahexaenoic acid-ethyl ester (DHA-E). This work was undertaken to determine the comparative effects of TAK-085 and EPA-E on blood pressure (BP) and autonomic function using radiotelemetry.
Methods: Telemetry devices were implanted into high-salt-loaded Dahl salt-sensitive hypertensive rats (DS rats) that were treated orally with (1)vehicle, (2)TAK-085, or (3)EPA-E once daily for 6 weeks.
Results: Over 6 weeks of drug treatment, TAK-085 prevented BP elevation in DS rats much more than EPA-E ($P<0.01$). The 24-hour averaged mean BP of the TAK-085 group after 6 weeks of treatment was significantly lower than that of the EPA group (162±7 vs 204±6 mmHg: $P<0.01$). Heart rate was reduced by TAK-085 more than by EPA-E. BP variability, defined as the coefficient of variance (CV) of systolic BP in DS rats, was significantly reduced by TAK-085 but not by EPA-E. The low frequency power of systolic BP, an index of vasomotor sympathetic tone, in DS rats was reduced by TAK-085 more than by EPA-E. Spontaneous baroreceptor reflex gain was increased by TAK-085 more than EPA-E. TAK-085, but not EPA-E, significantly reduced 24-hour urinary norepinephrine excretions in DS rats. TAK-085 increased 24-hour urinary sodium excretions more than EPA-E.
Conclusion: These results demonstrate that TAK-085 suppressed salt-sensitive hypertension more so than EPA-E, and this superiority of TAK-085 is mediated by the suppression of sympathetic activity, improvements in baroreceptor function, and natriuresis. Thus, TAK-085 seems to be effective for the prevention of salt-induced hypertension.



Time courses of 24-hour averaged MAP

P6153 | BEDSIDE
Amlodipine alone compared to amlodipine + acetylsalicylic acid on inflammation and endothelial damage markers in hypertensive patients

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Background: The use of acetylsalicylic acid (ASA) in primary prevention is still debated.
Purpose: To evaluate the effects of amlodipine alone, compared to amlodipine + ASA, on some inflammatory and endothelial damage markers in patients affected by essential hypertension.
Methods: We enrolled 213 hypertensive patients with mild to moderate hypertension [systolic blood pressure (SBP) $\geq$140 and $<$180 mmHg and diastolic blood pressure (DBP) $\geq$90 and $<$105 mmHg]. Patients were randomised to amlodipine 5 mg, or amlodipine 5 mg + ASA for three months; then, if adequate blood pressure control was not reached, amlodipine was up-titrated to 10 mg/day for further 3 months and compared to amlodipine 10 mg + ASA 100 mg.
We assessed the effects of the two treatments on some inflammatory parameters evaluating, at baseline, after 3 and 6 months these markers: high sensitivity C-reactive protein (Hs-CRP), adiponectin (ADN), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), myeloperoxidase (MPO), soluble CD40 ligand (sCDL40).
Results: After 3 months of therapy, no variations of the above cited markers were recorded with amlodipine alone. Patients treated with amlodipine 5 mg + ASA 100 mg, instead, showed a reduction of Hs-CRP, TNF-α, MPO, and sCDL40, and an increase of ADN, both compared to baseline ($p<0.05$ for all) and to amlodipine alone ($p<0.05$ for all). Regarding IL-1β, it decreased with amlodipine 5 mg + ASA 100 mg compared to baseline ($p<0.05$ for all), but no differences were recorded compared to amlodipine alone. One hundred and seven patients continued the study, and were up-titrated to amlodipine 10 mg + ASA 100 mg or to amlodipine 10 mg alone. We observed a decrease of Hs-CRP, TNF-α, MPO, and sCDL40 and an increase of ADN in both groups compared to baseline ($p<0.05$ for amlodipine alone, and $p<0.01$ for amlodipine + ASA). Values recorded with amlodipine 10 mg + ASA were better than the ones recorded with amlodipine 10 mg alone ($p<0.05$ for all). Regarding IL-1β, it decreased compared to baseline only with amlodipine 10 mg + ASA. No significant serious adverse events were reported.
Conclusion: The addition of ASA to anti-hypertensive therapy gave a better improvement of inflammatory parameters compared to amlodipine alone, suggesting a role of ASA in reducing inflammation and endothelial damage independently from the blood pressure reduction.

POSTER SESSION 7

NEW INSIGHTS IN ARRHYTHMIAS: MECHANISMS AND TREATMENT

P6154 | BENCH
The combined effects of ranolazine and low dose dronedarone on atrial vs. ventricular electrophysiology; a novel therapeutic hope?

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Introduction: Pharmacological rhythm control of atrial fibrillation (AF) in patients with structural heart disease is limited. Ranolazine (Ran) in combination with low dose dronedarone (Dron) remarkably reduced the AF-burden by of 59% in the HARMONY Trial (Heart Rhythm congress 2014). We thus aimed to investigate the underlying causes of these trial results.
Results: Human atrial cardiomyocytes (CM) were isolated from 18 patients with AF versus 18 in sinus rhythm (SR). LV myocardium was taken from 9 human failing (HF) hearts.
Patch clamp experiments revealed that Ran (5 μM), low dose Dron (0.3 μM), and the combination of both prolonged the APD90 at 1 Hz in human SR CM (Ran by 22%, Dron by 53%,(each $p<0.05$) and the combination by 16% ($p=0.08$)). Most importantly, in AF CM either Ran alone (by 24%, $p<0.05$) or the combination (by 37%, $p<0.001$) prolonged the typically abbreviated APD90. Interestingly, Ran and more pronounced the combination, but not Dron alone caused a remarkable hyperpolarisation of the atrial resting membrane potential. We further show in human LV HF CM that Ran alone and in combination with Dron did not significantly

change the APD. Similar to its atrial effects Ran and the combination, but not Dron caused a hyperpolarisation of the resting membrane potential ($p<0.05$) in human LV HF CM. The investigation of cellular arrhythmogenic triggers (EADs, DADs and spontaneous APs) in AF and in LV HF CM showed a reduction of DADs by the combination of Ran and Dron. The proarrhythmic SR-Ca2+-leak in SR and AF which underlies the occurrence of DADs was measured using confocal microscopy (Fluo 3). Ran alone caused a potent reduction of the SR-Ca2+-spark frequency (by 78.0%, $p<0.05$) in SR CM. Comparable results could be obtained with the combination (by 78.2% $p<0.05$) that also suppressed Ca2+ waves and spontaneous transients by ~60% ($p<0.05$). In AF CM preliminary data show a significant reduction of the SR-Ca2+-spark frequency of Ran by 54% ($p<0.05$) and the combination by 60% ($p<0.05$).

Conclusion: Our electrophysiological measurements of Ran alone and in combination with low dose Dron show APD prolongation, cellular hyperpolarisation and a reduced SR-Ca2+-leak in human atrial CM. Therefore, the combined inhibitory effects of Na currents in particular late Na current and K currents may explain the anti-AF effects observed in the HARMONY Trial. Therefore, the combination but also Ran alone may be promising new AF-treatment options especially for patients with heart failure and merit further clinical investigation.

P6155 | BEDSIDE
Digoxin use is associated with higher mortality among patients with atrial fibrillation with and without heart failure: insights from the ARISTOTLE trial

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Background: Despite limited data from randomized controlled trial, digoxin is widely used in pts with atrial fibrillation (AF). Recent studies, exploring whether digoxin increases mortality, have reported conflicting results.

Purpose: To evaluate whether digoxin is associated with survival in pts with AF with or without heart failure (HF). We also assessed the treatment effect (apixaban vs. warfarin) on clinical outcomes according to digoxin use.

Methods: We studied ARISTOTLE pts where information about digoxin and HF status at baseline (n=17897) were available. Event-rates by digoxin use and HF status were computed and the association between digoxin and mortality was assessed.

Results: At baseline 5824 pts (32%) were treated with digoxin and 6693 (37%) had HF. Digoxin use was associated with a significant increase in the risk of all-cause mortality among pts with and without HF. The beneficial effects of apixaban vs. warfarin were similar in pts on and off digoxin.

Event rates per 100 patient-year follow-up

Event-rates by digoxin status	Digoxin	No digoxin	Adjusted HR (95% CI) Digoxin vs. No digoxin
All-cause mortality			
Overall population	4.81	3.19	1.19 (1.03–1.37)
No HF	3.35	2.43	1.21 (0.98–1.51)
HF	6.24	4.98	1.18 (0.98–1.42)
Cardiovascular mortality			
Overall population	2.61	1.58	1.25 (1.03–1.53)
No HF	1.41	1.13	1.10 (0.78–1.53)
HF	3.78	2.62	1.34 (1.05–1.73)
Event-rates by apixaban vs. warfarin	**Apixaban**	**Warfarin**	**HR (95% CI) Apixaban vs. Warfarin***
Stroke/systemic embolism			
Digoxin	1.36	1.74	0.78 (0.58–1.07)
No digoxin	1.25	1.54	0.71 (0.65–1.02)
All cause mortality			
Digoxin	4.68	4.94	0.95 (0.80–1.13)
No digoxin	2.96	3.43	0.87 (0.75–1.00)
ISTH major bleeding			
Digoxin	2.21	2.88	0.76 (0.59–0.98)
No digoxin	2.12	3.10	0.68 (0.57–0.81)

*P for interaction: 0.866 for stroke/systemic embolism, 0.425 for all causemortality and 0.461 for ISTH major bleeding.

Conclusions: Digoxin use was associated with a significant increased risk of mortality in AF, irrespective of the presence of HF. The benefits of apixaban vs. warfarin were consistent and preserved regardless of digoxin use.

P6156 | BEDSIDE
Effects of combination therapy with nifekalant and mexiletine on electrical storm

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Background: Patients with electrical storm, which is a clinical emergency, are frequently required antiarrhythmic drugs. Amiodarone has been widely used for the treatment of electrical storm, but is ineffective in a certain number of patients and evidence showing the efficacy of other antiarrhythmic drugs for electrical storm is limited. Therefore, we aimed to study the efficacy of stepwise administration of nifekalant, a pure potassium channel blocker, and mexiletine as emergency treatment to control electrical storm.

Methods: This study included patients who received stepwise therapy with nifekalant and mexiletine for electrical storm. Nifekalant was initially administered, and mexiletine was subsequently added if nifekalant failed to control ventricular tachyarrhythmias.

Results: This study included 44 patients (age, 61±15 years; 10 women, 23%) with repetitive ventricular tachyarrhythmias who were treated with nifekalant. Underlying heart diseases were, myocardial infarction (n=9, 20%), cardiomyopathy (n=27, 61%), and other diseases (n=8, 18%). Nifekalant completely suppressed recurrences of ventricular arrhythmias in 28 patients (64%). There was no severe side effect of nifekalant, which required the discontinuation of the drug. In 9 of 16 patients in whom nifekalant was partially effective but failed to suppress ventricular arrhythmias, mexiletine was added to nifekalant. The addition of mexiletine prevented recurrences of ventricular tachyarrhythmias in 5 of 9 patients (56%). Mexiletine was discontinued in two patients because of neurological side effect (n=1) and ventricular fibrillation (n=1). There was no death associated with electrical storm. In total, the stepwise treatment with nifekalant and mexiletine was effective in preventing ventricular tachyarrhythmias in 33 of 44 patients (75%). There was no difference in cycle length of ventricular tachycardia, QRS interval, QT interval, mexiletine dose, nifekalant dose, or left ventricular ejection fraction between patients who responded to antiarrhythmic drugs and those who did not respond.

Conclusion: The stepwise therapy of nifekalant and mexiletine was highly effective in suppression of electrical storm.

P6157 | BEDSIDE
The changing landscape of oral anti-arrhythmic prescriptions for atrial fibrillation in England: 1998-2014

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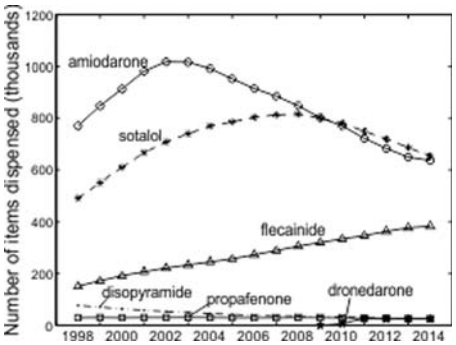
Background: An important decision in the management of atrial fibrillation (AF) is between a rate-control and rhythm-control strategy. If the latter is adopted options include oral anti-arrhythmic drugs (AAD) or catheter ablation. There have been increasing reports of the association between oral AADs (in particular Class Ia, Ic and III agents [Vaughan-Williams]) and higher mortality, which may affect prescribing behaviour.

Purpose: To describe the trend in oral AADs prescriptions in England 1998–2014.

Methods: We conducted a retrospective study using data from the Prescription Cost Analysis system, which holds information on every prescription dispensed in the community in England. We obtained data from 1998 to October 2014 for all Class Ia, Ic and III AADs. Betablockers (Class II) were not studied as they are not exclusively used for rhythm control in AF.

Results: Amiodarone and sotalol remain the most commonly prescribed AADs in England, though the use of both is decreasing (Figure). Over the study period two drugs have been discontinued: quinidine, tocainide and one introduced: dronedarone (2009). Dronedarone prescriptions peaked in September 2011 and our most recent data shows that amiodarone prescriptions are 25 fold those of dronedarone.



Trends in anti-arrhythmic drug use

Conclusion: There is a decline in use of amiodarone and sotalol consistent with the growing safety concerns with these drugs. Dronedarone has failed to make an impact on AAD prescribing. In contrast, flecainide, which now has stronger evidence for safety has had a linear increase in use. There remains a dearth of safe and effective new oral AADs for AF, which needs attention.

P6158 | BENCH
Effective suppression of atrial fibrillation by the antihistaminic agent antazoline: first experimental insights into a novel antiarrhythmic agent

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Background: In a few clinical case series, the antihistaminic antazoline (ANT) was reported to be highly effective and safe for rapid conversion of atrial fibrillation (AF) to sinus rhythm. We therefore aimed at analysing underlying mechanisms in an experimental whole-heart model.
Methods and results: 20 isolated and retrogradely perfused rabbit hearts were paced with cycle lengths from 350 to 150ms in the atrium. A standardized protocol employing atrial burst pacing induced AF in 5 of 20 hearts under baseline conditions (7 episodes). Thereafter, a combination of acetylcholine and isoproterenol was employed to enhance AF occurrence. Two monophasic action potential recordings on the left- and two on the right atrial epicardium showed a decrease of atrial action potential duration (aAPD, –25ms, $p<0.05$) and atrial effective refractory period (aERP; –52ms, $p<0.01$) after infusion of both acetylcholine (1μM) and isoproterenol (1μM) as compared with baseline. This led to induction of AF in 14 of 20 hearts (145 episodes). Simultaneous infusion of ANT (20μM) led to a complete suppression of AF in all 20 hearts. Treatment with ANT also led to a significant increase of aAPD (+41ms, $p<0.01$ as compared with acetylcholine/isoproterenol-treatment) and aERP (+74ms, $p<0.05$) leading to a marked increase of atrial post-repolarization refractoriness (aPRR), defined as the difference of aERP and aAPD (+33ms, $p<0.01$).
Results: were compared to 13 rabbits treated with flecainide employing the same experimental protocol. Flecainide also induced a significant increase of aPRR and resulted in induction of AF in 7 of 13 hearts (51 episodes) while 11 of 13 hearts were inducible during sole treatment with acetylcholine and isoproterenol (93 episodes)
Conclusion: In the present experimental study, administration of ANT was highly effective in suppressing AF and seems to represent a promising novel therapeutic option in AF. Of note, it was more effective than the established agent flecainide. The antiarrhythmic effect could be explained by a significant increase in post-repolarization refractoriness as a result of a more marked increase of aERP as compared with aAPD. Further systematic clinical studies are necessary to investigate the potential benefit of ANT.

P6159 | BENCH
Selective late sodium current inhibition abolishes torsades de pointes arrhythmias in the chronic atrioventricular block dog model by reducing repolarization and spatial dispersion of repolarization

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Introduction: GS-458967 (GS) is a selective and potent late sodium current (INaL) inhibitor.
Objective: We evaluated the antiarrhythmic efficacy of INaL inhibition by GS against dofetilide (D)-induced early afterdepolarizations (EADs) in vitro and Torsades de Pointes arrhythmias (TdP) in vivo and determined the underlying basis of the antiarrhythmic effect of GS.
Methods: In left and right ventricular (LV and RV) cardiomyocytes isolated from sinus rhythm (SR) and chronic AV block (cAVB) dogs, 1) INaL current density, 2) IC50 of INaL blockade by GS and 3) concentration-dependent effect of GS (100–1000 nM) to suppress D-induced EADs were determined.
In 11 cAVB dogs GS 0.1 mg/kg was given IV after inducing arrhythmias by D (25 μg/kg). QRS and QTc intervals from surface ECG were measured along with monophasic action potential duration (MAPD) from LV and RV. In 2 dogs mapping of electrical activity was performed. A total of 165 electrograms were recorded from 64 needle electrodes inserted in LV and RV. Spatial dispersion of repolarization (SDR) was determined at baseline, before D-induced TdP and after GS administration. An arrhythmia score (AS) was calculated according to their severity occurring after D and GS. Plasma levels of GS were measured.
Results: In cardiomyocytes the magnitude of INaL was 1) greater in LV vs. RV of SR cells (0.30±0.10 vs. 0.21±0.10 pA/pF, $p<0.05$*), 2) reduced in cAVB vs. SR of LV cells (0.18±0.05 vs. 0.30±0.10 pA/pF*) but not in RV. IC50 values of GS for INaL were 188±15 and 230±10 nM in SR and cAVB cardiomyocytes, respectively. GS concentration-dependently suppressed D-induced EADs similarly in SR and cAVB myocytes (2/14, 5/17* and 10/17* at 100, 300 and 1000 nM, respectively).
In cAVB dogs, GS (787±265 nM) completely abolished D-induced TdP (8/11 after D vs. 0/11* after GS) reducing AS from 33.1±29.4 to 2.1±1.1*; some single ectopic beats remained present. This effect was associated with a significant shortening of the repolarization parameters QTc and LVMAPD (from 618±43 and 454±94 ms after D to 576±38* and 393±60 ms* after GS, respectively). In mapped animals, D increased SDR (from 15±1 to 69±6 ms) prior to occurrence of TdP. The antiarrhythmic effect of GS was accompanied by a reduction of SDR (32±4 ms).
Conclusions: INaL inhibition with GS completely abolished occurrence of TdP, while some ectopic activity in vivo, and some EADs in isolated cardiomyocytes remained. GS seems to exert its antiarrhythmic effect by decreasing both the repolarization time and its spatial dispersion.
Acknowledgement/Funding: Gilead Sciences, Inc.

P6160 | BENCH
Genetic analysis of desmosomal gene mutations in Han Chinese patients with ARVC

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Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a cardiomyopathy that primarily involves the right ventricle. Mutations in desmosomal genes have been associated with ARVC. But its prevalence and spectrum are much less defined in the Chinese population, especially Han Chinese, a majority ethnic group in China; also the genotype-phenotype correlation regarding left ventricular involvement is still poorly understood. The aim of this study was to elucidate the genotype in Han Chinese patients with ARVC and the phenotype regarding cardiac left ventricle involvement in mutation carriers of ARVC. 48 Han Chinese patients were recruited into the present study based on the Original International Task Force Criteria of ARVC. Clinical data were reassessed according to the modified criteria published in 2010. A total of 36 subjects were diagnosed with ARVC; 12 patients were diagnosed with suspected ARVC. Five desmosomal genes (PKP2, DSG2, DSP, DSC2 and JUP) were sequenced directly from genomic DNA. Among the 36 patients, 21 mutations, 12 of which novel, were discovered in 19 individuals (19 of 36, 53%). The distribution of the mutations was 25% in PKP2, 14% in DSP, 11% in DSG2, 6% in JUP, and 3% in DSC2. Multiple mutations were identified in 2 subjects (2 of 36, 6%); both had digenic heterozygosity. Eight mutations, of which six were novel, were located in highly conserved regions. Seven mutations introduced a stop codon prematurely, which would result in premature termination of the protein synthesis. Two-dimensional echocardiography showed that LDVd and LDVs parameters were significantly larger in nonsense mutation carriers than in carriers of other mutations. In this comprehensive desmosome genetic analysis, 21 mutations were identified in five desmosomal genes in a group of 48 local Han Chinese subjects with ARVC, 12 of which were novel. PKP2 mutations were the most common variants. Left ventricular involvement could be a sign that the patient is a carrier of a nonsense cardiac desmosome gene mutation.
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P6161 | BEDSIDE
Genotype/phenotype relationship in a large cohort of long QT syndrome patients

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Introduction: Congenital long QT syndrome (LQTS) is a hereditary disease characterized by prolonged QTc and a risk of cardiac arrest.
Purpose: The aim of this study is to report the experience of the referral center of our hospital.
Methods: Patients were recruited from 19 tertiary centers in France between 1997 and 2014. Clinical data and 12-lead ECG were collected. The results of genetic screening were analyzed according to the symptoms and the length of QTc interval (Table). Genetic screening was performed using dHPLC-DNA sequencing, HRM for at least KCNQ1, KCNH2 and SCN5A.
Results: The population consisted in 456 probands affected by LQTS according to the Schwartz score (298 females, sex-ratio=1.9) with a mean age at diagnosis of 34±20 years. In this cohort, 214 patients (47%) were symptomatic: 54 resuscitated SCD (12%), 191 (42%) syncopes and 47 (10%) ventricular arrhythmias. Heart rate was 67±18 bpm, PR 151±51 mm, QRS 87±17 mm and QTc 486±55 mm.
Genetic screening was positive for 263 patients (58%): 122 mutations (27%) in

Abstract P6161 – Table 1. Genetic screening of LQTS patients according to clinial presentation

	QTc <480 ms			QTc >480 ms		
	Number of patients	Number of mutations	% of mutated patients	Number of patients	Number of mutations	% of mutated patients
Asymptomatic	143	86	60%	99	69	70%
Symptomatic	109	39	36%	105	69	66%

KCNQ1, 103 mutations (23%) in KCNH2, 29 mutations (6%) in SCN5A and 10 mutations in minor genes of LQTS.
QTc duration was similar in asymptomatic patients with (483±45 ms) or without mutation (QTc 476±49 ms), NS. QTc duration was longer in symptomatic patients with (514±68 ms) than without (470±47 ms) mutations.
Conclusion: We identified a mutation in 58% of patients suspected for LQTS. The frequency of mutations is lower in the symptomatic with QTc<480ms group, probably related to the weight according to symptoms in the Schwartz score. In patients with a QTc>480ms, genetic analysis identified a high percentage of mutations independently of the presence of symptoms.

P6162 | BENCH
Single nucleotide polymorphisms discriminates between symptomatic and asymptomatic LQTS2 patients: A DNA-based patient classification

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Aim: We evaluated if specific genomic signatures exist in LQTS2 patients which could assist in discriminating disease severity between symptomatic and asymptomatic individuals carrying hERG mutations.
Methods and results: Genomic DNA was collected from multiple symptomatic and asymptomatic LQTS2 patients bearing heterozygous mutations in KCHN2 gene that encodes the IKr potassium ion channel. Using next generation sequencing (NGS), KCNH2 gene in LQTS2 patients was sequenced along with healthy patient cohorts. Skin fibroblasts from selected patients were reprogrammed to generate transgene-free human induced pluripotent stem cells (hiPSC). These hiPSC were differentiated into cardiomyocytes for confirmational studies. Expectedly, multi-electrode array analysis indicating corrected field potential duration (cFPD) demonstrated cardiomyocytes from LQTS2 patients (asymptomatic and symptomatic, 628±73 ms, n=26) showed delayed repolarization as compared to controls (355±48 ms, n=15). Although symptomatic cardiomyocytes showed longer cFPD (689±89 ms, n=10) as compared to asymptomatic (601±109, n=16), no statistical difference was documented. Interestingly, NGS based SNP analysis identified 11 SNPs within intragenic regions of KCNH2 gene only in LQTS2 patients which were absent in controls. These NGS results were further validated by Sanger Sequencing across multiple LQTS2 patients. More interestingly, there were 8 SNPs that could specifically discriminate between asymptomatic and sympotomatic LQTS2 patients based on their QTc interval and Schwartz score. These results provide insights in understanding the differences between symptomatic and asymptomatic LQTS2 clinical presentations.
Conclusions: Understanding mechanisms governing subtle differences between symptomatic and asymptomatic patients would provide unparalleled insights in developing new diagnostic tools for patient management. Our study leverages on the presence of SNPs which could act as a genetic marker which could distinguish between asymptomatic and symptomatic LQTS2 patients and provide better clinical regimes as well as understanding disease penetrance in LQTS2.
Acknowledgement/Funding: NRF-CRP-2008-02, NMRC/BNIG/1074/2012, GCR/2012/006, GCR/2013/008, SHF/FG569P/2014 and SHF/FG630S/2014

P6163 | BEDSIDE
Sustained QTc shortening by GS-6615 in patients with LQT3

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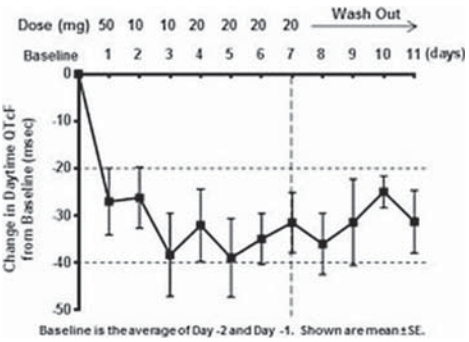
Introduction: In patients with LQT3, enhanced cardiac late sodium current (INa,L) causes prolongation of QT interval. GS-6615 is a selective inhibitor of INa,L that has been shown to shorten the action potential duration and QTc interval in experimental models of LQT3. We determined the effect of GS-6615 on QTc shortening and durability in patients with LQT3.
Methods: Five patients with LQT3 and QTc >480 msec at screening were admitted to the CRC of the University of Rochester. GS-6615 was administered orally at 50 mg on Day 1, 10 mg on Days 2–3, 20 mg on Days 4–7, and followed by washout on Days 8–11. Standard 12-lead ECG were collected over 12 hours each day. The daytime QTc interval for each day was calculated as AUC0–12(QTc)/12 hours and the baseline was defined as the average of Days –2 and –1.



Results: The baseline mean (±SE) daytime QTc interval was 525±16 msec, which was shortened by 26–39 msec during seven days of dosing (Figure). After stopping GS-6615, QTc remained below baseline during the 4 days of washout, possibly due to the long half-life of GS-6615. On Day 1, the median (Q1, Q3) value for the maximal shortening of QTc interval relative to pre-dose was 53 (40, 70) msec, which was observed at 4 (3, 5) hours post-dose. GS-6615 did not affect heart rate and blood pressure.
Conclusion: GS-6615 caused a sustained shortening of QTc in LQT3 patients and was well tolerated. A clinical study to evaluate the long-term safety and efficacy of GS-6615 in patients with LQT3 is currently ongoing.
Acknowledgement/Funding: Gilead Sciences Inc.

P6164 | BEDSIDE
Inflammation in ARVC: new pathophysiological insights

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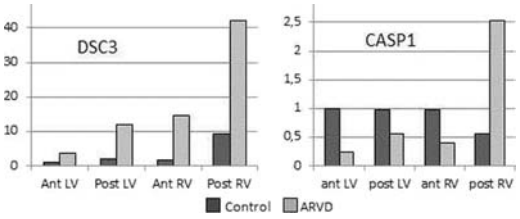
Introduction: Mutations in the DSC2 gene cause Arrhythmogenic Right Ventricular Dysplasia (ARVD). The mechanisms by which these mutations confer histologic substrate remain unknown. A metabolic function of inflammasome/casp1 in adipose tissue has been demonstrated.
Materials and methods: Fragments of cardiac tissue from 2 patients were collected after macroscopic and histopathological examination the patients' hearts. A 63-year-old patient with ARVD caused by a DSC2 mutation (p.Arg132Cys) underwent heart transplantation. The diseased heart genome-wide expression profiling was compared with that of a non-diseased donor heart. The retained genes of interest were listed and classified according to their biological functions using Ingenuity Pathways Analysis (Ingenuity Systems Inc., Mountain View, CA). RT-qPCR and Western Blot (WB) were used to confirmed genes of interest.
Results: Transcriptomic and RT-PCR data first revealed a down-expression of DSC2 mRNA and an unexpected overexpression of DSC3 mRNA in the posterior right ventricle of the ARVC patient (Fig) In the ARVD heart, DSC3 was found to be cleaved. Prediction software revealed that this cleavage could be due to Caspase-1. We observed an overexpression of Casp1 (fig) and other elements of inflammasome (CARD16, NLRP3) in the posterior RV of the ARVC patient. A down-expression of DSG2, DSP and RyR2 was also documented. Biological pathways analysis identified a relationship of Casp1 with apoptosis (BCL2, FOS), fibrogenesis (Col3A1, Col4A1, Col4A2, MMP9) and adipogenesis (IGF1, ADIPOQ) in the ARVC heart.



DSC3 and CASP1 RT-PCR in heart samples

Conclusion: This is the first study that shows a switch DSC2/DSC3 in an ARVC patient with a DSC2 mutation. Casp1, activated owing to desmosome instability, could play a central role in ARVC physiopathology.

P6165 | BENCH
Genomewide expression profiling of micro-RNA in atrial fibrillation

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Background: microRNAs (miRNAs) are small ribonucleic acid molecules involved in post-transcriptional regulation of gene expression. The involvement of miRNAs in the pathophysiology of atrial fibrillation (AF) is under research.
Aim: To investigate the participation of miRNAs in the pathophysiology of the AF by comparing their genomewide expression profile according to the rhythm and left atrial volume (LAv).
Methods: Observational study of patients with mitral valve disease requiring surgical treatment. Genomewide miRNA expression profile was characterized in left atrial samples by deep sequencing and compared according to the rhythm and LAv by nonparametric tests, linear correlation and hierarchical clustering analysis. Target genes of the differentially expressed miRNAs were predicted (miRWalk) and their potential biological effects were analyzed in regard to myocardial physiology and recognized involvement in other human diseases (ontology analysis).
Results: Eighteen patients were studied: 5 with permanent AF (Pe-AF), 5 with paroxysmal AF (Px-AF) and 8 with no history of atrial arrhythmia (SR). Significant variation of 42 miRNAs' levels was observed in relation, simultaneously, to cardiac rhythm and LAv, 36 of such miRNAs being overexpressed. Among them

stood out miR-891a, whose tissue levels were strongly correlated with the LAv (Pearson R=0.88; P<0.001) and were significantly higher in patients with Pe-AF [median: 4.7 rpm; interquartile range (IQR): 3.1–5.2] than in those with Px-AF (1.2 rpm; IQR: 0.6–1.3) or SR (0.0 rpm; IQR: 0,0–0.4) - P=0.001. About 13,542 potential gene targets of the differentially expressed miRNAs were identified: 23 of them were simultaneous targets of at least 9 miRNAs, including KCNA1 (K+ voltage-gated channel) TAB1 (TGF-β activated kinase 1/MAP3K7 binding protein 1), TCF21 (involved in cardiac morphogenesis) and ASPH (involved in Ca2+ storage and release by sarcoplasmic reticulum). The predicted gene targets are strongly associated with the regulation of ionic currents, muscle contraction, cell signalling pathways, cell programming, inflammation and thrombotic propensity, and included genes known to be involved in long QT syndrome, dilated cardiomyopathy, neurological electrical disturbances, diabetes and thrombophilia.
Conclusions: The global expression profile of miRNA is significantly changed during AF progression. We identified a group of differentially expressed miRNAs with relevant predicted gene targets, suggesting the involvement of post-transcriptional regulation changes in the AF pathophysiology.

ARRHYTHMIAS AND CARDIOMYOPATHIES

P6166 | BEDSIDE
Lamin A/C gene mutations underlie Arrhythmogenic Cardiomyopathy with atrio-ventricular block

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Background: Arrhythmogenic Cardiomyopathy (AC) is an inherited heart muscle disease characterized by ventricular arrhythmias and an increased risk of sudden death. Mutations in genes mainly encoding desmosomal components are involved in approximately 50% of AC cases, however mutations in extra-desmosomal genes can cause cardiomyopathies with overlapping AC features.
Methods: A 76 years-old man diagnosed with biventricular AC died in the Hospital for heart failure. Since young age he had frequent syncopal episodes, mainly during effort. The 12 lead- ECG showed low QRS voltages in limb leads and right precordial negative T-waves from V1 to V4, the Eco-color Doppler examinations evidenced severe right ventricular dilatation with global hypokinesia and mild left ventricular dilatation with mild systolic disfunction. Angiography showed no lesions in the coronary arteries. At 72 yrs the patient was implanted with a pacemaker for complete AV block. At the age of 74 years he received an implantable cardioverter-defibrillator (ICD) for secondary prevention because he suffered by a syncopal episode due to ventricular tachicardia (VT) with left bundle branch morphology and superior axis. During the follow-up the patient received an appropriate ICD intervention in response to VT. Conventional genetic screening was performed by bidirectional Sanger sequencing of all major desmosomal encoding genes on an ABI310 Genetic analyzer and subsequently whole exome sequencing (WES) was carried out by using TruSeq technology on a Illumina HiSeq2000 platform.
Results: Conventional genetic screening failed to detect genetic variations in desmosomal genes associated with the disease. WES identified a heterozygous point mutation c.949G>A, p.E317K in the lamin A/C gene (LMNA). This genetic variant, absent in the 1000 Genomes and Exome Variant Server datasets and predicted to be deleterious by Polyphen and SIFT, has been previously associated with autosomal dominant dilated Cardiomyopathy and atrio-ventricular block. The mutation was also detected in the proband's daughter and son, who exhibited an AC-like pattern.
Conclusion: This study highlights that LMNA gene mutations may mimic the AC phenotype but always accompanied with atrio-ventricular block. A comprehensive genetic test enables a clear differential diagnosis in cardiomyopathies.

P6167 | BEDSIDE
Progression of cardiac arrhythmia in familial amyloidotic polyneuropathy, portuguese type, after liver transplant

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Background: Cardiovascular complications are common in Familial Amyloidotic Polyneuropathy (FAP) and, although liver transplant (LT) has been shown to improve the survival of patients (pts), it has also been reported progression of the disease after the procedure.
Purpose: The aim of this study was to evaluate the progression of cardiac conduction disorders in pts with FAP, portuguese type, submitted to LT and prophylactic permanent pacemaker (PM) implantation before the procedure.
Methods: We enrolled 117 pts with FAP due to transthyretin Val30Met mutation, submitted to LT and prophylactic PM implantation, between 2001 and 2012, and that were evaluated in our institution between December 2013 and November 2014. We analyzed symptoms, ECG and PM records.
Results: In our sample, 69% of the pts were female, median age at disease onset was 32 years old (IQR 27–36) and median time between disease onset and LT was 4 years (IQR 2.5–5). By the time of LT, 90% were in stage 1 (according with Coutinho neurological clinical staging) and 43% already had clinical manifestations of cardiovascular involvement. Median time from disease onset to the follow-up visit was 11 years (IQR 8–15).
At the follow-up visit, only 8.8% had a normal ECG. One third had paced rhythm, 44% 1st degree AV block, 45% impaired intraventricular conduction (IIVC), 37% poor R wave progression and 18% low voltage QRS. Only 4 pts had atrial fibrillation or flutter. Compared with the ECG's from previous years (median 4 years before), there was a significant increase in the frequency of 1st degree AV block (16% vs 44%, p<0.001), IIVC (24% vs 45%, p<0.001) and poor R wave progression (16% vs 37%, p<0.001).
All pts had dual chamber pacemaker and 73% were programmed on DDD mode, with algorithms for minimizing ventricular pacing. 5 (4.8%) pts were pacemaker-dependent (PMD), 20% had ventricular pacing ≥50% of time (50% with 2nd or 3rd degree AV block) and 18% had atrial pacing ≥50% of time. All pacemaker-dependent pts had been transplanted, at least, 8 years before and mean age at the last follow-up visit was 44±10 years old. Pacemaker-dependency and high percentage of pacing were significantly associated with longer time of disease, worse neurologic stage at follow-up visit and global progression of the disease. High percentage of ventricular pacing was also associated with 1st degree AV block (80% vs 35%, p=0.002) and IICV (86% vs 42%, p=0.043).
Pacemaker complications, requiring surgical intervention, occurred in 9 pts.
Conclusion: Cardiac conduction disease progresses in FAP pts in spite of LT, with the development of arrhythmia requiring PM.

P6168 | BEDSIDE
Characteristics of supra- and ventricular arrhythmias in 94 patients with genetically proven myotonic muscular dystrophy and no clinically overt cardiac dysfunction

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Purpose: Patients with myotonic muscular dystrophy (dystrophia myotonica, DM) are at risk for myocardium damage and sudden cardiac death due to diverse arrhythmias, especially progressive atrioventricular (AV) conduction abnormalities. However, there is limited data on potential life-threatening ventricular arrhythmias (VA) in these patients, especially according to the type 1 and type 2 DM.
Methods: A group of 94 consecutive pts (47 F, 47 M) aged 42.3±14.0 yrs with genetically confirmed DM (mean disease duration 9.6 yrs) and 40 sex- and aged-matched healthy controls underwent electrocardiography, echocardiography and 24-h Holter monitoring. Type 1 (DM1) was diagnosed in 51 pts, while type 2 (DM2) in 43 pts.
Results: All controls and 85 DM pts (91%) had preserved left ventricular function at echocardiography (LVEF >55%, no valvular dysfunctions). Due to previously detected advanced AV conduction defects 2 pts with DM had a pacemaker implanted. DM pts presented more frequently benign and potentially life threatening VA and also 1st degree AV block (AVB) than controls (Table). In opposite to AVB, all types of tachyarrhythmias were more frequently observed in DM2 than in DM1 patients. Moreover, 4 DM1 pts had persistent or paroxysmal atrial fibrillation.

Parameter	DM (n=94)	Controls (n=40)	p	DM 1 (n=51)	DM 2 (n=43)	p
Short supraventricular tachycardia	18	2	0.04	3	15	0.005
Benign ventricular arrhythmia (bi-trigeminy and/or couplets)	22	3	0.03	7	15	0.03
Potentially malignant ventricular arrhythmia (non-sustained ventricular tachycardia and/or R-on-T premature ventricular contractions)	14	1	0.04	4	10	0.045
1st degree atrioventricular block	18	0	0.002	15	3	0.008
2nd degree atrioventricular block	5	2	0.9	4	1	0.4

Conclusions: In the large group of DM patients we observed significantly more frequent diverse arrhythmias (including potentially life-threatening ventricular arrhythmias) which warrants their close cardiac monitoring. Supraventricular and ventricular arrhythmias were more frequently observed in DM2 patients. However, DM1 subjects when compared to DM2 presented more AV conduction defects.

P6169 | BEDSIDE
Phenotype-genotype correlation of Lamin (LMNA A/C) associated dilated cardiomyopathy

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Dilated cardiomyopathy (DCM) caused by mutations in the lamin A/C (LMNA) gene is often associated with conduction disorders and cardiac arrhythmias.
Aim: The purpose of this study was to identify LMNA mutations, estimate their frequency among Belarus patients (pts) with sporadic DCM and phenotype-genotype correlation analysis.
Methods: We enrolled 173 pts with sporadic DCM. Of these 92 (53,2%) pts had a primary manifestation of conduction disorders and cardiac arrhythmias (aged

42,3±11,7; men 89,1%; NYHA 2,7±0,4; LVEF 25,9±11,1%; LBBB 59,8%; AV block 21.7%; sVT+nsVT 64,1%; AF 34,8%). Genetic analysis of 1,3,5,8–10 exons of LMNA was performed by SSCP and sequencing in 92 pts. Genetic testing, age, gender, NYHA, 6-MWT, serum CK, EchoCG and ECG/HM-ECG (QTdisp, HRT, microvolt T-wave alternans (mTWA)) were analyzed.
Results: In 28 (30,4%) pts with DCM were identified changes in gene LMNA. So at 23 pts was detected replacement c.1698 C>T in exon 10, including two homozygous carriers T/T. Two different mutations were identified in 2 pts in exon 3: c.612G>A and c.569G>C; the latter is a result of substituted arginine residue by proline - Arg190Pro. Another missense mutation was identified in 9th exon Thr528Arg (c.1247S>T). In addition, two patients were identified as carriers simultaneously three nucleotide changes in the gene LMNA: c.639+73C>T and c.639+56G>A, located in intron and c.861T>C in exon 5. One patient had mutation in exon 1 - c.150S>T. These identified mutations could change the function of lamin A/C directly or indirectly and clinically manifest as “lamine-phenotypes” DCM. Genetic and phenotypic (clinical, morphofunctional) parameters were included in the correlation and univariate dispersive analysis. As a result, carriers of mutations in the LMNA gene were associated with a positive test mTWA ($p<0.005$), ↑CK levels ($p<0.01$), nsVT ($p<0.05$) and AV block ($p<0.01$); a negative correlation was detected with LVEF ($p<0,05$). As a result of univariate dispersive analysis, LVEF and nsVT were lost their significance (F=2,95; p=0.056), while mTWA (F=9,6; p=0,000), ↑CK (F=6,43; p=0.015), and AV block (F=5,7; p=0.019) confirmed the predictive accuracy of these phenotypic findings.
Conclusions: Thus, 1/3 DCM pts of Belarus developed a phenotype with arrhythmias and conduction disoders caused by lamin gene anomalies. Given the high risk of SCD pts with lamin-associated DCM, detection elevated level of sCK, AVblock and abnormal mTWA will allow to select a group of sporadic DCM pts for obligatory genetic screening in order to determine of risk stratification.

P6170 | BEDSIDE
Cardiac magnetic resonance and arrhythmic risk stratification of cardiomyopathy associated with lamin A/C mutations: results from a 5 year study

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Background: Mutations in the LMNA gene, encoding nuclear proteins lamin A/C, have been associated with cardiac disease and high risk of sudden cardiac death (SCD) from both brady- and tachyarrhythmias. The implant of a cardioverter defibrillator (ICD) is to date the only effective intervention, but no specific guidelines are available.
Purpose: We designed a clinical protocol including extensive cardiological examination and strict follow-up (FU) of patients bearing LMNA gene mutations to define a risk stratification protocol for arrhythmic events.
Methods: To date, 17 patients (age 41±16; 59% males) bearing LMNA gene mutations have been enrolled in our center and followed for 5±2 years. All the patients had a baseline ECG and underwent cardiac magnetic resonance (CMR) at the time of genetic diagnosis. Patients fulfilling criteria for dilated cardiomyopathy -EF <45% and moderate or severe left ventricular (LV) dilatation- were excluded (n=4). We termed early cardiomyopathy (ECM) the finding of late gadolinium enhancement (LGE) on CMR in the absence of the criteria defined above. Regular FU including 2/year ECG, echocardiogram and 24h-Holter monitoring was obtained.
Results: All the patients were asymptomatic. Eight of them (62%) had a normal CMR. ECM phenotype was seen in the other 5 cases (38%), all with a midwall LGE distribution pattern involving mid-basal segments of interventricular septum (IVS) and posterior-inferior LV wall. At presentation, 4 patients in the ECM group (80%) had 1st degree atrioventricular (AV) block and/or QRS duration >120 ms. Moreover, at 2.5±0.5 years FU, 2 of them developed 2nd degree AV block. On the contrary, all the patients with normal CMR had no evidence of any conduction delay ($p<0.01$). Due to family history of SCD, 7 patients (4 ECM + 3 normal) underwent ICD implantation in primary prevention. To date, no ICD shocks were seen in both groups. However, at 4.0±1.0 years, 3 patients in ECM group (60%) vs. 1 patient in normal group (13%) showed episodes of non-sustained ventricular tachycardia (NSVT) on Holter or ICD recording (p = n.s.). Interestingly, serial echocardiograms showed no significant changes in LV volumes and systolic function in both groups.
Conclusion: In carriers of LMNA mutations, CMR detects an early form of cardiomyopathy involving IVS. The presence of LGE identifies patients at a higher risk of both AV conduction worsening and, later, new-occurrence of NSVTs. Based on the incidence of major arrhythmic events, long-term FU will allow us to define the correct timing of ICD implant in this population.

P6171 | BENCH
Cardiac hypertrophy is associated with mutations in SCN5A gene

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Background: The SCN5A gene encodes the alpha subunit of the Nav1.5 sodium channel, which is responsible for the inward sodium current (INa). Genetic alterations in the SCN5A gene may affect the structure, function or level of expression of the Nav1.5 sodium channel. These diverse and often functionally opposite alterations of cardiomyocyte electrical excitability result in various cardiac arrhythmias, such as long QT syndrome (LQTS), Brugada syndrome, sick sinus syndrome, progressive cardiac conduction defect, idiopathic ventricular fibrillation, sudden infant death syndrome (SIDS), and mixed arrhythmogenic syndromes. It was recently demonstrated that the phenotypic expression of SCN5A genetic mutations could be expanded from electrical disorders with an apparently normal heart to cardiomyopathies. Currently, more than 10 mutations in the SCN5A gene have been described which lead to the development of DCM and/or atrial cardiomyopthy in conjunction with a wide range of cardiac arrhythmias and conduction disorders.
Methods: We did perform DNA diagnostics for primary arrhythmias since 1998 year, and 232 unrelated families underwent molecular genetic testing, including sequencing of SCN5A gene by Sanger or within PGM Ion Torrent target genes resequencing. Twenty-one mutations in 22 unrelated families in SCN5A gene were found, one proband have carried two mutations in two SCN5A alleles inherited from both parents. Detailed clinical and instrumental examinations including ECG, EchoCG, cardiac MRI, and neurological examination were performed for SCN5A mutation carriers (probands) regardless of underlying diagnosis of primary arrhythmia.
Results: The screening had revealed 4 patients (18%) with undoubted structural cardiac remodeling (Table 1).

Table 1. Cardiac remodeling in SCN5A-pos

Mutation	Age, y.o.	Gender	Primary diagnosis	Type of remodelling
p.I388F	32	F	PVC	ARVC
p.E446K	54	M	CCD	Dilatedcardiomyopathy
p.S1431R + p.A572D	16	F	SSS	Cardiac hypertrophy
p.P2005A	20	F	LQTS, VF, SCD	Cardiac hypertrophy

Conclusion: It seems that the prevalence of different variants of cardiac remodeling in SCN5A-mutations carriers is higher than previously thought. In this study we did find cardiac hypertrophy in patients with SCN5A mutation what had not been published before.

P6172 | BEDSIDE
Association of genetic variants with atrial fibrillation in Japanese individuals

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Purpose: Recent genome-wide association studies (GWASs) identified various genes and loci that confer susceptibility to coronary artery disease or myocardial infarction among Caucasian populations. Given that myocardial ischemia is an important risk factor for atrial fibrillation, we hypothesized that certain polymorphisms may contribute to the genetic suscep-tibility to atrial fibrillation through affecting the susceptibility to coronary artery disease. The purpose of the present study was to examine a possible association of atrial fibrillation in Japanese individuals with 29 polymorphisms identified as susceptibility loci for coronary artery disease or myocardial infarction in the meta-analyses of GWASs in Caucasian populations.
Methods: Study subjects comprised 5460 Japanese individuals (305 subjects with atrial fibrillation, 5155 controls) who visited the participating hospitals between 2002 and 2012. Subjects with atrial fibrillation who had apparent structural heart diseases were excluded from the study. Genotypes of polymorphisms were determined by the multiplex bead-based Luminex assay.
Results: Comparisons of allele frequencies by the chi-square test revealed that rs11556924 (C→T, Arg363His) of the zinc finger, C3HC-type containing 1 gene (ZC3HC1, P=0.0076), rs599839 (G→A) of the proline/serine-rich coiled-coil 1 gene (PSRC1, P=0.0084), rs964184 (C→G) of the ZPR1 zinc finger gene (ZPR1, P=0.0281), and rs2075650 (G→A) of the translocase of outer mitochondrial membrane 40 homolog gene (TOMM40, P=0.0407) were significantly ($P<0.05$) associated with atrial fibrillation. Multivariable logistic regression analysis with adjustment for age, gender, body mass index, and the prevalence of smoking, hypertension, diabetes mellitus, and dyslipidemia revealed that rs11556924 (P=0.0066; odds ratio, 1.95; additive model) and rs599839 (P=0.0047; odds ratio, 1.57; dominant model) were significantly associated with atrial fibrillation, with the minor T and G alleles, respectively, representing risk factors for this condition. Similar analysis revealed that rs964184 (P=0.0127; odds ratio, 0.72; additive model) and rs2075650 (P=0.0067; odds ratio, 0.67; additive model) were also significantly related to atrial fibrillation, with the minor G allele of both polymorphisms being protective against this condition.
Conclusions: ZC3HC1, PSRC1, ZPR1, and TOMM40 may be susceptibility loci for atrial fibrillation in Japanese individuals. Determination of genotypes of these polymorphisms may probe informative for assessment of the genetic risk for atrial fibrillation in such individuals.

P6173 | BENCH
Transcriptional profile and functional analysis of aged atrial fibrillation

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Background: Aging is known as a very important factor to increase the incidence of atrial fibrillation (AF) and to confer the risk of thromboembolism, however, the pathogenesis of aged atrial fibrillation remain poorly understood.
Methods and results: Samples of right atrial appendage were collected from patients undergoing aortic valve replacement. Patiens with mitral valve diseases, rheumatic valve diseases, left atrial dimension >50mm were not included. Patients were divided into six groups: aged 40 in sinus rhythm (SR-40), aged 50 in sinus rhythm (SR-50), aged 60 in sinus rhythm (SR-60), aged 70 in sinus rhythm (SR-70), aged 60 in AF (AF-60) and aged 70 in AF (AF-70). We performed genome-wide whole transcriptomic profiling using Illumina Human HT-12 mRNA microarrays. Among four SR groups, we found 257 genes accociated with atrial aging were significantly up-regulated and 304 genes were significantly down-regulated. Among SR-60, SR-70, AF-60 and AF-70, 62 genes accociated with atrial fibrillation were significantly up-regulated and 56 genes were significantly down-regulated. 10 genes were identified with both atrial aging and atrial fibrillation. Functional classification based on Gene Ontology Database were conducted and demonstrated these genes were strikingly accociated with immunomodulatory regulation and electrophysiological remodeling.
Conclusion: Our study first revealed 10 genes and several signaling pathways significantly involved in aged AF-related transcriptional expression, which may yield novel insight into aged AF pathogenesis.

P6174 | BEDSIDE
Exercise-induced changes in Brugada ECG

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Purpose: Exercise is reported to induce ST-segment changes in Brugada patients, and anecdotally to induce ventricular arrhythmias. We aimed to assess ECG responses to exercise in our Brugada patients and correlate them with clinical data.
Methods: A treadmill exercise test according to Bruce protocol was performed, using 12 lead ECG, placing right precordial leads V1, V2 in 2 nd intercostal space
Results: 53 Brugada patients (42 men, 11 women, mean age 45 years) performed the test. They had a spontaneous Brugada pattern (11) or a drug induced (ajmalin) pattern (42). During the test the heart rate increased reaching a medium of 96.4% of the maximal (range 80–107%)
The baseline ECG showed a type 1 Brugada pattern in 3 patients: at maximum effort 2 presented an increase of the J wave amplitude, 1 developed a decrease of the J wave amplitude, all 3 returned to baseline levels in the recovery phase.
The other patients presented a type 2 Brugada ripolarization at the baseline. 6 of them (12%) developed a type 1 at maximal effort. During the recovery phase type 1 pattern gradually disappeared, returning to the baseline ripolarization. All but one of these 6 patients had previously exhibited a type 1 Brugada ECG spontaneously.
There were no serious arrhythmias, 7 (13%) presented isolated ventricular premature beats, 5 with a left bundle block morphology and 2 with right bundle block morphology
Conclusions: Stress test in Brugada patients seems to be a safe and useful tool. The appearance of an exercise induced type 1 Brugada ECG was non infrequent (12%). In our series exercise triggered a type 1 Brugada ECG mostly in patients that had already shown an intermittent spontaneous type 1. Although we had no serious ventricular arrhythmias, the appearance of an exercise induced type 1 ECG questions the safety of exercise in Brugada patients.

P6175 | BENCH
Spatial reproducibility of complex fractionated atrial electrograms depending on the direction and configuration of bipolar electrodes: a patient specific in-silico left atrial modeling study

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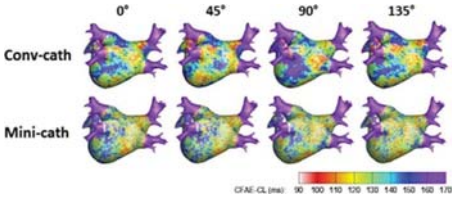
Introduction: Although 3D-complex fractionated atrial electrogram (CFAE) map is useful in radiofrequency catheter ablation for persistent atrial fibrillation (AF), directions and distance of bipolar electrodes may affect the areas of CFAE.
Purpose: We compared spatial reproducibility of CFAE by changing catheter directions and electrode distance in patient-specific in-silico modeling of left atrium (LA).
Methods: We conducted this study by importing a persistent AF patient's heart CT image to 3D-homogeneous human LA modeling and tested spatial distribution of CFAE-cycle lengths (CLs) at 400,000 nodes. Electrogram morphology and CFAE-CL in each node and the ratio of consistent sites with CFAE-CL<120ms were compared in 16 different orientations of virtual bipolar conventional catheter (conv-cath: size 3.5mm, inter-electrode distance 4.75mm), and also tested with virtual mini catheter (mini-cath: size 1mm, inter-electrode distance 2.5mm).
Results: 1. Depending on the catheter orientations, electrogram morphology changed and CFAE-CLs were variable (conv-cath: 11.5±0.7% variation, mini-cath: 7.1±1.2% variation, $p<0.001$). 2. However, those measured by mini-cath were less influenced by catheter directions than with conv-cath ($p<0.001$). 3. There were moderate spatial correlations of CFAE-CL (conv-cath: r=0.3055±0.2194, mini-cath: 0.6074±0.0733, $p<0.001$) and consistency of CFAE area (conv-cath: 22.3±1.4%, mini-cath: 38.3±4.6%, $p<0.05$) in 16 variable orientations of virtual bipolar catheters.



CFAE map depending on catheter direciton

Conclusions: Electrograms and CFAE distribution are affected by catheter orientations and electrode configurations in this in-silico LA model. However, there was moderate spatial consistency of CFAE areas, and narrow spaced bipolar catheter was less influenced by catheter direction than conventional catheter.

P6176 | BENCH
PITX2 and atrial fibrillation: from palpitations to methylation

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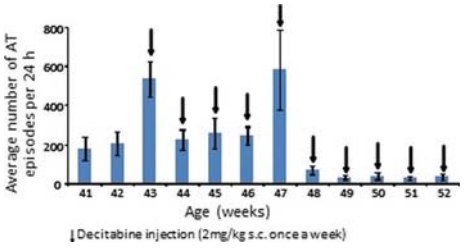
Background: Pitx2 is a transcription factor located in proximity to the human 4q25 familial atrial fibrillation (AF) locus. The mechanisms underlying PITX2 regulation in AF remain unknown.
Purpose: To determine the role of methylation in PITX2 regulation in the left atrial muscle.
Methods: Transcriptomic analysis was used to identify the altered genes in myocardial left atrium (LA) of AF patients. Quantitative RT-PCR of PITX2 was also performed in fourteen subjects and in four aging spontaneously hypertensive rats (SHRs). Using bisulfite sequencing of DNA, the methylation status of the PITX2 promotor region embedded in CpG islands was analysed in eleven patients, in eleven aging SHRs and in two normotensive Wistar-Kyoto (WKY) rats. In five SHR rats, the antiarrhythmic action of a hypomethylating drug, decitabine (5-Aza-2'-deoxycitidine), was studied. Reversion of the hypermethylated PITX2 promotor region with this drug was also evaluated.
Results: Microarray data showed that PITX2 was down-regulated in myocardial LA of AF patients (–5.40 fold changes AF patients/ controls). Quantitative RT-PCR confirmed the PITX2 dysregulation in AF patients and in SHRs (significantly negatively correlated with age. Spearman r=–0.86, $P<0.01$). Methylation of the PITX2 promotor region was documented in 100% of AF patients and in 50% of aging SHRs. Decitabine decreased the atrial tachycardia (AT) occurrence (figure) and reversed the hypermethylation of PITX2 promotor region in 3 out of 5 SHR rats.



Effect of decitabine

Conclusions: These data suggest that in the left atria of AF patients and of SHRs, methylation of the PITX2 promotor region may underlie down-regulation of this gene. Additional studies are needed to confirm the anti-arrhythmic effect of PITX2 demethylation.

P6177 | BENCH
LED flash-induced termination of anatomical reentry in optogenetically modified transverse rat ventricular tissue slices

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Background: Reentry is an important mechanism of ventricular arrhythmias in patients with structural heart disease. Termination often requires implantable cardioverter defibrillator shocks with significant impact on quality of life and prognosis. Optogenetics, which rely on light-gated ion channel expression and activation

can modulate electrophysiological properties and may provide a new and unique means to analyse and counteract cardiac arrhythmias. Whether optogenetic interventions can influence anatomically determined reentry is unknown. We studied the effects of optogenic interventions on reentry in a novel in situ model.
Methods and results: Hearts from 2 day-old Wistar rats and a dedicated vibratome setup were used to produce 150 μm-thick transverse ventricular tissue slices, which were plated onto 0.4 μm-pore membranes (Millicell culture insert). Within 4 hours slices were genetically modified with lentiviral vectors encoding a depolarizing current-producing, light-activated Ca^{2+}-translocating channelrhodopsin (CatCh-group) or eYFP as control. After 4 days, the effects of CatCh activation by 470 nm-light pulses from a LED which was positioned centrally below the specimen, was investigated by optical mapping using Di-4-ANEPPS as voltage-sensitive dye. During electrical stimulation action potential duration (APD80) and conduction velocity (CV) showed no significant differences between controls and CatCH-group (129±37ms vs. 126±43ms; 6.9±1.0cm/s vs. 6.8±0.8cm/s). However, only in the CatCh-group, 10ms-LED flashes evoked action potentials up to 4 Hz. Reentry was induced in controls (80%, n=5) and in the CatCh-group (100%, n=6) by programmed electrical stimulation (S1/S2-protocol). Reentry circuit cycle lengths were comparable (162±12ms vs.178±7ms, ns) and sustained unless terminated on purpose. Global illumination by longer duration LED flashes (500–1500ms) terminated reentry in 5 out of 6 slices in CatCh, but in none of the controls ($p<0.01$). Localized illumination, targeting the critical part of the reentrant circuit, could also terminate the arrhythmia in CatCh-expressing slices. In both situations, depolarization-induced conduction block terminates the arrhythmia.
Conclusion: This is the first study to show that stable anatomically determined reentry circuits in transverse rat ventricular tissue slices can be terminated effectively by expression of light-gated ion channels that are subsequently activated by LED flashes. These results can provide novel practical and mechanistic insights into the optogenetic control of arrhythmic activity in ventricular tissue.

ATRIAL FIBRILLATION: BASIC MECHANISMS

P6178 | BENCH
Increased cellular inflammation and chemotactic activity of epicardial adipose tissue in atrial fibrillation

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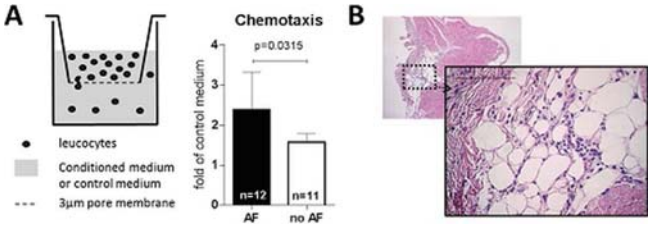
Background: There is growing evidence that epicardial adipose tissue (EAT) might be involved in the pathophysiology of atrial fibrillation (AF). We previously demonstrated a fibrotic remodeling of atrial EAT associated with AF.
Purpose: In this study we assessed inflammatory changes of atrial EAT induced by AF.
Methods: In a sheep model of long-term persistent AF, induced by atrial tachypacing, we specifically addressed the role of AF in altering EAT. First, the presence of inflammatory cells in the adipose tissue was assessed on Haematoxylin Eosin stained sections. Second, atrial EAT was cultured and the conditioned medium was used in a chemotactic assay (Figure A). Peripheral blood mononuclear cells (PBMC) were prepared from fresh blood and a total of 500 000 PBMCs were added to the upper chamber. The migration test was performed for 120 minutes in a cell culture incubator.
Results: Small lymphoid aggregates were observed in the fatty infiltrations (Figure B), more frequently in AF than control sheep (AF: 6 out of 15 sheep or 7% (14/211) of fatty infiltrations vs control: 1 out of 11 sheep or 1% (1/103) of fatty infiltrations, p=0.043). The chemotaxis assay demonstrated increased chemotactic capacity on the PBMCs, the predominant type of immune cell observed in the fatty infiltrations.



Conclusion: The increased chemotactic capacity, in combination with increased inflammatory aggregates, indicate a pro-inflammatory state of the atrial EAT induced by AF.
Acknowledgement/Funding: Research Fund – Flanders (FWO)

P6179 | BENCH
Profibrotic and inflammatory atrial remodeling of zucker diabetic fatty rats is aggravated by rapid pacing

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Purpose: Atrial fibrosis is a critical substrate in the initiation and maintenance of atrial fibrillation (AF). The pathomechanism of AF is multifactorial and related to concomitant diseases. The detailed mechanisms, which trigger atrial remodeling of extracellular matrix (ECM) in diabetic atrial tissue, remain incompletely investigated.
Methods: Zucker Diabetic Fatty (ZDF) rat is an animal model that mimics human T2DM. Left and right atrial tissue samples from male rats (obese ZDF; n=29) and their non-diabetic controls, lean ZDF (n=24), were analysed at the age of 3 months (onset of diabetes) and 6 months (advanced stage). To study the molecular changes in response to pacing we prepared atrial slices and put into the culture on the membrane of the cell culture inserts. To resemble AF, the tissue slices were stimulated in the electrical field at 5 Hz (vs.0.6 Hz) up to 20h. Then, atrial tissue was examined using transcriptome analysis, and at the transcriptional and protein level. We focused our investigation on components of ECM including collagens, fibronectin, and adhesion molecules (ICAM-1), growth factors (TGFb, CTGF, CYR61), metalloproteinases that remodel collagens (MMPs, ADAMs) and their naturally occurred inhibitors (TIMPs). Moreover the expression of tissue relevant cytokines was analysed.
Results: Transcriptome analysis revealed that atrial remodeling in T2DM is associated with a strong induction of growth factors: 3-fold in CTGF (connective tissue growth factor), and 3.7-fold in CYR61. Interestingly this up-regulation was observed at the onset of diabetes. With the progression of diabetes, the expression of TGFb, another marker of fibrosis, was significant elevated. Surprisingly, the synthesis of new collagens was not induced. However, the advanced stage of T2DM was associated with rise in the expression of fibronectin (3.3±0.40; $p<0.01$), and MMP9 (2.2±0.34, $p<0.05$). Moreover, atrial myopathy in T2DM is characterised by increased levels of cytokines (IL-6, IL-8, TNFα), and adhesion molecules (ICAM-1). The exposure of atrial diabetic tissue slices to stimulation in the electrical field caused further up-regulation in the expression of fibronectin, IL-8, and TNFα compared to non-diabetic atrial slices. The augmented ratio of MMP/TIMP indicated that diabetic atrial tissue was more prone to degradation processes of ECM during pacing.
Conclusions: T2DM promote pro-fibrotic and pro-inflammatory atrial remodeling processes that might serve as a pro-arrhythmogenic substrate. The “in vitro” stimulation of diabetic atrial tissue further aggravates this inflammatory process.
Acknowledgement/Funding: European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement HEALTH-F2-2010-261057

P6180 | BENCH
Inhibitions of late sodium current and calmodulin kinase II terminate atrial fibrillation induced by isoproterenol

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Introduction Inhibitions of late sodium current and Ca2+/calmodulin-dependent protein kinase II (CaMK II) may be new targets in treating atrial fibrillation (AF).
Purpose: The objective of this study was to determine the role of late sodium current and CaMK II in promoting triggered activities and AF in a rabbit whole heart model of inducible AF by isoproterenol (ISO).
Methods: Langendorff-perfused rabbit hearts were used to record right atrial monophasic action potentials (MAPs), ECG signals and 96-electrode atrial mapping. AF burden, AF inducible window, atrial effective refractory period (AERP), electrical conduction and activation pattern during sinus rhythm and AF were measured in hearts at a fixed pacing cycle length of 250 ms before and after exposure of ISO in the absence and presence of late sodium current (ranolazine and TTX) and CaMK II (KN-93) inhibitors.
Results: At basic stimulation cycle length of 250 ms, ISO (3–15 nM) increased AF burden and AF inducible window by 16±6s and 23±3 ms, and shortened AERP by 29±4 ms (n=12, $p<0.05$), respectively, in concentration-dependent manners. In the continued presence of 15 nM ISO, Ran (0.1–10 μM, n=10), KN-93 (0.01–6 μM, n=5) and TTX (0.01–3 μM, n=5) decreased AF burden by 16±1, 27±3, 20±3s, and AF inducible window by 22±1, 26±1, 20±5 ms, and prolonged from the baseline of the AERP by 30±6, 25±8, 15±4 ms ($p<0.05$), respectively, in similar concentration-dependent manners. In contrast, KN-92 (0.01–6 μM) did not alter the AF burden, AF inducible window and AERP (n=5, $p>0.05$). ISO (3, 6, 10, 15 nM, n=12) increased the incidence of premature beat (S2) -induced AF from 0% to 25%, 42%, 92% and 100%, respectively. In the continued presence of 15 nM ISO, Ran (3 μM, n=10), TTX (1 μM, n=8) at concentrations that inhibit late INa, and KN-93 (3 μM, n=5) abolished the inducible AF in 75%, 62.5% and 80% hearts studied. In hearts with sinus rhythm, ISO (15 nM), RAN (3 μM) or KN-93 (3 μM) did not alter the intraatrial conduction time and mean activation time. However, during AF in the presence of ISO, atrial activation pattern was disorganized with multi-ectopic activation sites. ISO (15 nM) increased intraatrial activation conduction time and mean activation time by 12±2 and 6±1 ms (n=5, $p<0.05$). Compared with ISO alone, Ran (3 μM) and KN-93 (3 μM) shortened intraatrial conduction time and mean activation time by 9±2, 10±2 ms, and 6±1, 7±2 ms, respectively (n=5, $p<0.05$).

Conclusions: Late sodium current and CaMK II pathways play important roles in the genesis of AF mediated by ISO. Inhibition of these pathways is effective in treating AF.

P6181 | BENCH
Pro-inflammatory skewing of inflammatory to regulatory T lymphocyte ratio in atrial fibrillation

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Background: The precise role of inflammation in the development and perpetuation of atrial fibrillation (AF) is yet to be fully uncovered. T and B lymphocytes, the main cellular effectors of adaptive immunity, have pivotal roles in orchestrating inflammation. Different subsets of lymphocytes either promote or prevent inflammation. We are investigating a unique subset of lymphocytes, the CD4+CD28null T cells that expand in patients with chronic inflammation. These cells secrete high levels of pro-inflammatory cytokines tumour necrosis factor-α (TNF-α) and interferon-g (IFN-g). The response of CD4+CD28null T cells is normally maintained under control by regulatory T cells (Tregs), a specialised subset of T lymphocytes with suppressive function that maintain immune homeostasis and prevent pathogenic immune responses. The role of CD4+CD28null and Treg cells has not been investigated in AF.
Purpose: We hypothesised that in AF the balance between pro-inflammatory and regulatory T lymphocytes is skewed in favour of inflammatory T cells.
Methods: We recruited 65 patients with idiopathic AF who lacked co-morbidities associated with inflammation (coronary artery disease, autoimmune diseases, diabetes, heart failure). Circulating CD4+CD28null T lymphocytes, Tregs and B cells were quantified by flow cytometry in AF patients and healthy controls (n=35). High sensitivity CRP, TNF-α and IFN-g levels were quantified in serum.
Results: CD4+CD28null T lymphocytes were significantly increased in the circulation of AF patients compared to controls ($p<0.0001$). In addition, AF patients had a marked reduction (p=0.0001) in Treg cells. The ratio of CD4+CD28null T lymphocytes to Tregs was also significantly increased. In contrast, no alterations were identified in circulating B cell subsets (total, mature and memory). The correlation between CD4+CD28null or Treg lymphocytes and serum levels of CRP, TNF-α and IFN-g was investigated.
Conclusions: Our findings demonstrate that specific subsets of T lymphocytes are deregulated in patients with AF. Pro-inflammatory CD4+CD28null T cells increase significantly in AF patients, whilst the anti-inflammatory Treg subset is markedly reduced. These innovative results suggest an imbalance in the mechanisms that maintain homeostasis in the immune response, which may promote inflammation in patients with AF. An in-depth understanding of the role of various lymphocyte subsets in the inflammatory response in AF may reveal novel therapeutic strategies to re-establish the equilibrium between pro- and anti-inflammatory mechanisms at work in this disease.

P6182 | BENCH
Tissue expression levels of miRNAs associated with fibrosis in patients with paroxysmal and persistent atrial fibrillation

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Background: Atrial structural remodeling includes atrial enlargement and fibrosis and forms a key substrate for atrial fibrillation (AF). MicroRNAs (miRNAs) are likely modulators of atrial remodeling and are potential targets for diagnosis or therapies.
Purpose: This study aims to explore the differential expression of miRNAs associated with fibrosis in human left atrial tissue of patients with paroxysmal and persistent AF.
Methods: Left atrial appendages of 10 patients with paroxysmal (n=6) and persistent AF (n=4) were retrieved during thoracoscopic pulmonary vein isolation. Total RNA was extracted from tissue and miRNA sequencing was performed on the Illumina Nextseq500. The differential expression of 5 established miRNAs (miR-21, miR-29b, miR-30c, miR-133, miR-590) known to suppress genes involved in structural remodeling was studied.
Results: MiRNA sequencing revealed miR-29b-3p to be downregulated in persistent AF compared to paroxysmal AF (LogFC –0.33, p 0.04). No differential expression was found for miRNA-21 (LogFC –0.4, p 0.21), miR-30c (LogFC 0.11, p 0.37), miR-133a/–133b (LogFC –0.03, p 0.83; LogFC –0.15, p 0.78) and miR-590 (LogFC –0.01, p 0.92).

Table 1. Differential expression of miRNAs

miRNA	Target gene	CPM paroxysmal	CPM persistent	Log fold change	P-value
miR-21	SPRY1	7.7±0.4	7.4±0.5	–0.4	0.21
miR-29b-3p	COL1A1, COL3A1, FBN	13.4±0.3	13.1±0.1	–0.33	0.04
miR-30c	CTGF	13.5±0.1	13.6±0.2	0.11	0.37
miR-133a/b	CTGF, TGF-β1, TGFR-2	15.8±0.2/ 0.4±0.8	15.8±0.2/ 0.4±0.7	–0.03/–0.15	0.83/0.78
miR-590	TGF-β1, TGFR-2	4.8±0.1	4.7±0.2	–0.01	0.92

Abbreviations: CPM, counts per million; SPRY1, sprouty-1; FBN, fibrillin; CTGF, connective tissue growth factor; TGF-β1, transforming growth factor β1; TGFR-2, transforming growth factor β receptor type 2.

Conclusion: This is the first study to report on whole miRNome sequencing in human left atrial tissue. Our preliminary results show miR-29b-3p to be downregulated in persistent compared to paroxysmal AF. The consequent upregulation of extracellular matrix genes may induce atrial fibrosis and turns miR-29b-3p into a potential target of therapy. Other miRNAs were not differentially expressed. These data emphasize the relevance of miRNAs, but a larger study population including non-AF controls and the concomitant exploration of gene expression is needed to establish the pathophysiological role in AF.
Acknowledgement/Funding: Netherlands Organisation for Scientific Research (NWO): VIDI Grant nr.016.146.310

P6183 | BENCH
Atrial fibrillation altered hepatic gene expression profiles in human and rat model

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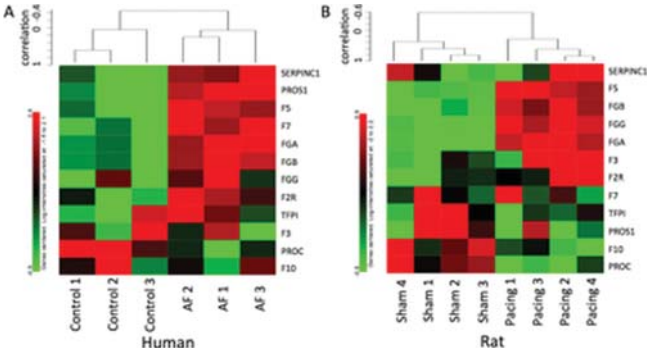
Background: Atrial fibrillation (AF) increases the risk of stroke, and is accompanied by systemically enhanced coagulation. The liver is a major source of prothrombotic molecules. These evidences imply the role of the liver on pathophysiology of AF-related thromboembolism.
Purpose: The aim of this study was to identify the change of hepatic gene expressions associated with AF in human and rat model.
Methods and results: We screened 465 consecutive patients with non-alcoholic steatohepatitis, who underwent liver biopsy from 2003 to 2013, and identified 3 patients with AF. Patients in sinus rhythm matched for age, sex, hepatic histopathological stage, served as a control group. Using cDNA microarray, we compared gene expression profiles of the liver in 2 groups. Of 54675 genes on the array, 46950 filtered genes demonstrated clear clusters for AF or control. Interestingly, among 354 BioCarta Pathways, the extrinsic prothrombin activation pathway including fibrinogen and coagulation factor VII showed the most prominent change (Figure A). To assess whether rapid atrial excitation per se affects hepatic gene expression profile, we subjected healthy Sprague-Dawley rats to 12-hour rapid atrial pacing at 1200 bpm and analyzed their livers. Hierarchical clustering with 13463 filtered genes showed clear clusters for the pacing or sham group. As with human AF, rapid atrial pacing in rat significantly altered the hepatic gene expressions associated with extrinsic prothrombin activation pathway (Figure B). In contrast, the genes related to fibrinolysis were augmented in human, but not in rat.



Heatmap of extrinsic coagulation pathway

Conclusions: AF affected hepatic gene expressions, predominantly involved in coagulation. These findings suggest the cardio-hepatic interaction in the AF-related thromboembolism.

P6184 | BENCH
Differential expression of microRNAs associated with electrical remodeling in left atrial tissue of patients with paroxysmal versus persistent atrial fibrillation

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Background: The pathophysiological substrate of atrial fibrillation (AF) is complex and incompletely understood. Electrical remodeling contributes to arrhythmogenesis, and is reflected in the expression of microRNAs (miRNAs) in atrial tissue.

Abstract P6184 – Table 1. Differential expression of miRNAs

miRNA	Target gene(s)	Effect	Expression levels (CPM)		p
			PAF	PersAF	
miRNA-1	KCEN1, KCNB2	Downregulating minK and Kv2.2	12.4±0.3	12.5±0.4	0.8
miRNA-26a/b	KCNJ2	Increase in I_{K1} and Kir 2.1 protein levels	15.9±0.2 / 12.7±0.1	15.8±0.1 / 12.7±0.1	0.3 0.8
miRNA-133b	CTGF	Increased TGFB1 and TGFR-2	0.4±0.8	0.4±0.7	0.8
miRNA-208a	Unknown		10.2±0.4	10.0±0.3	0.3
miRNA-328	CACNA1C, CACNB1	Decrease in I_{CaL}, reduced expression of Cav1.2 and CavB1 and APD shortening	6.4±0.4	6.4±0.3	1.0
miRNA-499a	KCNN3	Downregulating SK3	3.7±0.3	3.0±0.5	0.01

miRNA, microRNA; PAF, paroxysmal atrial fibrillation; PersAF, persistent atrial fibrillation; CPM, counts per million.

Purpose: With this first study to perform next-generation miRNA sequencing in human left atrial tissue we aim to determine whether miRNAs that are associated with electrical remodeling are differentially expressed in patients with paroxysmal versus persistent AF.
Methods: Left atrial appendages from patients with paroxysmal (n=6) and persistent AF (n=6) were retrieved during thoracoscopic surgery for AF. Total RNA was isolated and whole genome miRNA expression profiling was performed to evaluate differential miRNA expression. Seven miRNAs (miRNA-1, -26a/b, -133b, -208a, -328 and -499a) previously reported to be involved in electrical remodeling were studied.
Results: miRNA-499a showed lower expression in patients with persistent AF compared to paroxysmal AF (log fold change (logFC) –0.8, p 0.01). The following miRNAs were not differentially expressed (table); miRNA-1 (logFC 0.1, p 0.8, miRNA-26a (logFC –0.1, p 0.3) and –26b (logFC –0.02, p 0.8), miRNA-133b (logFC –0.1, p 0.8), miRNA-208a (logFC –0.2, p 0.3) and miRNA-328 (logFC<-0.01, p 1.0).
Conclusion: Expression of miRNA-499a, which downregulates the calcium-activated potassium channel 3 (SK3), is reduced in patients with persistent AF compared to paroxysmal AF. These data are consistent with upregulation of calcium-dependent potassium current and action potential duration shortening during AF. However, to appreciate the functional role of miRNA-499a and its potential role as a diagnostic or therapeutic tool, a larger study sample, including atrial tissue of patients without AF, is required.
Acknowledgement/Funding: unrestricted grant from Atricure Inc.

P6185 | BENCH
Effect of idarucizumab on bleeding time associated with dabigatran in combination with antiplatelet agents aspirin, clopidogrel and ticagrelor in a rat tail bleeding model

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Introduction: Idarucizumab is a selective, humanized antibody fragment (Fab) that specifically reverses the anticoagulant activity of dabigatran, a selective and reversible direct thrombin inhibitor.
Purpose: To determine if idarucizumab can reverse the prolonged bleeding time after treatment with dabigatran etexilate (DE) and antiplatelets (AP), such as aspirin (ASA), clopidogrel and ticagrelor, in a rat tail bleeding time model.
Methods: ASA (100 mg/kg), clopidogrel (4 mg/kg), ticagrelor (3 mg/kg) or vehicle was given orally to rats (–120 min). Ex vivo platelet aggregation was performed in platelet rich plasma with collagen (2 μg/mL), ADP (5 μM) or arachidonic acid (AA; 500 μM) agonists using light transmission aggregometry. AP (doses above) were then given 75 min after oral DE (30 mg/kg). Forty five min later (0 min), idarucizumab (33 mg/kg) or vehicle was given as an i.v. bolus and rat tail bleeding time was measured 15 min post-injection. Plasma levels of dabigatran were measured using diluted thrombin time (dTT, Hemoclot). Data presented as mean ± SE, n=6/group.
Results: The doses of antiplatelet agent given impaired ex vivo platelet aggregation by 40–60% using ADP for ticagrelor and clopidogrel and 100% for ASA using AA agonist, consistent with their mechanism of action. Dabigatran plasma levels were ~500 ng/mL in DE-treated animals and similar across groups. Control bleeding time was 137±11 sec and was significantly prolonged at least 2-fold when rats were treated with DE and each AP ($p<0.05$). Idarucizumab partially reversed the prolonged bleeding time induced by the combination of each antiplatelet together with dabigatran, though this was not returned to control, despite complete reversal of dabigatran anticoagulation.
Conclusion: This study demonstrated that in rats treated with both dabigatran and antiplatelet agents, idarucizumab specifically and effectively neutralized the activity of dabigatran. However, due to present antiplatelet activity the bleeding time was only partial reversed.

P6186 | BENCH
Exploration of the function of class I HDACs and class IIa HDACs in experimental atrial fibrillation

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Background: Atrial Fibrillation (AF), the most common persistent clinical tachyarrhythmia, is associated with altered gene expression resulting in functional loss and AF progression. Recent research showed Class I and Class IIa histone deacetylases (HDACs) to regulate pathologic and fetal gene expression causing cardiac contractile dysfunction and hypertrophy.
Purpose: Whether Class I and Class IIa HDACs are involved in AF progression is unknown. Therefore, we investigated their role in tachypacing-induced contractile dysfunction and pathological fetal gene expression in experimental model systems for AF and in clinical AF.
Methods: HL-1 cardiomyocytes were tachypaced (TP) at 5Hz and Ca2+ transient amplitude (CaT) was measured. Before TP, HL-1 cardiomyocytes were overexpressed with individual Class I HDAC (1/3) or Class IIa HDAC (4/5/7/9) with retro virus infection. Western blot was used to measure the expression of HDACs and HDAC5 phosphorylation. Confocal analysis was utilized to measure endogenous HDAC5 and transfected GFP-HDAC5 localization. Real time PCR was used to measure fetal gene expression in both HL-1 cardiomyocytes and human heart tissue.
Results: TP of HL-1 atrial cardiomyocytes resulted in a CaT reduction. Overexpression of HDAC class I member HDAC1 protected against TP-induced CaT reduction, whereas overexpression of HDAC3 reduced CaT both in control and tachypaced cardiomyocytes. Overexpression of Class IIa HDACs, HDAC5 and HDAC7, protected against TP-induced CaT reduction, while HDAC4 and HDAC9 did not. Notably, cardiomyocytes overexpressing a dominant negative HDAC5 or HDAC7 mutant, which bears a myosin enhancer factor 2 (MEF2) binding defect, were not protected against loss of CaT. Furthermore, TP increased phosphorylation of HDAC5, promoted its translocation from the nucleus to cytoplasm, and consequently increased MEF2-related fetal gene expression (β-MHC, BNP). In line with these experimental findings, patients with AF showed a significant increase in both phosphorylated HDAC5 and fetal gene expression (β-MHC, BNP).
Conclusion: Overexpression of HDAC1, HDAC5 and HDAC7 protects against tachypacing-induced CaT reduction in HL-1 cardiomyocytes. Furthermore, tachypacing induces HDAC5 phosphorylation and its nuclear export, resulting in MEF2 regulated fetal gene expression. These features are also present in AF patients. As HDAC5 is abundantly expressed in the heart, in contrast to HDAC1 and HDAC7, HDAC5 is a promising therapeutic target in clinical AF to attenuate pathological gene expression, contractile dysfunction and progression of the disease.
Acknowledgement/Funding: Dutch Heart Foundation (2013T096, 2013T144), LSH-Impulse (40-43100-98-008)

P6187 | BEDSIDE
Association of C34T AMP deaminase 1 gene polymorphism with permanent atrial fibrillation in patients with chronic heart failure

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Background: AMP deaminase (AMPD)-1 accounts for 30% of nucleotide catabolism in the heart and regulates the energetic metabolism in cardiomyocytes. The common C34T variant in the AMPD-1 gene induces a truncated protein (Glu12Stop), and a decrease in AMP catabolism, with adenosine accumulation and a potential to disrupt the energy equilibrium in cardiomyocytes. Adenosine (through action potential shortening) and impaired energetics are potential promoters of atrial fibrillation (AF).
Objective: In patients with chronic heart failure (CHF), we assessed the association between the C34T variant and the presence of permanent AF (perm-AF).
Methods: We included 197 patients with CHF. Blood was withdrawn upon HF stabilization and the C34T variant determined by direct gene sequencing. Chi-squared and t-test were used to assess differences between patients with and without perm-AF. The independent association between permAF and C34T was assessed by binary logistic regression analysis adjusted for pertinent variables.
Results: Of the 197 patients (61% men, mean age 69±10), 72.6% had hypertension, 51% diabetes and 56% were prior/current smokers. CHF was of ischemic origin in 49%. Left-ventricular ejection fraction (EF) was 37.8±16% and mean NYHA functional class 2.5±0.8. Eighty-four percent of patients were treated with ACEI/RAA and 85% with betablockers. Thirty-one patients (15.7%) had perm-AF. The C34T variant was present in 54 patients (27.4%). Patients with and without perm-AF did not differ except for a greater prevalence of ischemic etiology and

higher tobacco use in patients without perm-AF. The prevalence of C34T was significantly higher in patients with perm-AF (45.2% vs 24.1% in no perm-AF patients, p=0.016). Multivariable logistic regression analysis adjusting for age, sex, EF, treatment and classical factors associated with a worse outcome in CHF and AF confirmed that age (HR 1.05 [1.01–1.10]) and C34T (HR 2.62 [1.14–6.02]) were the only variables independently associated with perm-AF.
Conclusions: C34T variant in AMPD1 was independently associated with the presence of perm-AF in a population of HF-patients. Impaired cardiomyocyte energetics and adenosine accumulation could be involved in AF promotion in patients with the C34T variant.

P6188 | BEDSIDE
Increased platelet toll- like receptor- 2 and 4 expression in atrial fibrillation

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Background: Inflammation plays a major role in atrial fibrillation (AF) pathogenesis. Accumulating evidence suggest that platelets are of the immune cells involved in this process. Platelet responses, such as activation and aggregation, have been shown to be mediated by the Toll-like receptor (TLR)-2 and 4. However, platelet function mediated by TLR-2 and 4 have not been evaluated in AF patients, yet.
Purpose: In this study, we aim to compare platelet Toll-like receptor expression in patients with atrial fibrillation and sinus rhythm.
Methods: 30 patients with non- valvular AF and 31 healthy patients in sinus rhythm referred for routine check- up were included. Platelet TLR-2 and 4 expression were evaluated by flow cytometric analysis in peripheral venous blood samples.
Results: 61 subjects (55.7% male, 50.2±11.1 years) were included in the study. Platelet TLR-2 expression was higher in patients with AF when compared to those in sinus rhythm [20 (10- 64) vs. 4 (1–21)%, p<0.001]. Patients with AF also had higher expression of TLR-4 when compared to those with sinus rhythm [19 (8–65) vs. 4 (1–22)%, p<0.001] (Figure).

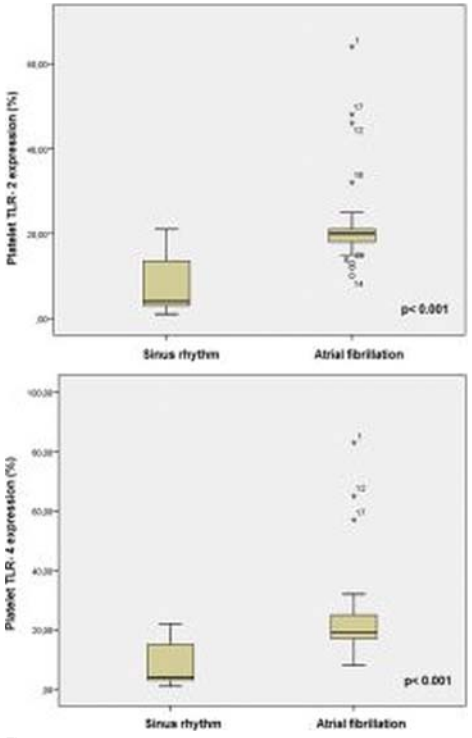

Figure 1

Conclusions: Our study shows that there is enhanced expression of the Toll-like receptor- 2 and 4 on platelets in atrial fibrillation. Demonstrating whether the increased biological platelet activity via the TLRs is responsible for initiation and/or maintenance of AF or thrombogenesis merit further studies.

P6189 | BENCH
Novel HSP-inducing compounds restoring cardiomyocyte function in atrial fibrillation

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Background: Atrial Fibrillation (AF) is the most common clinical tachyarrhythmia associated with significant morbidity and mortality. AF is a persistent disease, caused by a progressive, often age-related, derailment of proteostasis resulting in structural remodeling and contractile dysfunction of cardiomyocytes. It has been widely acknowledged that the progressive nature of the disease hampers the effective functional conversion to sinus rhythm in patients and explains the limited efficacy of current drug therapies. Previously, we identified that inducers of heat shock proteins (HSPs), such as geranylgeranylacetone (GGA) by inducing Heat Shock Proteins (HSPs) expression, suppresses derailment of proteostasis and remodeling of cardiomyocytes. As a result, GGA attenuates the AF substrate in cellular, Drosophila melanogaster and animal experimental models. Clinical application of GGA is however hampered by the high dosage needed, because of its high LogP value. Therefore, the aim of the current study was to identify novel HSP-inducing compounds, which protect against AF remodeling.
Methods and results: We synthesized 83 GGA-derivatives and explored their action (at 10μM) in HL-1 cardiomyocytes pretreated with a mild heat shock to activate heat shock factor-1 (HSF-1) (43°C 10 min, 10 min recovery 37°C). We identified 30 GGA-derivatives, that significantly induced HSP70 expression, and other HSF-1 related HSPs, including HSP25, HSP90, HSP40, but not Grp78 (HSPA5, not HSF-1 related). The magnitude of induction was comparable or higher compared to GGA. Next, HL-1 cardiomyocytes were pretreated with the most potent HSP70-inducing GGA-derivatives (n=13) for 8 hrs, followed by 8 hrs tachypacing (5 Hz) or normal pacing (1 Hz) and contractile function was determined by measuring calcium transients (CaT). Tachypacing significantly reduced the amplitude of CaT, and 7 GGA-derivatives revealed a significant protective effect against CaT loss, which was improved or comparable to GGA.
Conclusion: We identified novel GGA derivatives with improved HSP-inducing and cardioprotective properties compared to GGA. Ultimately, these HSP-inducing compounds may prevent expansion of the structural remodeling during AF, resulting in improved outcome of cardioversion and/or delay in progression towards permanent AF.
Acknowledgement/Funding: Dutch Heart Foundation (2013T096, 2013T144), LSH-Impulse (40-43100-98-008)

ANTICOAGULATION AND ATRIAL FIBRILLATION I

P6190 | BEDSIDE
Mediterranean diet does not affect anticoagulation quality in non-valvular atrial fibrillation

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Purpose: It is still unclear if atrial fibrillation patients on treatment with oral vitamin K antagonists must follow a diet poor in fruits and vegetables, which are rich of vitamin K, to avoid interference with anticoagulation. Aim of the study was to assess if Mediterranean diet, which is rich in fruit and vegetables, affects the anticoagulation stability in patients with AF.
Methods: Prospective, observational single-center cohort study including 553 non-valvular atrial fibrillation patients on treatment with oral vitamin K antagonists. Adherence to Mediterranean diet was evaluated with a validated nine-items dietary questionnaire. Anticoagulation control was assessed by time in therapeutic range.
Results: Mean follow-up was 32.8±20.3 months. Mean number of INR controls for each patient was 70.0±41.4; mean days between two controls were 18.9±7.1; 38730 blood samples were analyzed. In the whole cohort mean time in therapeutic range was 65.5±17.8% and mean Mediterranean score was 5.19±1.6. No difference of time in therapeutic range was found in patients with low (<5) and high (>5) adherence (65.3±17.6 vs. 65.7±18.2 p=0.790) or comparing patients from zero (no adherence) to nine (maximum adherence) (p=0.345). No correlation between adherence and time in therapeutic range was found (R=0.056, p=0.185). Weekly amount of vitamin K anticoagulants needed to achieve therapeutic range did not differ between patients with low and high adherence to Mediterranean diet.
Conclusions: Mediterranean diet does not interfere with time in therapeutic range and may be advised for patients with atrial fibrillation on treatment with oral vitamin K antagonists.

P6191 | BEDSIDE
Economic analysis of rivaroxaban and vitamin K antagonists in cardioversion for atrial fibrilation in Spain

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Background: Restoration of sinus rhythm in atrial fibrillation (AF) may be achieved by electrical cardioversion (ECV). Safe ECV requires therapeutic anti-

coagulation before and after the procedure to minimise the risk of embolic stroke. Vitamin K antagonists (VKA) have been the oral anticoagulants of choice for many years, but warfarin or acenocoumarol pharmacological effects are unpredictable and have a narrow therapeutic window. As a result ECV may be cancelled due to inadequate INR levels in the previous month. ECV cancellations lead to treatment delays and ECV waiting list at an increased hospital costs. The objective was to determine the frequency and cost of ECV cancellations due to inadequate anticoagulation in Spain.

Methods: Cost analysis and budget impact analysis were performed, from the Spanish National Health Service (NHS) perspective. Were considered as costs of ECV cancellation the day hospital cost and the procedure cost itself. The unit costs and population data were obtained from Spanish sources. ECV cancellation rates with rivaroxaban (0.2%) and VKA (44.2%) were obtained from the clinical trial X-VeRT. Monte-Carlo simulations (one simulation per patient of a hypothetical cohort of 1,000 patients) were developed to simulate the healthcare costs avoided with rivaroxaban versus VKA, simulating the effect of changes in different parameters to describe real-life distributions.

Results: The cost of a cancellation of cardioversion was estimated at €256.44 (95% CI €76.55 to €576.15). Considering that approximately 100% of the ECV are currently performed with VKA, 70% of AF are non-valvular AF and that all of these could be done with rivaroxaban, the annual budget saving for the NHS would be €292,124 (95% CI €88,155 to €663,476).

Conclusions: The cancellation rate of ECV is high and is costly with VKA. Replacing VKA with rivaroxaban with a predictable anticoagulation effect appears to be useful and cost saving.

Acknowledgement/Funding: Bayer HealthCare

P6192 | BEDSIDE

Patient profile of oral anticoagulation (OAC) use in people with non-valvular atrial fibrillation (NVAF): Findings from REACT-AF 2 study in UK primary care data

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Background: Atrial fibrillation (AF) is the most common arrhythmia, affecting more than 4.5 million people in Europe, currently affecting approximately 2% of the UK population. Owing to recent developments in OAC treatments, there is a need to generate real-world evidence on patients prescribed OACs for AF.

Purpose: To describe the characteristics of patients with NVAF who are newly prescribed OACs in routine clinical practice in the UK.

Methods: This was a retrospective cohort study of patients with NVAF who were newly prescribed OAC treatment (apixaban, rivaroxaban, dabigatran and vitamin K antagonists (VKAs)) from 1st Dec 2012 to 31st Oct 2014 using UK primary care data from CPRD database. Newly prescribed OAC therapy was defined as initiation of OAC treatment during the study period and having had no prior prescriptions of the same OAC. Demographic and clinical characteristics (HAS-BLED score and CHA2DS2-VASc score) were examined at the starting date of the new OAC (index date) in the overall cohort and within each cohort defined by the OAC treatment.

Results: In total, 16,067 patients were included in the study. 94.8% of patients received only one newly prescribed OAC therapy during the study period, of those 5.6% were treated with apixaban, 8.5% with dabigatran, 18.7% with rivaroxaban and 67.2% with VKA. 55.2% of patients were males. The mean age of the total cohort was 74.6 years. The distribution of age, previous OAC status, HAS-BLED, and CHA2DS2-VASc by OAC treatment groups are reported in table 1 below.

Table 1. Distribution of demographics and clinical characteristics at index date

OAC therapy	Age >70	Previous OAC	HAS-BLED score >3	CHA2DS2-VASc score >2
Apixaban (N=1,023)	72.6%	47.1%	50.1%	89.3%
Rivaroxaban (N=3,165)	75.6%	49.8%	50.1%	89.2%
Dabigatran (N=1,555)	68.0%	52.3%	43.0%	83.7%
VKA (N=10,324)	70.6%	1.0%	41.7%	86.9%
Total cohort (N=16,067)	71.4%	18.5%	44.0%	87.2%

Conclusion: NVAF patients newly prescribed an OAC in the UK were predominantly males, over 70 years old. Overall, most patients had a high risk of stroke. The proportion of patients with high bleeding risk was slightly lower in those prescribed VKA compared to the other OACs.

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P6193

P6194 | BEDSIDE

CCP survey about management of thromboembolic events in atrial fibrillation prevention

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Pourpose and methods: To evaluate knowledge and application of 2012 ESC Atrial Fibrillation (AF) guidelines, we sent a questionnaire to 50840 cardiologists, subscribers of the CCP E-Journal, with 15 questions concerning anticoagulation management.

Results: The responders were 2428 (4.7% of total), 70.3% male, 51.8% from 30 to 50 years old, 70.3% from Europe, 56.1% working in hospital and 22.6% in out-of-hospital practice. 91.9% declare to use regularly the CHA2DS2-Vasc Score. Of the physicians not using the score 35.2% has difficulties in remembering it, and 23.1% lacks of knowledge. CHADS score was still used from 28.1%. HAS-BLED Score is not beeing used by 24.9% of the responders, mainly (35.4%) due to memory difficulties, or to lack of knowledge (22.8%). In patients with concomitant AF and stable CAD, 33.8% of physicians uses warfarin, 29.9% NOACs, 20.3% ASA and warfarin, 13.1% ASA and NOACs. 30.4% of physicians thinks anticoagulation compatible with an age >90 years, but 14.8% believe 75 years the highest age compatible with OAC. The majority of responders (37.7%) uses NOACs as first line treatment, and 30.5% after VKA management problems. Patients wish is the reason for NOACs choiche for 21.9% of responders. 6.9% of responders is not using NOACs at all, mainly due to reimbursment problems in his country (31.5%) or lack of experience with this drugs (25.1%). 61.7% of responders declares to know and apply or to know and apply partially (35.9%) the 2012 ESC Guidelines on AF.

Conclusions: Many of the results of the questionnaire are quite satisfying. A large percentage of responders is using the CHA2DS2-Vasc Score. A good percentage of responders thinks anticoagulation compatible with very old ages, while only 14.8% consider the highest age 75 years. Realtively few responders don't use NOACs, mainly due to lack of reimbursement of their NHSs. Finally a very large percentage knows the guidelines and applies them, at least partially. On the other hand about one fourth doesn't use the HAS-BLED Score. The answer concerning the use of antithrombotic drugs in stable CAD is difficult to analize: the choice of VKA and NOACs is adequate, while the association chosen by one third of responders of ASA and VKA or ASA and NOACS in stable conditions is not indicated in the guidelines. Our results indicate that 2012 AF ESC guidelines are accepted and known by the medical community. This is encouraging, however there is still a large room for improvement.

P6195 | BEDSIDE
Effect of renal function on the cost-effectiveness of high-dose edoxaban compared to adjusted-dose warfarin for stroke prevention in non-valvular atrial fibrillation patients

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Background: Post-hoc analysis suggests high-dose edoxaban may provide inferior anticoagulation to adjusted-dose warfarin in non-valvular atrial fibrillation (NVAF) patients with good renal function. To date, no cost-effectiveness analysis of edoxaban has taken these data into account.
Purpose: To assess the cost-effectiveness of high-dose edoxaban versus adjusted-dose warfarin for the prevention of stroke in patients with NVAF at differing categories of creatinine clearance (CrCl).
Methods: Our Markov model compared the cost-effectiveness of high-dose edoxaban (60 mg once daily, 30 mg once daily in patients with a CrCl≤50 mL/min) and adjusted-dose warfarin (target international normalized ratio (INR) range of 2.0–3.0) at CrCls of ≥80 mL/min, >50–<80 mL/min and CrCl 30–50 mL/min. The model was performed from a United States (US) societal perspective; and assumed NVAF patients initiated therapy at 70 years of age, had a moderate-to-high risk for ischemic stroke (mean CHADS2 of 3) and no contraindications to anticoagulation. Data sources included regulatory agency subgroup analyses of the Edoxaban versus Warfarin in Patients with Atrial Fibrillation (ENGAGE-AF) trial and other published anticoagulation studies. Outcome measures included lifetime costs (direct and indirect) in 2014 US dollars, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs). The robustness of our model's conclusions were tested using Monte Carlo simulations (MCS).
Results: High-dose edoxaban was found to be an economically dominant alternative to adjusted-dose warfarin in NVAF patients with a CrCl<80 mL/min (Table). In patients with a CrCl≥80 mL/min, warfarin was the dominant strategy. Monte Carlo simulation suggested these conclusions were robust to uncertainty in included inputs.
Conclusions: Our Markov model suggests high-dose edoxaban is a dominant economic strategy when compared to adjusted-dose warfarin for the prevention of stroke in patients with NVAF, a moderate-to-high risk of stroke and a CrCl<80 mL/min.

P6196 | BEDSIDE
Validation of the SAMe-TT2R2 score in a nationwide, unselected population of nonvalvular atrial fibrillation patients on vitamin K antagonists

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Introduction: The SAMe-TT2R2 score (sex female, age <60 years, medical history [more than two comorbidities], treatment [interacting drugs, eg, amiodarone for rhythm control], tobacco use [doubled], race non-caucasian [doubled]) has been proposed to identify patients with nonvalvular atrial fibrillation (AF) who maintain a high average time in therapeutic range (TTR) on vitamin K antagonists treatment (VKA). This score has been validated in several studies, either monocentric or including selected populations in a specialized setting. Our objective was to validate this score in a nationwide, unselected cohort of AF patients, and to quantify the ability of the score in predicting a good anticoagulation control.
Methods: The CALIFA study ("Quality of Anticoagulation and associated comorbidities in patients with non-valvular atrial fibrillation in the cardiology outpatient clinic", in Spanish: "Calidad de la Anticoagulación y comorbilidades asociadas en pacientes con Fibrilación Auricular no valvular en consultas de cardiología") was designed by the Research Agency of the Spanish Society of Cardiology to analyze the prevalence of poor control of anticoagulation with VKA in patients with non valvular AF in Spain, as well as potential factors associated with this poor control. It is a national, multicenter, observational, cross-sectional and retrospective analysis of consecutive cases in non valvular AF patients receiving VKA. From November 2013 to March 2014 we included in this study the first 10 patients with AF on VKA consecutively seen in 120 outpatient cardiology clinics in Spain. The SAMe-TT2R2 score was calculated for each patient and TTR in the preceding 6 months was estimated by Rosendaal method.
Results: 1056 patients were recruited (mean age 73.6±9.8 years, 42% female). Mean value of TTR was 63.8±25.9% (median 66.8%, interquartile rank 45.6%-85.4%). We found a progressive decline in mean TTR from a score of 0 (67.5%±24.6%) to ≥4 (52.7±28.7%, p<0.01). The score was able to discriminate which patients had a good anticoagulation control (TTR ≥65%) with a C-statistic of 0.57 (95% CI 0.53–0.60, p<0.0005). A SAMe-TT2R2 score of 0–1 was associated with a good anticoagulation control with a sensitivity, specificity, positive and negative predictive values of 64%, 48%, 58% and 54%, respectively; and the odds ratio of having a TTR<65% if the score was ≥2 was 1.64 (CI95% 1.33–1.95, p<0.001).
Conclusion: In this nationwide, non selected population with AF on VKA, the SAMe-TT2R2 score had a significant, although moderate, ability to identify patients with a good anticoagulation control.
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P6197 | BEDSIDE
Clinical and demographic characteristics according to dosage among non-valvular atrial fibrillation patients newly initiated on novel oral anticoagulants

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Background: Apixaban, dabigatran, and rivaroxaban are Non-Vitamin K Oral Anticoagulants (NOACs) approved in the United States for stroke prevention in non-valvular atrial fibrillation (NVAF). Each drug has two approved dosages-(1) apixaban 5 mg and 2.5 mg twice a day (BID), the latter if any two of the following three conditions are present: age ≥80, body weight ≤60, serum creatinine ≥1.5mg/dL; 2) dabigatran 150 mg and 75 mg BID, the latter if CrCl 15–30 mL/min; 3) rivaroxaban 20 mg and 15 mg once a day (OD) with an evening meal, the latter if CrCl ≤50 mL/min).
Objective: To describe the baseline clinical and demographic characteristics of NVAF patients newly initiated on apixaban, rivaroxaban, and dabigatran by dose in the real world setting.
Methods: Using Humedica de-identified Electronic Health Records (EHR) data, adult NVAF patients with ≥1 prescription for a NOAC between January 1, 2013 and June 30, 2014 were identified. Index date was the date of the first observed NOAC prescription among treatment naïve AF patients following a 12-month baseline period. Strength of the index NOAC was used as proxy for dose.
Results: A total of 10,885 patients were identified (2,038 on apixaban; 6,407 on rivaroxaban; 2,440 on dabigatran). The majority of patients were on the "standard dose" for all the NOACs (apixaban 5 mg, rivaroxaban 20 mg, and dabigatran 150 mg) as shown in Table 1. Differences in patient demographic and clinical characteristics across different NOACs are described in Table 1.
Conclusion: For each NOAC, the majority of patients received the standard dose, with the reduced dose strategy more commonly prescribed to patients who were elderly, had renal disease, or had greater CHA2DS2-VASc or HAS-BLED scores.
Acknowledgement/Funding: Funded by Pfizer, Inc.

Abstract P6195 – Table 1

Comparators	CrCl, mL/min	% of All Patients in ENGAGE-AF	Costs, $	QALYs	Incremental Costs, $	Incremental QALYs	ICER, $/QALY	% of 10,000 MCS Iterations Edoxaban ICER <$50,000/QALY
Warfarin	30–50	19.0	123,516	10.11	–16,993	0.20	Edoxaban Dominant	73
Edoxaban			106,523	10.31				
Warfarin	>50–<80	43.5	123,516	10.11	–33,535	0.51	Edoxaban Dominant	>99
Edoxaban			89,981	10.62				
Warfarin	≥80	37.5	123,516	10.11	3,022	–0.14	Warfarin Dominant	14
Edoxaban			126,538	9.97				

Abstract P6197 – Table 1. Baseline characteristics by dose

	Apixaban (n=2,038)			Rivaroxaban (n=6,407)				Dabigatran (n=2,440)		
Characteristic	2.5 mg (11.7%)	5 mg (53.2%)	Missing (35.1%)	10 mg (7.4%)	15 mg (11.8%)	20 mg (49.9%)	Missing (30.9%)	75 mg (14.0%)	150 mg (70.6%)	Missing (15.4%)
Age, mean ± SD	79.6±7.4	69.4±9.9	70.2±11.1	72.3±10.5	77.1±8.1	67.7±10.8	69.6±11.2	76.6±8.5	69.5±10.0	69.5±11.4
Sex: female	63.0%	43.5%	44.8%	51.7%	56.0%	41.1%	44.8%	57.0%	40.8%	40.4%
Renal disease	18.5%	6.3%	8.2%	9.1%	21.1%	5.6%	7.9%	16.7%	6.4%	5.3%
CHA_2DS_2-VASc Score, mean±SD	3.8±1.4	2.6±1.5	2.8±1.7	3.0±1.6	3.6±1.5	2.4±1.5	2.7±1.6	3.6±1.5	2.7±1.6	2.4±1.5
HAS-BLED score, mean ± SD	2.1±1.0	1.6±1.0	1.7±1.0	1.8±1.0	2.1±1.0	1.5±1.0	1.7±1.0	1.9±1.0	1.6±0.9	1.4±1.0

Note: All comparisons by dose group (excluding missing dose) within the three cohorts were significant at p<0.0001.

P6198 | BEDSIDE
Guideline adherence to anticoagulation for atrial fibrillation: a study in indigenous and non-indigenous Australians

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Background: Atrial fibrillation (AF) is a leading cause of preventable stroke in Australia. Given anticoagulation therapy can significantly reduce this stroke risk, we sought to characterise anticoagulation use in Indigenous and non-Indigenous Australians with AF.
Methods: Administrative, clinical and prescription data from patients with AF were linked. Anticoagulation use was characterised according to guideline-recommended risk scores and Indigenous status.
Results: 19,613 individuals with AF were studied. Despite a greater prevalence of other risk factors, Indigenous Australians were significantly younger than their non-Indigenous counterparts ($p<0.001$) and thus had lower CHADS2- (1.19±0.32 vs 1.99±0.47, $p<0.001$) and CHA2DS2VASc-scores (1.47±0.03 vs 2.82±0.08, $p<0.001$). Correspondingly, the percentage of Indigenous Australians with CHADS2≥2 (39.6% vs 44.1%, $p<0.001$) and CHA2DS2VASc-scores≥2 (62.9% vs 78.8%, $p<0.001$) was also lower. Indigenous Australians, however, had greater rates of under- and over-anticoagulation. Overall, 72.1% and 68.9% of Indigenous and non-Indigenous Australians with CHADS2 scores≥2, and 76.3% and 71.3% with CHA2DS2VASc scores≥2, were under-anticoagulated. Similarly, 27.4% and 24.1% of Indigenous and non-Indigenous Australians with CHADS2 scores=0, and 24.0% and 16.7% with CHA2DS2VASc-scores=0, were over-anticoagulated. In multivariate analyses, Indigenous Australians were more likely to receive under- or over-anticoagulation according to CHADS2- or CHA2DS2VASc-score ($p=0.045$ and $p<0.001$ respectively).
Conclusion: Anticoagulation for AF is frequently not prescribed in accordance with guideline recommendations. Under-anticoagulation in those at high stroke risk, and over-anticoagulation in those at low risk, is common and more likely in Indigenous patients with AF. Improving adherence to guideline recommendations for anticoagulation in AF may reduce both ischaemic and haemorrhagic strokes in Indigenous and non-Indigenous Australians.

P6199 | SPOTLIGHT
Inadequacy of oral anticoagulation is a crucial factor for development of dementia in patients with permanent atrial fibrillation

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Purpose: The aim of the present prospective study was to identify risk factors for significant dementia in patients with permanent atrial fibrillation (AF)
Methods: We enrolled 212 patients with at least 1 year of permanent AF referred to our outpatients clinic from September 2013 to May 2014. Exclusion criteria was the presence neurological disease, pregnancy, bleeding disorders, neoplasm. Presence of cardiovascular risk factors (hypertension, diabetes mellitus type II, dyslipidemia, smoking status) and previous cardiovascular events (ischemic heart disease, stroke, and heart failure) were also collected
All patients were submitted to Short Portable Mental Status Questionnaire (SPMSQ) (score from 0 to 10): significant dementia was defined as score >5.
Results: Significant dementia was higher in patients on antiplatelet (AT) therapy (n=25/212) than warfarin (n=187/212). In entire cohort, risk factors at multivariate analysis were: AT therapy (OR=3.4; 95CI 1.4–8.5; p=0,008), CHADsVASC score (1.5; 95CI 1.2–2.1; p=0,003), age (1.08; 95 CI 1.03–1.14; p=0.003). In patients taking warfarin, time in therapeutic range (TTR) was predictive for significant dementia (AUC 0.85±0.03) with following cut-offs of TTR: ≤50% (sensitivity 63%, specificity 93%); ≤60% (sensitivity 90%, specificity 62%); ≤70% (sensitivity 93%, specificity 34%). In order to evaluate the influence of age and duration of atrial fibrillation in warfarin patients, this group was split into 2 subgroups: age≤75 years (45 cases), where the length of disease has not been found out as risk factor. In the remaining 142 patients older than 75 years, the duration of AF was protective for dementia (OR=0.88, 0.83–0.94, $p<0.001$), probably due to better TTR. Infact, among 142 patients on warfarin >75 years, 60 with dementia showed lower TTR than 82 without dementia: 45±15% vs 64±14%, $p<0.002$; in this subgroup, correlation between TTR and duration of AF was significant ($r=0.561$; $p<0.001$).
Conclusion: In patients with AF, oral anticoagulation with a high TTR might be crucial to reduce the likelihood to develop significant dementia.

P6200 | BEDSIDE
Hemostasis POC tests are affected by dabigatran, rivaroxaban and apixaban treatments in patients with atrial fibrillation

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Background: The rapid monitoring of anticoagulant effect of direct oral anticoagulants (DOA) -dabigatran, rivaroxaban, apixaban- might be required in specific conditions to prevent the risk of bleedings or thrombosis. As clinical application of DOAs is gradually growing, it might be noteworthy to know their influence on hemostasis Point-of-Care Testing (POCT).
Purpose: This study was aimed to assess the DOA effect on the POC parameters in patients with atrial fibrillation.
Methods: Whole blood was taken just before (TTrough) and 3 hrs after the administration (Tmax) (TTrough: 110 -dabigatran-, 57 -rivaroxaban- and 30 -apixaban-patients; Tmax, 62, 18 and 18 patients). ACT, aPTT, PT, thromboelastometry and platelet function analysis were performed. Dabigatran and rivaroxaban plasma levels were measured with Hemoclot technique and Biophen DXaI, respectively.
Results: At TTrough, patients showing normal clotting times were: ACT, 2/110 (dabigatran), 9/57 (rivaroxaban) 7/30 (apixaban); aPTT, 5/57 (rivaroxaban), 5/30 (apixaban). Rivaroxaban or apixaban patients showed prolonged PT. At Tmax, all patients showed ACT, aPTT and PT significantly prolonged ($p<0.001$), except for 3/18 (ACT) and 5/18 (aPTT) patients on apixaban. Dynamic parameters of ROTEM tests (EXTEM, INTEM, ECATEM) were significantly prolonged ($p<0.001$); no change was observed in PFA-200-CTs. Significant relationships were observed between plasma drug concentration and clotting parameters (at least, $p=0.01$).
Conclusions: DOAs exhibit distinct effects on clotting and platelet function POCT. Use of clotting POCT might provide information in emergency clinical setting to evaluate the impact of these drugs on clotting system, when rapid medical decision should be taken.

P6201 | BEDSIDE
Dabigatran and rivaroxaban have different risk factors for bleeding in atrial fibrillation patients

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Background: It is unclear whether dabigatran and rivaroxaban have different risk factors for bleeding.
Purpose: To compare the risk factors for bleeding of dabigatran and rivaroxaban.
Methods: We enrolled consecutive patients with atrial fibrillation (AF) who received dabigatran or rivaroxaban. Selection of dabigatran or rivaroxaban depended on each physician's discretion. In this study, bleeding was defined as a reduction in the hemoglobin≥2.0 g/dl. We compared the risk factors for bleeding including age, gender, incidence of customary dose and antiplatelet therapy, CHADS2 and HAS-BLED scores, body weight, creatinine clearance (CLCr), prothrombin time (PT) and activated partial thromboplastin time between (APTT) between patients with and without bleeding in dagibatran and rivaroxaban groups, respectively. Uni and multivariate analyses were performed to determine the risk factors of bleeding.
Results: The dabigatran group consisted of 177 patients and the rivaroxaban group consisted of 179 patients. Multivariate analysis revealed that CLCr was the only independent factor correlated with bleeding in the dabigatran group while in the rivaroxaban group, the CHADS2 score and use of antiplatelet therapy were the independent factors correlating with bleeding (Table).
Conclusions: To avoid bleeding, dabigatran should be prescribed with caution in patients with lower CLCr and rivaroxaban should be prescribed with caution in patients with higher CHADS2 scores and patients using antiplatelet therapy.

Abstract P6201 – Risk factors for bleeding

	Dabigatran group				Rivaroxaban group			
	Bleeding (n=28)	No bleeding (n=149)	Univariate analysis (p value)	Multivariate analysis (p value)	Bleeding (n=27)	No bleeding (n=152)	Univariate analysis (p value)	Multivariate analysis (p value)
Age	72.2±12.4	71.4±9.5	0.732		74.6±9.0	72.8±9.1	0.336	
Male (%)	46.4	57.8	0.051		18.5	63.2	>0.001	0.334
Customary dose (%)	46.4	38.3	0.528		48.1	63.8	0.137	
CHADS2	2.1±1.0	1.6±1.2	0.045	0.345	3.0±1.7	2.0±1.3	0.008	0.023
HAS-BLED	1.9±12	1.6±1.12	0.150		2.6±1.2	2.1±1.4	0.091	
Body weight (kg)	56.6±15.0	61.4±13.5	0.138		55.7±14.1	61.4±12.1	0.091	
CLCr (ml/min)	64.7±15.0	76.6±24.1	0.024	0.031	64.7±15.0	76.6±24.1	0.024	0.417
Antiplatelet therapy (%)	21.4	8.1	0.043	0.133	40.7	11.2	>0.001	0.005
PT	60.4±13.9	60.5±12.6	0.977		71.6±20.8	70.1±19.2	0.754	
APTT	10.2	14.0	0.330		33.3±7.1	34.2±8.1	0.756	

ANTICOAGULATION AND ATRIAL FIBRILLATION II

P6202 | BEDSIDE

Management of anticoagulation in patients with non-valvular atrial fibrillation in general practice in UK: Evolution and characteristics of patients not treated with antithrombotic therapy

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Background: Prior to the 2012 ESC guidance, the CHADS2 score was recommended to stratify stroke risk in patients with non-valvular atrial fibrillation (NVAF). Emerging evidence suggests that the CHADS2 score does not reliably identify patients at truly low risk. Recent guidelines recommend the CHA2DS2-VASc score, which includes additional stroke risk factors (age 65 to 74, arterial disease and female sex) and better identifies "truly low-risk" patients with NVAF.
Aim: Describe changes over time from 2012–15 in the proportion and characteristics of NVAF patients not treated with oral antithrombotic therapy (OAT) for thromboembolic prophylaxis (TEP) in the UK.
Methods: We undertook four cross-sectional analyses on 1 April of each year from 2012–15 (index dates), using the UK's Clinical Practice Research Datalink (CPRD). Each analysis included all patients with NVAF with a CHA2DS2-VASc ≥2. We defined oral anticoagulant (OAC) and antiplatelet agent (APA) treatment by GP prescriptions or INR measurements in the 90 days before index date and identified co-morbidities from GP records (Read codes). We calculated the proportion (with 95% confidence intervals) of patients receiving OAC (± APA), APA alone, or no OAT and evaluated the trend over time in the proportion of patients with no OAT using a mixed regression model. Data are presented for the years 2012–14. Results for 2015 will be available for the ESC congress.
Results: We identified 67,327, 66,364 and 62,840 NVAF patients eligible for anticoagulation on the 2012, 2013 and 2014 index dates, respectively. A decrease was observed between 2012–14 in the proportion of NVAF patients not treated with OAC (49.8, 46.8, 42.5%), due to a downward trend in the proportion of patients on APA alone (34.2, 31.2, 27.7%). However, similar proportions of patients remained without OAT (15.6, 15.7, 14.8%). In 2012, patients with no OAT included more patients under 65 compared with OAC-treated patients (15 vs 6.7%), more women (54.9 vs 43.3%), and more patients with CHA2DS2-VASc score of 2 (24 vs 10.6%). 65.6% of these patients had never been treated with OAC. Similar patterns were observed in 2013 and 2014.
Conclusion: Despite the ESC 2012 guidance and the introduction of novel OACs in the UK, the proportion of patients with no OAT did not change between April 2012 and April 2014 among NVAF patients eligible for anticoagulation. Lack of TEP was more frequent in patients under 65, women and patients with CHA2DS2-VASc of 2. Further analysis (1 April 2015) will examine early changes following the 2014 NICE guidance.
Acknowledgement/Funding: This study was funded by Bristol-Myers Squibb Pharmaceuticals Ltd

P6203 | BEDSIDE

Safety and efficacy of the direct factor Xa inhibitor rivaroxaban for peri-procedural anticoagulation in catheter ablation of atrial fibrillation: A systematic review and meta-analysis

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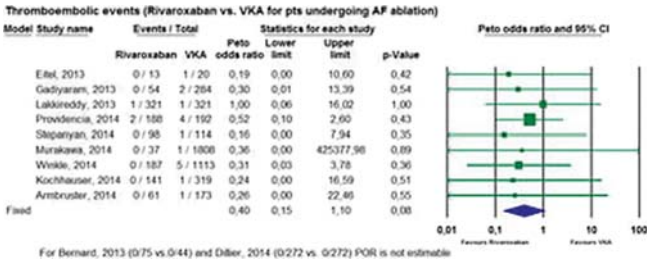
Introduction: The novel oral anticoagulant rivaroxaban is being used more frequently in patients (pts) undergoing catheter ablation of atrial fibrillation (AF). For rare outcomes such as procedure-related thromboembolic or bleeding events, a meta-analysis of the literature may be the best way to obtain reliable evidence on peri-procedural safety and efficacy of rivaroxaban until proper randomized clinical trials become available.
Purpose: To provide detailed analysis of the currently available study reports on the safety and efficacy of peri-procedural rivaroxaban in pts undergoing AF ablation.
Methods: We performed a systematic search (2004–2014) of the English literature for studies comparing peri-procedural rivaroxaban therapy with vitamin K antagonists (VKAs) reporting detailed data on bleeding and/or thromboembolic complications. The Peto Odds Ratio (POR) was used to pool data into a fixed-effect meta-analysis.
Results: A total of 6,234 pts undergoing catheter ablation were included in 12 observational studies of whom 1,487 were receiving rivaroxaban and 4,747 VKAs. A total of 59 minor bleeding events were reported in 1,233 pts (4.79%) in the rivaroxaban group and in 133 of 3,330 pts (3.99%) in the VKA group (POR 0.77, 95% confidence interval (CI), 0.55 to 1.07, p=0.12, I^2=0%). Major bleeding events occurred in 22 of 1,487 cases (1.48%) in the rivaroxaban and 87 of 4,747 (1.83%) in the VKA group (POR 0.77, 95% CI, 0.47 to 1.28, p=0.31, I^2=0%) The risk of thrombo-embolic events trended to be lower in the rivaroxaban group (3 vs. 17, POR 0.40, 95% CI, 0.15 to 1.10, p=0.08, I^2=0%).
Conclusion: The risk of rivaroxaban-associated bleeds and thromboembolism is similar to that of VKA in pts undergoing AF ablation. Hence, rivaroxaban may be an alternative to VKA in this clinical scenario.



P6204 | BEDSIDE

Dabigatran plasma concentration measurement in patients with atrial fibrillation: is it helpful for choosing the optimal dose?

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Purpose: According to current ESC guidelines for the treatment of patients with atrial fibrillation, the standard dose of dabigatran, if this oral anticoagulant is chosen, should be 150 mg bd, with the lower 110 mg bd dose considered for patients with certain clinical characteristics, like age >80, GFR 30–49 ml/min or high bleeding risk. In our country, due to regulatory approval issues, the 110 mg dose was available well before the 150 mg dose. Therefore, once the higher dose became available, a clinical decision whether to increase the dose or not, in patients already on the low dose, had to be made. The aim of our study was to investigate whether by measuring dabigatran plasma concentration we could identify patients who should or should not switch to the recommended 150 mg dose.
Methods: We measured aPTT and dabigatran plasma trough (11.7±1.0 hrs post last dosing) concentration by Hemoclot in 43 consecutive patients receiving 110 mg bd. Group A included 22 patients who had clinical characteristics suitable for the 150 mg bd dose. Group B included 21 patients with at least one clinical characteristic suggesting the lower dose. Plasma levels ≥200 ng/ml were considered high and ≤30 ng/ml were considered low.
Results: There was a good correlation between dabigatran concentration and aPTT (r=0.6, p<0.001). Group A patients in comparison to group B were younger (age 70.4±7.9 vs 78.9±7.8, p=0.001), with non-significantly higher creatinine clearance (80±25 vs 73±18 ml/min, p=0.3), lower CHA2DS2VASc (3±1 vs 4±1, p=0.02) and HASBLED (2±1 vs 3±1, p<0.001) scores. Dabigatran levels in groups A vs B were 84.4±50.1 vs 74.0±48.7 ng/ml (p=0.5). There was significant overlap of values with the 10th and 90th percentile values being 30 and 170 vs 30 and 154 ng/ml, respectively. 11 patients had low levels (4 in group A and 7 in group B) and only 2 patients had high levels (1 in group A and 1 in group B and both receiving amiodarone). An aPTT value ≤40 sec was measured in 9 of the 11 patients (82%) with dabigatran concentrations ≤30 ng/ml as compared to 5 of the 32 patients (16%) with concentrations >30 ng/ml (p<0.001).
Conclusion: Patients receiving dabigatran 110 mg bd can have low drug concentrations. A low aPTT value may identify patients who deserve further drug concentration measurement with a view to increase the dosage at 150 mg bd, if low drug levels are indeed confirmed, even in cases considered eligible for the low dose by clinical characteristics alone.

P6205 | BEDSIDE

Ability of bleeding risk scores for stratification of bleeding events in elderly patients with atrial fibrillation

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Background: In stroke prevention of patients with atrial fibrillation (AF), major bleeding is a main concern which can impact decision for thromboembolic prophylaxis, especially among the elderly. HAS-BLED, HEMORR2HAGES and ATRIA are scores created to evaluate the bleeding risk in AF patients. ESC recommends using HAS-BLED score for all patients whilst geriatrics may prefer using HEMORR2HAGES since it includes relevant items of comorbidities seen in elderly patients. The objective of this study was to estimate and compare predictive ability of these scores in AF patients with a specific attention in the elderly (≥75 years).
Methods: All patients with AF seen in our institution were identified and followed up between 2000–2010 for mortality, stroke and bleeding events. Rate of bleeding events was calculated for the low, moderate and high risk subgroups of patients using the HAS-BLED score and we then compared its predictive value with previously published bleeding risk schemas (HEMORR2HAGES, ATRIA). Hazard ratios were calculated and predictive abilities of the scores as continuous variable

or as categorical variable (low, moderate or high risk) were compared using the c-statistic with 95% CI.
Results: Among 8120 consecutive patients with AF including 46% elderly patients, 791 severe bleeding events were recorded during a follow-up of 877±1052 days. Bleeding occurred more commonly in patients with higher HAS-BLED, HEMORR2HAGES and ATRIA scores. Overall, HAS-BLED significantly had higher c-statistics (0.60, 95% CI 0.59–0.61) than HEMORR2HAGES (0.58, 95% CI 0.57–0.59, p=0.04) and ATRIA (0.58 95% CI 0.57–0.59, p=0.04). In elderly patients, the c-statistic was lower for all 3 scores and was not significantly different between HAS-BLED (0.57, 95% CI 0.55–0.58), HEMORR2HAGES (0.55 95% CI 0.53–0.56, p=0.32) and ATRIA (0.55 95% CI 0.53–0.56, p=0.13).
Conclusion: All 3 scores demonstrated only modest performance in predicting bleeding (c-stats from 0.53 to 0.60) although the HAS-BLED score performed better than the HEMORR2HAGES and ATRIA scores. In addition, all 3 scores showed lower performance in predicting bleeding within elderly population. HAS-BLED and other bleeding risk scores performed equally to predict bleeding events among elderly patients. Given its simplicity but similar performance, the HAS-BLED score may be an attractive alternative to HEMORR2HAGES score for the estimation of bleeding risk in specific elderly population.

P6206 | BEDSIDE
Differences in clinical outcome of patients with paroxysmal and sustained atrial fibrillation under oral anticoagulation therapy - results from the thrombEVAL study

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Background: Oral anticoagulation therapy (OAC) for prophylaxis of stroke is recommended for patients at risk with paroxysmal (PAF) and sustained (SAF; ie, persistent and permanent) atrial fibrillation (AF). It is controversial whether AF patterns translate into differences in clinical outcome under OAC.
Purpose: We compared the outcome in patients with paroxysmal and sustained AF in a regular medical care cohort under OAC.
Methods: ThrombEVAL is an investigator-initiated, prospective, multi-center cohort study (NCT01809015). Data were obtained from clinical visits and computer-assisted personal interviews according to standard operating procedures with quality control. Study monitoring was carried out by an independent institution. Information on study endpoints was validated by medical records and adjudicated by a review committee.
Results: The analysis comprised 541 patients with PAF and 840 patients with SAF. Mean CHADS2 score was 2.3±1.3 for PAF and 2.5±1.3 for SAF patients. Mean follow-up time in both cohorts was 11.6±5.1 and 10.8±4.9 months respectively. There was a significant difference between event rates for net clinical benefit outcome (composite of thromboembolic events, major and clinically-relevant non-major bleeding, death) between both samples with 46 events/100 patient-years (py) for PAF and 104 events/100 py for SAF patients (rate ratio (RR): 0.60, 95% CI 0.42/0.86; p=0.004). Bleeding events, defined as major bleeding or non-major clinically-relevant bleeding, were less frequent in PAF patients (RR: 0.52, 95% CI 0.32/0.82; p=0.004). There was no significant difference for thromboembolic events (RR: 0.57, 95% CI 0.23/1.29; p=0.21). Hospitalizations occurred 19% less often (RR 0.81, 95% CI 0.70/0.92; p=0.002) and all-cause mortality was 37% lower in PAF patients as compared to SAF patients (RR 0.63, 95% CI 0.40/0.95; p=0.028). After adjustment for age, sex, traditional cardiovascular risk factors and comorbidities, Cox regression modelling demonstrated a worse outcome for patients with SAF: hazard ratios were 1.51 (95% CI 1.05/2.18; p=0.028) for net clinical benefit outcome, 1.84 (95% CI 1.16/2.93; p=0.001) for clinically-relevant bleeding, 1.32 (95% CI 0.86/2.02; p=0.21) for all-cause mortality and 1.33 (95% CI 1.09/1.62; p=0.005) for hospitalization.
Conclusions: Patients with sustained AF under oral anticoagulation therapy inherited a worse specific and non-specific clinical outcome in comparison to patients with paroxysmal AF. AF patterns predict clinical outcome under OAC therapy and need to be further investigated for application in risk stratification.
Acknowledgement/Funding: Ministries of Health and Economics, Rhineland-Palatinate, Germany; Federal Ministry of Education and Research, Germany.

P6207 | BEDSIDE
Direct acting oral anticoagulants are more effective than Vitamin-K-antagonists for the resolution of established left atrial thrombi in patients with atrial fibrillation

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Background: Left atrial appendage thrombus formation (LAAT) occurs in a relevant subset of patients with non-valvular atrial fibrillation (AF), despite oral anticoagulation (OAC) with Vitamin K antagonists (VKA), and LAAT is associated with a 5-fold increased risk in stroke. The objective of this study was to assess resolution rates of LA thrombi under anticoagulant therapy with the new direct acting OAC (DOAC) in a patient cohort with therapeutic failure of VKA.
Methods and results: In this prospective monocenter registry 69 patients were identified with LAAT despite VKA treatment and 50 subjects completed follow-up procedures (age 73.2±9.8 years, CHADS2VA2Sc 4.4±1.5, 64% male). The patients had a high prevalence of cardiomyopathy with a reduced mean left ventricular ejection fraction (LVEF) of 42.8±16.4%, including 32% of patients with LVEF $<$35%. Echocardiography confirmed a so called "thrombogenic milieu" in all patients with spontaneous echo contrast grading $>$2 in all cases and reduced LAA peak emptying velocities (22±10cm/s). Mean LAAT width and length was determined with 0.9±0.3 and1.6±0.5cm. In a first step all patients received intensified VKA therapy with targeted INR ranging between 2.5–3.5 for six weeks. In cases with persistent LAAT after this follow-up (FU) period, alternative therapeutic options were discussed with the patient, and if consenting, VKA was switched to DOAC (n=31) with either dabigatran (n=11), rivaroxaban (n=10), or apixaban (n=10). FU was performed after six and 12 weeks under DOAC treatment including transesophageal echocardiography (TEE).Overall VKA showed a poor capability for midterm thrombus resolution after six weeks of intensified anticoagulant treatment. We identified 9 cases (18%) with LAAT disappearance, and one patient experienced massive LAAT expansion (2%). After switching anticoagulant treatment to DOAC, LAAT resolution was observed in 18 out of 31 patients (58%), incuding six patients out of 10, which were treated with rivaroxaban (60%), 7 out of 10 under anticoagulant therapy with dabigatran (70%), and in five out of 10 patients under apixaban (50%). When comparing the absolute LAAT resolution rates of VKA (18%) with DOAC (58%), this difference reached statistical significance ($p<0.0005$). We observed no major bleeding complication during FU in patients treated with either VKA or DOAC.
Conclusion: These preliminary results of a single-centre registry give interesting insights in promising characteristics of all three so far available DOACs. These substances might enable effective anticoagulant treatment of patients with therapeutic failure of VKA therapy.

P6208 | BEDSIDE
Stroke and bleeding risk-associated use of antithrombotic therapies for stroke prevention in atrial fibrillation in routine clinical practice: the BALKAN-AF Survey

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Background: In contrast to other European regions, real-world data on the management of atrial fibrillation (AF) in the Balkan countries are scarce.
Purpose: We report an interim analysis from the Balkan-AF survey addressing the stroke and bleeding risk-associated use of oral anticoagulation (OAC) and antiplatelet drug therapies (APT) for stroke prevention in AF in routine clinical practice.
Methods: A 12-week prospective "snapshot" survey (December 2014-February 2015) of consecutive non-valvular AF patients seen by internal medicine specialists or cardiologists was conducted in Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Montenegro, Romania and Serbia (a region with $\sim$45 million inhabitants). Each country participated with university/non-university hospitals and outpatient clinics in- and outside the capital cities. Data were collected via an electronic case report form.
Results: Of 2080 patients (mean age 69.1±10.8, range 18–96 years), 936 (45.0%) were female. Mean CHA2DS2-VASc and HASBLED scores were 3.4±1.9 and 2.0±1.2, respectively. Overall, OAC was prescribed to 1512 patients (72.6%) and APT to 611 patients (28.4%). Whilst no antihrombotic therapy was advised for 206 patients (9.9%), there were 1263 patients (60.7%) with OAC only, 249 (11.9%) with OAC + APT, 97 (4.7%) with dual APT and 265 patients (12.7%) with single APT.
On univariate analysis, the overall use of OAC was not significantly associated with stroke risk as measured by the CHA2DS2-VASc score (OR 1.00; 95% CI,0.95–1.05, p=0.944), but there was a significant positive association with the risk of bleeding (HASBLED score), OR 1.14;95% CI, 1.04–1.23, p=0.002. Overall

use of APT was significantly associated with the CHA2DS2-VASc (OR 1.12;95% CI,1.11–1.23, p<0.001), but not with the HASBLED (OR 1.07;95% CI,0.99–1.16, p=0.076). With increasing CHA2DS2-VASc score, use of OAC monotherapy was less likely (OR 0.93;95% CI,0.88–0.97, p=0.001), in contrast to dual APT (OR1.21;95% CI,1.08–1.35, p=0.001), with no significant association with the HASBLED score.

Conclusions: Use of antithrombotic therapies for AF-related stroke prevention in daily clinical practice in the Balkan-AF survey was not based on individual patient stroke and bleeding risk scores. Although internal medicine specialists and cardiologists prescribed OAC to 73% of AF patients, better understanding of treatment principles is necessary to improve the management of AF-related stroke risk.

Acknowledgement/Funding: The BALKAN-AF Survey was supported by Pfizer, Bayer and Boehringer Ingelheim.

P6209 | BEDSIDE

Predictors of LAA thrombi in patients with atrial fibrillation and low CHA2DS2-VASc score

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Purpose: In patients with atrial fibrillation (AF), LAA morphology has been suggested to modify thrombogenesis. We tested the hypothesis that LAA thrombi in low-risk patients are associated with LAA characteristics.

Methods: Of 2069 patients who underwent AF ablation, 25 (1.2%) had a prior LA thrombus and a low CHA2DS2-VASc score (≤1). Those patients were matched for the CHA2DS2-VASc criteria with 94 thrombus free patients and CT data were compared. LAA measurements, morphology (Cactus, Chicken-Wing, Windsock, Cauliflower) and takeoff in relation to the respective takeoff of the adjacent pulmonary vein (PV) were determined. The LAA flow and the heart rate (HR) at the presence of the thrombus and after its resolution was compared.

Results: In univariate analysis, patients with prior thrombus had a higher incidence of Non-Chicken-Wing LAA (84% vs. 61%, p=0.03), a tendency for reduced LAA flow (46±18 vs. 54±17 cm/s, p=0.08), higher LAA (9±6 vs. 7±3 ml, p=0.1) and LA volume (138±49 vs. 121±38 ml, p=0.06), while clinical (HR: 76±25 vs. 82±26 bpm, p=0.48) or other LAA characteristics were similar between groups. Logistic regression revealed that LAA volume (OR: 1.2/ml, CI: 1.04–1.37, p=0.01) and Non-Chicken-Wing LAA (OR: 5.99, CI: 1.5–23.3, p=010) were independent predictors of thrombi. Intra-group analysis of the study group revealed that in the presence of a thrombus, tachyarrhythmia (89±29 vs. 76±25 bpm, p=0.03) and reduced LAA flow (34±17 vs. 46±18 cm/s, p=0.015) were more common than after its resolution.

Conclusion: A higher volume and Non-Chicken-Wing LAA predispose to thrombus formation whereas tachyarrhythmia and reduced LAA flow facilitate its perpetuation. These findings may have implications for anticoagulation of AF patients with low CHA2DS2-VASc scores.

P6210 | BEDSIDE

Treatment consistency across levels of baseline renal function with rivaroxaban compared with warfarin: insights from ROCKET AF

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Background: ROCKET AF confirmed the non-inferiority of rivaroxaban vs. warfarin in preventing stroke and systemic embolism (SE) in patients with nonvalvular atrial fibrillation (AF).

Purpose: To evaluate the consistency of treatment effect across a range of baseline renal function in ROCKET AF participants, including those with high creatinine clearance (CrCl).

Methods: ROCKET AF included 14,264 patients with nonvalvular AF randomized to rivaroxaban or dose-adjusted warfarin. The primary endpoint was the composite of stroke or SE. The major safety endpoint was the composite of major bleeding and clinically relevant non-major bleeding. We stratified patients into subgroups based on baseline renal function: CrCl 30–50 mL/min, 50–80 mL/min, and 80 mL/min.

Results: Compared with those with CrCl ≤50 mL/min or CrCl 50–80 mL/min, patients with CrCl ≥80 mL/min were younger (79 vs. 74 vs. 65; p<0.001) and less likely female (55% vs. 41% vs. 27%; p<0.0001). Rates of stroke or SE decreased with increasing CrCl (Table). There was no difference in the hazard ratio of rivaroxaban vs. warfarin across CrCl levels (p=0.85 for interaction). Similarly, rates of major bleeding decreased with increasing CrCl (Table), with no difference in the hazard ratio of rivaroxaban vs. warfarin across CrCl levels (p=0.17).

Conclusions: Rivaroxaban is non-inferior to warfarin with regard to both the primary endpoint and the safety analysis of major bleeding across all ranges of renal function, including those with high CrCl.

Acknowledgement/Funding: ROCKET AF was supported by Janssen Pharmaceuticals and Bayer Healthcare

ANTICOAGULATION AND ATRIAL FIBRILLATION III

P6211 | BEDSIDE

Early assessment of bleeding-related hospital readmissions among nonvalvular atrial fibrillation patients treated with the new oral anticoagulants using an electronic medical record database in the US

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Background: Randomized clinical trials have demonstrated that new oral anticoagulants NOACs are efficacious for reducing stroke risk among patients with nonvalvular atrial fibrillation (NVAF), although the reductions in stroke and bleeding risk vs. warfarin were different.

Purpose: To assess bleeding-related hospital readmissions among hospitalized NVAF patients treated with the 3 NOACs, dabigatran, rivaroxaban, and apixaban, in the US

Methods: Patients (≥18 years) with a hospital discharge diagnosis of AF who received apixaban, dabigatran, or rivaroxaban during hospitalization were identified from the Cerner Health Facts hospital database between 1/1/2012 and 8/31/2014. Patients were grouped into 3 cohorts depending on NOAC received. Patient characteristics and hospital resource use associated with the initial hospitalizations and bleeding-related readmissions within 30 days were evaluated and compared among patients treated with the 3 NOACs at the unadjusted and regression adjusted levels.

Results: Among NVAF patients included in the study population, 1,813 were treated with apixaban, 6,637 with rivaroxaban, and 5,751 with dabigatran during hospitalization. Patients who received apixaban were older, had greater severity of comorbidity, and had higher stroke and bleeding risks (Table). After controlling for patient characteristics, including stroke/bleeding risks, in comparison with treatment with apixaban, the odds of bleeding-related 30-day hospital readmissions were estimated at 1.68 (p=0.03) and 1.33 (p=0.25) for patients treated with rivaroxaban and dabigatran respectively. In comparison with use of apixaban, the use of rivaroxaban and dabigatran were associated with longer average hospital stay for bleeding-related readmissions (0.07 days, p=0.07; 0.08, p=0.03).

Clinical Characteristics

	Apixaban	Rivaroxaban	Dabigatran	p-value
Age (years), mean [SD]	74.9 [11.7]	72.1 [12.6]	72.4 [12.2]	<0.001
Charlson Comorbidity Index (CCI), mean [SD]	2.7 [2.3]	2.4 [2.3]	2.5 [2.2]	<0.001
$CHADS_2$ score, mean [SD]	2.4 [1.2]	2.1 [1.2]	2.2 [1.1]	<0.001
HAS-BLED score, mean [SD]	2.5 [1.0]	2.3 [1.0]	2.4 [1.0]	<0.001

SD, standard deviation.

Conclusion: In this early assessment, after controlling for patient characteristics, treatment with rivaroxaban vs. apixaban was associated with significantly greater risk of bleeding-related 30-day readmissions.

Acknowledgement/Funding: Bristol-Myers Squibb and Pfizer

Abstract P6210 – Table 1

	P*	CrCl 30 to 50*		CrCl >50 to <80*		CrCl ≥80*	
Outcome		Rivaroxaban	Warfarin	Rivaroxaban	Warfarin	Rivaroxaban	Warfarin
Stroke or systemic embolism							
N		1,587	1,592	3,113	3,168	2,373	2,324
Event rate, per 100 pt-yrs (total events)		2.86 (78)	3.50 (96)	2.21 (124)	2.46 (138)	1.52 (66)	1.68 (72)
HR (95% CI) for rivaroxaban vs warfarin	0.85	0.81 (0.60, 1.10)		0.90 (0.71, 1.15)		0.91 (0.65, 1.26)	
Major bleeding							
N		1,599	1,610	3,128	3,177	2,376	2,332
Event rate, per 100 pt-yrs (total events)		4.71 (106)	4.59 (107)	3.48 (170)	3.77 (186)	3.08 (118)	2.39 (93)
HR (95% CI) for rivaroxaban vs warfarin	0.17	1.02 (0.78, 1.34)		0.93 (0.75, 1.14)		1.28 (0.98, 1.68)	

*CrCl cut points chosen to coincide with existing FDA analyses.

P6212 | BEDSIDE
Characteristics of patients initiating oral anticoagulant therapy for management of non-valvular atrial fibrillation (NVAF)

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Background: Non-vitamin K oral anticoagulants (NOACs) have recently being approved around the world for the prevention of stroke among NVAF patients. There is a need to generate data on treatment patterns and performance of NOACs compared to warfarin in "real world" settings.
Purpose: To describe the baseline clinical and demographic characteristics of NVAF patients initiating apixaban, rivaroxaban, dabigatran or warfarin in the US.
Methods: A retrospective cohort study was conducted using Humedica de-identified Electronic Health Records (EHR) data (January 1, 2013 to June 30, 2014) to identify a population of adult NVAF patients newly initiated with a NOAC or warfarin. The index date was defined as the date of the first observed OAC after a 12-month baseline period. Descriptive summary statistics were used to compare patient characteristics between treatments.
Results: A total of 35,757 patients were identified (2,038 on apixaban; 6,407 on rivaroxaban; 2,440 on dabigatran; 24,872 on warfarin). Patients initiating warfarin were older ($p<0.0001$) and had more comorbidities on average than those initiating NOACs as shown in Table 1. NOACs were more likely to be prescribed by cardiologists and for commercially insured patients (both $p<0.0001$).

Table 1. Baseline characteristics

Characteristic	Apixaban (N=2038)	Dabigatran (N=2440)	Rivaroxaban (N=6407)	Warfarin (N=24,872)
Age in years (mean±SD)	70.9±10.6	70.5±10.3	69.8±11.0	74.0±9.6
Gender Female	46.3%	43.0%	44.8%	44.4%
CHA_2DS_2-VASc Score, (mean±SD)	2.8±1.6	2.8±1.6	2.7±1.6	3.2±1.6
Bleeding history	6.7%	7.4%	8.9%	10.2%
Stroke history (inpatient)	2.0%	0.9%	2.0%	1.4%
Health Plan: Medicare	36.0%	43.1%	35.2%	36.7%
Health Plan: Commercial	23.7%	25. 1%	25.6%	12.8%

Conclusion: In a US-representative database, clinical and demographic differences in the NVAF patient profiles exist across the different OACs. NOAC users were younger and had fewer co-morbid conditions at baseline compared to warfarin users.
Acknowledgement/Funding: Funded by Pfizer, Inc.

P6213 | SPOTLIGHT
Temporal trends in thromboembolism and bleeding in patients with non-valvular atrial fibrillation between 1996 and 2011

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Background and aim: Warfarin is an efficient drug for prevention of thromboembolic complications, but poses administrative challenges because of its narrow therapeutic window and tendency to interact with other pharmacologic drugs. We examined how hospitalization caused by bleeding and thromboembolic (TE) events associated with warfarin therapy have developed from 1996 to 2011 for patients with non-valvular atrial fibrillation.
Methods: All Danish patients discharged from first-time hospitalization for non-valvular atrial fibrillation in 1996–2011 were identified from nationwide administrative registers. Patients were classified as using either warfarin or not using anticoagulant medication. Patients were censored at the time of event or initiation of treatment with novel oral anticoagulants. The risks of bleeding and thromboembolism were analyzed by multivariable Poisson regression adjusted for sex, age, aspirin consumption, CHA2DS2-VASc (TE) and HAS-BLED (bleeding) risk score.
Results: 161,147 patients (mean age of 73.0 years and 52% male) were included. Figure 1 illustrates the relative risk of events for different years stratified by warfarin therapy. In general, the relative risk has decreased for both endpoints, both for patients with and without warfarin therapy. However, the risk of thromboembolic events has declined more among patients receiving warfarin, compared to patients not on warfarin therapy (p for interaction <0.0001).

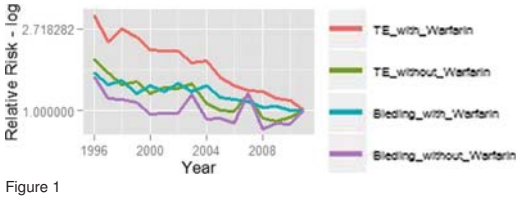

Figure 1

Conclusion: The relative risks of hospitalization due to bleeding or thromboembolic complications have decreased from 1996 to 2011 for patients with non-valvular atrial fibrillation, and this decline was particularly pronounced among patients on warfarin therapy. If this is related to better drug management needs to be explored in future studies.

P6214 | BEDSIDE
Antithrombotic management in patients with atrial fibrillation undergoing stent implantation: what is the impact of the ESC guidelines adherence?

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Background: Patients with atrial fibrillation (AF) who undergo percutaneous coronary intervention (PCI) and stenting transiently require triple antithrombotic therapy according to current ESC guidelines. The purpose of this study was to assess guidelines implementation and predictive factors of the prognosis related to ESC guidelines adherence.
Methods: Consecutive AF patients referred for PCI with stent were enrolled from 2011 to 2013. Prescription of antithrombotic treatment (ATT), and occurrence of bleeding, myocardial ischemia, stroke and death were obtained by screening hospitalization reports and standardized questions during followed up.
Results: Among 259 AF patients with PCI and stenting (age 76±10 years; CHA2DS2-VASc score 4.3±1.7), 40% had acute coronary syndrome and 60% had elective PCI. During a follow-up of 633±352 days, there were 53 (34%) undergoing elective PCI who were guidelines adherent, 10 (20%) for non ST elevation myocardial infarction (NSTEMI) and 8 (15%) for STEMI. Permanent AF (OR 0.45; 95% CI 0.23–0.89; p=0.02), medical history of valvular heart disease (OR 0.51; 95% CI 0.26–0.98; p=0.04), heart failure (OR 0.49; 95% CI 0.25–0.94; p=0.03) and use of OAC before hospitalization (OR 0.48; 95% CI 0.24–0.96; p=0.04) were associated with guideline adherence.
OAC and APT underuse was associated with an increased risk of death (OR 3.73; 95% CI 1.47–10.10; p=0.005 and OR 7.35; 95% CI 2.27–26.68; p=0.0009, respectively). APT overtreatment was significantly associated with a lower risk of death (OR 0.23; 95% CI 0.08–0.59; p=0.002).
Conclusion: Guidelines for antithrombotic therapy in patients with AF who undergo PCI and stent implantation are still poorly followed in clinical practice. OAC underuse was associated with an increased risk of death in this population.

P6215 | BEDSIDE
Real-world bleeding risk among non-valvular atrial fibrillation (NVAF) patients prescribed apixaban, dabigatran, rivaroxaban and warfarin: analysis of electronic health records

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Background: With the recent approval of three non-Vitamin K antagonist oral anticoagulants (NOACs) for stroke prevention among patients with non-valvular atrial fibrillation (NVAF), we need to understand how these medications perform in "real-world" settings.
Purpose: To evaluate bleeding rates among NVAF patients initiating an oral anticoagulant (OAC).
Methods: Using Humedica de-identified Electronic Health Record data, newly anticoagulated adult NVAF patients with treatment initiation date (index date) between January 1, 2013 and June 30, 2014 were identified. Based on index prescription, patients were assigned to apixaban, rivaroxaban, dabigatran, and warfarin cohorts and were followed up until the earliest of OAC switch, bleeding event (based on ICD-9-CM codes), last encounter, or 180 days post-index. Given the nature of the prescription data collected in the EHR system, it was not possible to account for discontinuation. Kaplan-Meier curves and Cox proportional hazard analysis were used to calculate the bleeding hazard ratios (HR) for the different OAC therapies, adjusting for age, sex, region, stroke risk, and baseline co-morbidities (i.e., Charlson score, bleeding, stroke, myocardial infarction, renal disease, heart failure, malignancy, and pulmonary embolism).
Results: A total of 35,757 patients were selected (2,038 on apixaban; 6,407 on rivaroxaban; 2,440 on dabigatran; and 24,872 on warfarin). After adjusting for baseline clinical and demographic characteristics, rivaroxaban (adjusted HR: 1.46; 95% CI: 1.23–1.75) and warfarin (HR: 1.34; 95% CI: 1.13–1.58) initiation cohorts were associated with statistically significant higher risk of bleeding compared to apixaban during the study period. No significant difference was observed between apixaban versus dabigatran (HR 0.91; 95% CI: 0.73–1.13) in this 2013–14 cohort study.
Conclusion: Patients initiating rivaroxaban and warfarin were estimated to have higher bleeding risk than patients on apixaban. The results showed no statistically significant difference in bleeding rates between apixaban and dabigatran.
Acknowledgement/Funding: Funded by Pfizer, Inc.

P6216 | BEDSIDE

Real-life use of non-vitamin K antagonist oral anticoagulants in comparison with vitamin K antagonists for non-valvular atrial fibrillation: data from a prospective cohort

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Current guidelines recommend non-vitamin K antagonist oral anticoagulants (NOACs) or vitamin K antagonists (VKAs) for patients with non-valvular atrial fibrillation (NVAF). Clinical features of patients prescribed with NOACs or VKAs in real-life remain undefined.

Purpose: To evaluate differences between NVAF patients prescribed with NOACs or VKAs in real-life.

Methods: Consecutive patients with NVAF prescribed with NOACs from August 2013 to January 2015 were included in a multicenter prospective cohort and compared with a random sample of patients with NVAF receiving VKAs.

Results: Overall, 1494 patients with NVAF (5.4% new detected, 17.3% paroxysmal, 8.8% persistent, 68.5% permanent) were included: 1021 receiving NOACs (reduced doses in 483 patients) and 473 VKAs. The mean CHA2DS2VASC score was higher in patients treated with rivaroxaban or apixaban compared with patients treated with dabigatran (both $p<0.001$) or VKAs (both $p<0.001$). Similarly, the mean HASBLED score was higher in patients treated with rivaroxaban or apixaban as compared with patients treated with dabigatran (both $p<0.001$) or VKAs (both $p<0.001$). These differences were mostly accounted for by a lower mean age in dabigatran patients compared to rivaroxaban, apixaban or VKAs patients and by a higher prevalence of previous stroke, previous major bleeding and labile INR in patients prescribed with NOACs compared with VKAs. Patients prescribed with reduced doses of NOACs have increased CHA2DS2VASC or HASBLED compared to patients treated with VKAs or standard doses of NOACs.

Real-life NOAC vs VKA:patient's features

		Warfarin (N=473)	NOACs (N=1021)		
			Dabigatran (N=386)	Rivaroxaban (N=356)	Apixaban (N=279)
Age, years	mean ± SD	79.5±8.2	76.8±8.2*	79.3±8.9	79.0±7.8
$CHADS_2$ score	mean ± SD	2.5±1.1	2.4±1.2	2.8±1.2*	2.8±1.3*
CHA_2DS_2-VASC score	mean ± SD	4.1±1.4	4.1±1.5	4.6±1.5*	4.5±1.5*
HASBLED score	mean ± SD	2.4±1.0	2.5±1.2	3.1±1.1*	3.1±1.1*
Previous TIA/stroke	n (%)	87 (18.4)	118 (30.6)*	107 (30.1)*	96 (34.4)*
Labile INR	n (%)	96 (20.3)	99 (25.6)	122 (34.3)*	73 (26.2)
Previous major bleeding or predisposition	n (%)	80 (16.9)	95 (24.6)*	133 (37.4)*	117 (41.9)*

*$p<0.05$ compared with warfarin.

Conclusion: Patients prescribed with rivaroxaban or apixaban in real-life have a higher thrombotic and haemorrhagic risk in comparison to patients receiving dabigatran or VKAs.

P6217 | BEDSIDE

Real world comparison of major bleeding risk among non-valvular atrial fibrillation patients newly initiated on apixaban, dabigatran, rivaroxaban or warfarin

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Background: Limited evidence is available about the real-world safety of apixaban versus other anticoagulants.

Purpose: To compare the major bleeding risk among newly anticoagulated non-valvular atrial fibrillation (NVAF) patients initiating apixaban versus warfarin, dabigatran or rivaroxaban.

Methods: Retrospective cohort from MarketScan® commercial & Medicare supplemental US database from 01/01/2013 to 12/31/2013 was used for this comparative assessment. Major bleeding was defined as: (i) bleeding requiring hospitalization (IP) and (ii) inpatient or outpatient bleeding (IP/OP). Cox model estimated Hazard ratios (HR) of major bleeding adjusted for age, gender, baseline comorbidities and comedications.

Results: Among 29,338 patients, 2402 (8.19%) were on apixaban, 4,173 (14.22%) on dabigatran, 10,050 (34.26%) on rivaroxaban and 12,713 (43.33%) on warfarin. warfarin (72.5±11.9 yrs) and apixaban (69.3±12.3 yrs) patients were older and sicker versus rivaroxaban (67.3±12.2 yrs) and dabigatran (66.8±12.1 yrs). Patients initiated on warfarin (IP bleeding HR: 1.93, 95% CI: 1.12–3.33, P=0.018; IP/OP bleeding HR: 1.62, 95% CI: 1.20–2.18, P=0.0015) or rivaroxaban (IP bleeding HR: 2.19, 95% CI: 1.26–2.79, P=0.0052; IP/OP bleeding HR: 1.70, 95% CI: 1.26–2.29, P=0.0006) had greater risk of major bleeding versus those on apixaban after adjusting for other risk factors. Patients initiating dabigatran (IP bleeding HR: 1.71, 95% CI: 0.94–3.1, P=0.079; IP/OP bleeding HR: 1.28, 95% CI: 0.92–1.79, P=0.1441) had numerically greater risk of major bleeding versus those on apixaban (Figure).

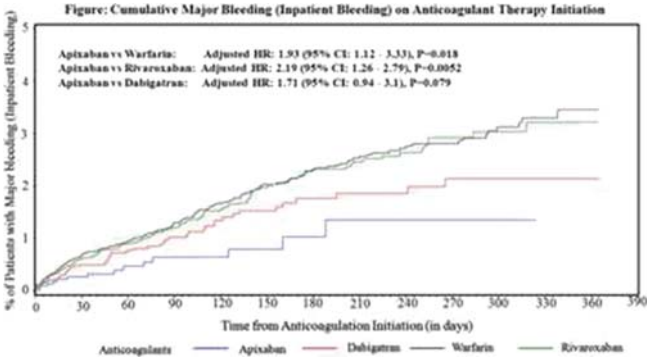

Figure 1

Conclusion: Among newly anticoagulated NVAF patients in the real world setting, initiation with rivaroxaban or warfarin was associated with significantly greater risk of major bleeding as compared to initiation on apixaban.

Acknowledgement/Funding: The study is supported by Bristol-Myers Squibb and Pfizer Inc.

P6218 | BEDSIDE

Higher amounts of heparin use with oral factor Xa-Inhibitor compared to oral vitamin K antagonist and thrombin-inhibitor during ablation procedure for atrial fibrillation

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Background: In practice guidelines, an approach of performing catheter ablation for atrial fibrillation (AF) under uninterrupted oral vitamin K antagonist (VKA) is recommended because of higher risk of bleeding in intravenous heparin bridging therapy. Recent studies have reported that non-VKA oral anticoagulants are equivalent to VKA, warfarin for preventing thromboembolism and bleeding during the perioperative period of AF ablation. In this study, we compared amounts of heparin use during the procedure and safety outcomes after the ablation among oral anticoagulants.

Methods: We included 273 consecutive patients who underwent catheter ablation procedure for elimination AF with either paroxysmal or persistent pattern. Ninety-one patients were under uninterrupted oral VKA (warfarin), 91 under oral direct thrombin-inhibitor (dabigatran), and 91 under direct oral factor Xa-inhibitor (rivaroxaban). We compared amounts of heparin use during the procedure and event rates of bleeding and systemic thromboembolism among three anticoagulants therapy.

Results: Significantly higher amounts of heparin were needed in the rivaroxaban group (252 U/kg ± 91 U/kg) compared to the warfarin group and the dabigatran group (187±59 U/kg and 218±55 U/kg, respectively; $p<0.05$ with ANOVA analysis). Major or minor bleeding event was seen in one (1.1%) of the rivaroxaban group, six (6.6%) of the warfarin group, and three (3.3%) of the dabigatran group. There was no significant difference among three anticoagulants groups ($p=0.168$). Thromboembolic event was seen in one of the rivaroxaban group (1.1%) and none of other two groups.

Conclusions: This study demonstrates that oral direct factor Xa-inhibitor rivaroxaban needs significantly higher amounts of heparin use compared to oral VKA warfarin and direct thrombin-inhibitor dabigatran in perioperative management for AF ablation. However, it may not lead to an increase in bleeding complications.

P6219 | BEDSIDE

Management of anticoagulation in patients with non-valvular atrial fibrillation in general practice in UK: Evolution and characteristics of patients treated with antiplatelet therapy alone

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Background: Oral anticoagulation (OAC) therapy for thromboembolic prophylaxis (TEP) is recommended for high-risk patients with non-valvular atrial fibrillation (NVAF), i.e. those with CHA2DS2-VASc ≥2. Evidence suggests that aspirin is less effective for TEP, with a risk of major bleeding comparable to OACs. Consequently, recent guidelines (ESC 2012, NICE 2014) recommend limited or no use of antiplatelet therapy for TEP in AF.

Aim: Describe changes over time from 2012 to 2015 in the proportion of NVAF patients treated with aspirin or other antiplatelet agents (APA) for TEP.

Methods: We undertook four cross-sectional analyses on 1 April of each year from 2012–15 (index dates), using the UK Clinical Practice Research Datalink

(CPRD), a primary-care database. Each cross-section included all NVAF patients eligible for OAC under 2014 NICE guidance (CHA2DS2-VASc ≥2). We defined OAC and APA treatment by GP prescriptions and/or INR measurement in 90 days before index date and identified co-morbidities from GP records (Read codes). We calculated the proportion (with 95% confidence intervals) of patients receiving OAC (± APA), APA alone, or no antithrombotic agent and evaluated the trend over time in the proportion receiving APA only using a mixed regression model. Data are presented for the years 2012 to 2014. Results for 2015 will be available for the ESC congress.

Results: We identified 67,327, 66,364 and 62,840 eligible patients on the 2012, 2013, and 2014 index dates, respectively. From 2012–14, the proportion of patients on APA alone trended downwards over time: 34.2% (33.8–34.6), 31.2% (30.9–31.6), and 27.7% (27.3–28.1) respectively. The proportion on OAC trended upwards (50.2, 53.2, 57.5%), whilst the proportion of untreated patients remained stable (15.6, 15.7, 14.8%). The reduction in the proportion on APA alone was greater in newly diagnosed patients (38.1, 31.2, 23.8%) than in those diagnosed ≥12 months (33.7, 31.2, 28.2%). Characteristics (age, gender, CHA2DS2-VASc, HAS-BLED) were similar between patients on APA alone and on OAC. More than 70% of the patients on APA alone had never been treated with OAC. Findings were similar across UK regions.

Conclusion: Since the updated ESC guidance and the introduction of NOACs in the UK, the use of APA for TEP in AF has begun to decrease, most notably in newly diagnosed patients. However, use of APA for TEP remained high in early 2014. A further analysis (1 April 2015) will examine early changes following publication of new guidance by NICE in June 2014.

Acknowledgement/Funding: This study was funded by Bristol-Myers Squibb Pharmaceuticals Ltd

ANGINA PECTORIS STABLE I

P6220 | BEDSIDE
Long-term cost-effectiveness of diagnostic tests for assessing stable chest pain

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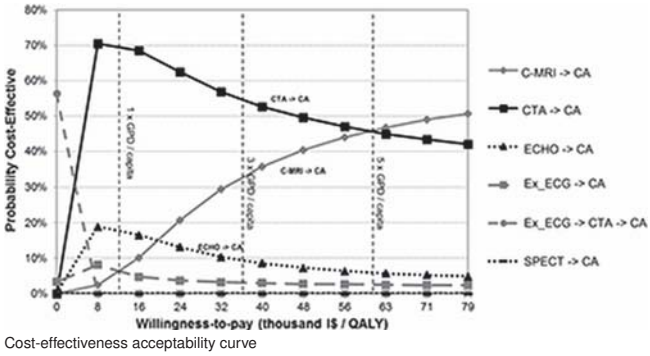
Background: Several tests are available for diagnosing coronary artery disease (CAD), with varying accuracy and cost. Choosing one test over another can influence healthcare costs and patient prognosis.

Purpose: Assess long-term health and economic impacts of diagnostic test selection.

Methods: State-transitions (Markov) model including several diagnostic strategies, based on either exercise electrocardiogram (Ex-ECG), stress echocardiogram (ECHO), single-photon emission computed tomography (SPECT), tomography angiography (CTA) or stress cardiac magnetic resonance (C-MRI) as initial test. Cost data were derived from Brazilian public health system (SUS) reimbursement values, and estimated from the private sector for tests not currently reimbursed (CTA and C-MRI). We used the SUS perspective and a lifetime horizon.

Results: Diagnostic strategy had a small but measurable impact in quality-adjusted life-years (QALY) gained. Switching from Ex-ECG to CTA-based strategies improved outcomes at an incremental cost-effectiveness ratio (ICER) of 3,100 international dollars (I$) per QALY. ECHO-based strategies resulted in cost and effectiveness almost identical to CTA, and SPECT-based strategies were dominated because of much higher cost. Strategies based on C-MRI were the most effective, but ICER versus CTA was higher than proposed WTP threshold. Invasive strategies were dominant in high pretest probability setting.



Cost-effectiveness acceptability curve

Conclusions: Coronary computed tomography is a cost-effective alternative for the diagnosis of CAD and should be included in the Brazilian public health system. Stress echocardiography has a similar performance and is an acceptable alternative for most patients, while invasive strategies should be reserved for patients at high risk.

Acknowledgement/Funding: This study was supported by the CNPq (MCT/MS), under the Brazilian National Institute for Science and Technology (INCT)'s HTA Program.

P6221 | BEDSIDE
High-sensitive troponin T as a predictor of short-term outcome in coronary artery disease patients with glucose metabolism disorder, ARTEMIS study

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Background: Several novel biomarkers of inflammation, myocardial damage and fibrosis predict cardiovascular events and mortality in general population and in patients with coronary artery disease (CAD) or congestive heart failure (CHF). The prognostic value of these novel biomarkers in patients with stable coronary artery disease (CAD) at increased risk for future cardiac events due to impaired glucose metabolism is not well established.

Methods: Serum levels of high-sensitive troponin T (hs-TnT), brain natriuretic peptide (BNP), high-sensitive C-reactive protein (hs-CRP), galectin-3 and soluble suppressor of tumorigenicity-2 (sST2) were analyzed in 1137 patients with angiographically verified stable CAD and with either type 2 diabetes, impaired glucose tolerance or fasting glycaemia. The patients were followed-up for 2 years. The primary endpoint was a composite of cardiac death and hospitalization for CHF and the secondary endpoint was acute coronary syndrome (ACS).

Results: The primary endpoint occurred in 40 patients (3.5%), of whom 15 (1.3%) were cardiac deaths and 25 (2.2%) hospitalizations for CHF, whereas 72 patients (6.3%) suffered ACS during the follow-up. Increased hs-TnT (≥14 ng·L-1) was the strongest univariate predictor of the primary endpoint with hazard ratio (HR) of 24.5 (95% confidence interval [CI]: 8.7–69.0; $p<0.001$) and remained so when adjusted for established risk markers (age, sex, prior myocardial infarction, body mass index, CCS class, echocardiography, microalbuminuria, lipid and glucose status) and the other predictive novel biomarkers (HR: 9.9; 95% CI: 3.2–30.8; $p<0.001$). In this multivariate model hs-CRP (HR: 2.9; 95% CI: 1.3–6.5), BNP (HR: 3.1; 95% CI: 1.4–6.8) and sST2 (HR: 3.0; 95% CI: 1.4–6.6) also predicted the primary endpoint ($p<0.01$ for all). Categorical net reclassification index for the addition of hs-TnT to establish risk markers was 0.231 (95% CI: 0.067–0.394; p=0.006) and continuous 1.169 (95% CI: 0.925–1.412; $p<0.001$). Integrated discrimination improvement for this model 0.054 (95% CI: 0.031–0.077, $p<0.001$), whereas C-index improved from 0.794 to 0.895. None of the variables predicted ACS.

Conclusions: In patients with stable CAD and abnormal glucose metabolism, hs-TnT is an independent predictor of composite endpoint of cardiac death and hospitalization due to CHF and gives additional prognostic value over the traditional risk markers.

Acknowledgement/Funding: Finnish Technology Development Center (TEKES), the Sigrid Juselius Foundation, and the Foundation for Cardiovascular Research, Helsinki, Finland

P6222 | BEDSIDE
Diagnostic significance of duration of myocardial early systolic lengthening in patients with stable coronary artery disease

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Background: Previous researches indicated that ischemic myocardium with reduced active force will lengthen when left ventricular (LV) pressure rises during early systole before onset of systolic shortening in patients with coronary artery disease (CAD).

Purpose: The purposes of this study were to investigate whether the duration of LV early systolic lengthening (ESL) could identify patients with CAD, and to examine the relationship between fractional flow reserve (FFR), which is used for decision-making of optimal therapy, and the duration of LV ESL.

Methods: We prospectively examined 75 patients with suspected CAD. Two-

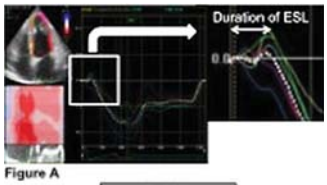

Figure A

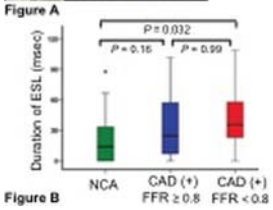

Figure B

dimensional speckle tracking echocardiography at rest was performed the day before coronary angiography or percutaneous coronary intervention. Apical 3 views were used to examine the duration of ESL. The duration of ESL was defined as time from onset of the Q wave on electrocardiography to maximum myocardial systolic lengthening (Figure A).
Results: Thirty-five patients revealed normal coronary angiogram (NCA), and 40 patients, who underwent FFR, had CAD. In patients with significant CAD, 17 patients showed the value of FFR ≥0.8 and 23 patients showed the value of FFR <0.8. The duration of ESL was 39.6±29.5 ms in patients with FFR <0.8, 36.4±23.2 ms in patients with FFR ≥0.8, and 20.9±22.2 ms in patients with NCA (P=0.020) (Figure B). However, the duration of LV ESL did not show the significant correlation with the value of FFR (R2 <0.1, P=0.12).
Conclusions: Duration of myocardial ESL was significantly prolonged in patients with significant CAD determined by FFR <0.8 compared with patients with NCA. ESL at rest might be a useful parameter to identify patients with CAD, whereas this new parameter could not predict an FFR in those patients.

P6223 | BEDSIDE
High-frequency QRS analysis compared to conventional ST-segment analysis in a large series of patients with chest pain and normal ECG managed with the propensity score matching for cardiovascular risk

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Background: The novel analysis of high-frequency QRS components (HF/QRS) has been proposed in patients with chest pain (CP) and normal ECG referred for exercise tolerance test (ex-ECG). Aim of the present study was to compare the prognostic value of the ex-ECG to the ex-HF/QRS in the emergency setting.
Methods: Patients with CP and normal ECG, normal troponin and normal echocardiography were considered. All patients underwent ex-ECG for conventional ST-segment-analysis and HF/QRS-analysis. A decrease ≥50% of the signal of HF/QRS intensity recorded in two contiguous leads, at least, was considered as index of ischaemia, as ST-segment depression ≥2 mm or ≥1 mm and CP on ex-ECG. Exclusion criteria were QRS duration ≥120 msec and inability to exercise. Baseline characteristics were adjusted with the propensity score matching for possible confounders. SPSS software allowed estimation of the propensity-score using logistic regression and specifying nearest neighbor matching in cardiovascular risk-factors and TIMI-score, GRACE-score, CHA2DS2VASc-score. The primary endpoint was the composite of coronary stenosis ≥70% or acute coronary syndrome, revascularization, and cardiac death at the 6-month follow-up.
Results: Out of 624 patients (age 61±15 years) considered, 589 were analyzed after matching. The percentage of age-adjusted maximal predicted heart rate was 88±10 and the maximal systolic blood pressure was 169±22 mmHg. Twenty-two patients achieved the end-point. On the univariate-analysis the presence of known cardiovascular disease, the CHA2DS2VASCs-score, the GRACE-score, the positive ex-HF/QRS and the positive ex-ECG were predictors of the end-point. However only the ex-HF/QRS (OR 29, 95% CI 7–127, p<0.001) remained predictor of the endpoint after the multivariate-analysis. The ex-HF/QRS showed higher sensitivity (91% vs 27%; p=0.02), lower specificity (74% vs 95%; p=0.09), and comparable negative predictive value (99 vs 97%; p=0.78) when compared to ex-ECG. Receiver operator characteristics analysis showed the larger area of HF/QRS (0.83, 95% Confidence Intervals, CI 0.75–0.90) over ex-ECG (0.57, CI 0.44–0.70) and CHA2DS2VASCs-score (0.65, CI 0.54–0.77), GRACE-score (0.65, CI 0.54–0.76), TIMI-score (0.63, CI 0.52–0.74); p=0.03 on pairwise comparison with C-statistic.
Conclusions: In patients with CP submitted to risk-stratification with the ex-ECG, the novel ex-HF/QRS analysis showed a valuable incremental sensitivity in diagnostic over ST-segment analysis.

P6224 | BENCH
Relationship between 24 hour pulse pressure dipping and cardiovascular risk assessment in patients with CHD

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Introduction: Elevated values of systolic (SBP), diastolic (DBP) blood pressure and pulse pressure (PP) are known to be powerful risk factors in cardiovascular (CV) diseases. The purpose of this study was to determine the association between PP and Major Advanced CV Events (MACE), and all cause and CV mortality in different age groups of patients with CAD confirmed by angiography.
Patients and methods: To the PROGNOSIS study there were included 1345 subjects. From total group of 1345 subjects, 891 with significant coronary artery stenosis ≥70% finally were included to the study. During baseline visit the following data were obtained: 1. two sphygmomanometric BP values; 2. 24-hour ABPM. PP was calculated as SBP minus DBP. The percentage decrease in mean PP during the nighttime period was calculated as 100x[daytime PP mean – nighttime PP mean]/daytime PP mean. Using this percentage ratio, subjects were classified as dippers or non-dippers (nighttime relative PP decline ≥or <10%, respectively). From the time of the baseline visit to 31 December 2013 (median follow-up 8.3 years), the survival state was ascertained. The primary endpoint was cardiovascular mortality and secondary all-cause mortality. A COX proportional hazards model was used to examine the association between PP and PP dipping and risk of MACE, revascularization, CV and total mortality after adjusting for sex, diabetes, smoking or non smoking status and LDL cholesterol.
Results: The study group was divided to age subgroups: <65 y. (n=461, 352 male), 65–74 y. (n=330, 191 male), ≥75 y. (n=100, 67 male). There were 245 all-cause deaths including 114 CV deaths during the follow-up period. MACE occurred in 442 subjects, but revascularisations (PCI or CABG) were performed in 578 subjects. A Cox proportional regression analysis confirmed the relationship between PP dipping and risk of MACE HR (95% CI, 0.98 (0.96–0.99)), revascularization HR (95% CI, 0.98 (0.97–0.99)) only in group of the oldest subjects.
Conclusions: In contrast to younger CAD patients, PP dipping is related to MACE, CV and total mortality in very elderly CAD subjects.

P6225 | BEDSIDE
In-plaque microchannel volume as a quantitative surrogate marker of plaque vulnerability: study with 3D optical coherence tomography and color-coded intravascular ultrasound

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Background and purpose: It has been documented that neovascularization in atherosclerotic plaques is associated with plaque vulnerability. This study was to examine tissue characteristics of plaque with micro-channels detected by three-dimensional optical coherence tomography (3D-OCT). The tissue of the plaque around the channel was assessed by use of a commercially available color-coded intravascular ultrasound, iMap software.
Methods: A total of 71 coronary vessel was enrolled from April 1st, 2012 to March 31st, 2014 at Nihon University Hospital. Micro-channel was defined as a tiny tubule with a diameter of 50 to 300 micrometers detected over 3 or more frames in OCT. We measured total areas of cross section (surrogate of total luminal volume) of micro channels from all the frames, in which the channel was detected. The i-Map software classified the plaque component into fibrotic, lipidic, necrotic, and calcified areas. The software analyzed the tissue characteristics of the whole cross-sectional areas of distance of 0.5mm apart within the plaque (length >5.0mm) around the micro-channels. Plaques with advanced calcified lesion of an angular span >90 degree, with a poor image quality, or with a significant deficit of echo-intensity were excluded.
Results: The total of cross-sectional areas of micro channel was significantly correlated with percent area of lipidic as well as necrotic components. (lipidic; r=0.626, p=0.005, necrotic; r=0.598, p=0.011) Its area was not correlated with percent area of fibrous as well as calcified component
Conclusions: The greater the lumina volume of micro-channel was, the more the percent content of lipidic/necrotic tissue area was within the plaque with micro-channel. These data suggested that micro-channels within coronary plaque might be significantly and quantitatively related to plaque vulnerability.

P6226 | BEDSIDE
Ranolazine added to standard-of-care treatment in the management of stable angina: cost-effectiveness analysis from the United Kingdom perspective

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Background: The prevalence of stable angina in the United Kingdom is about 1.3 million people. Stable angina is associated with a profound impact on quality-of-life and economic outcomes; with afflicted patients reporting their health to be twice as poor as those who previously suffered a stroke, and direct treatment costs approaching £700 million per year. Ranolazine has been shown to decrease angina symptom frequency and nitroglycerin consumption; and thus, has a positive impact on patient functioning. At present, the cost-effectiveness of ranolazine for stable angina has not been assessed from a UK perspective.
Purpose: To assess the cost-effectiveness of ranolazine when added to standard-of-care (SoC) antianginals compared with SoC alone in patients with stable coronary disease experiencing ≥3 attacks/week (weekly or daily angina).
Methods: A Markov model utilizing a UK health-system perspective, a 1-month cycle length, and a 1-year time horizon was developed to estimate costs (£2014) and quality-adjusted life years (QALYs) for patients receiving and not receiving ranolazine (500 mg twice daily for one week, followed by 1,000 mg twice daily, thereafter). Patients entered the model in 1 of the 4 angina frequency health states based upon Seattle Angina Questionnaire angina frequency (SAQAF) scores (100=no; 61 to 99=monthly; 31 to 60=weekly; and 0 to 30=daily angina) and were allowed to transition between states or to death based upon probabilities derived from the randomized, controlled Efficacy of Ranolazine in Chronic Angina (ERICA) trial and other published studies. Patients not responding to ranolazine in

month 1 (not improving ≥1 SAQAF health state) were assumed to discontinue ranolazine and behave like SoC patients.
Results: Ranolazine patients accrued a mean of 0.701 QALYs at a cost of £5,502. Those not receiving ranolazine accrued 0.662 QALYs and at a cost of £5,318. The incremental cost-effectiveness ratio (ICER) for the addition of ranolazine was £4,717/QALY. The ICER was most sensitive to ranolazine cost; exceeding £20,000/QALY when the cost of ranolazine increased >53% above base case. The ICER did not change appreciably when indirect costs were included (£3,439/QALY) in the model or mortality rates were assumed to increase with worsening severity of SAQAF health states (£5,171/QALY). Monte Carlo simulation found ranolazine cost-effective in >99% of 10,000 iterations assuming a £20,000/QALY willingness-to-pay threshold.
Conclusion: Ranolazine added to SoC in patients with weekly or daily angina appears cost-effective from a UK health-system perspective.
Acknowledgement/Funding: The Menarini Group

P6227 | BEDSIDE
Four-year clinical outcome of drug-eluting stent following rotational atherectomy for heavily calcified lesions

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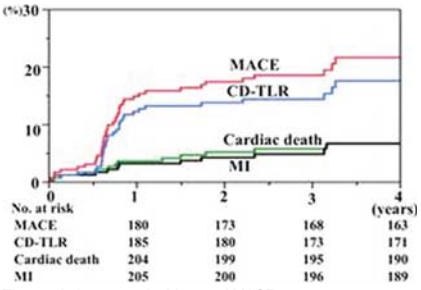
Background: Long term clinical outcomes after drug-eluting stent (DES) following rotational atherectomy (RA) for heavily calcified lesions remains unclear. The aim of this study is to assess long-term clinical outcomes after DES following RA.
Methods and results: We enrolled 213 consecutive patients with 245 lesions treated with DES following RA. Clinical follow-up information at 4 years was obtained 98.4%. Angiographic success rate was 98.9%. Mean age was 71.8+11.8 years, 50.2% had diabetes mellitus (DM), 21.8% had hemodialysis, and total stent length was 38.7+21.4 mm. The cumulative 4-year incidence of MACE, defined as cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CD-TLR) was 21.8%. The incidence of cardiac death, MI, and CD-TLR were 6.9%, 6.9%, and 17.8%. Definite stent thrombosis rate was 3.5%. MACE and CD-TLR risk was maximal within 1 year. In a multivariate analysis, significant predictors of MACE were DM (hazard ratio [HR] 1.90; 95% confidential interval [CI] 1.01–3.75; p=0.049), and ejection fraction <35% (HR 2.89; 95% CI 1.17–6.20; p=0.02).



The cumlative 4-year incidence of MACE

Conclusions: Incidence of MACE and CD-TLR was maximal within 1 year after DES implantation following RA and decreased thereafter. Patients implanting DES following RA with DM or low ejection fraction had poor clinical outcome.

P6228 | BEDSIDE
Modifiable risk factors associated with mild cognitive impairment in patients with stable coronary heart disease in the STABILITY trial

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Background: Decreased cognitive function is a major cause of disability in the elderly and is more prevalent in patients with cardiovascular disease.
Purpose: To evaluate associations between modifiable cardiovascular risk factors and mild cognitive impairment (MCI) in patients with chronic coronary heart disease (CHD) who participated in the global STabilization of Atherosclerotic plaque By Initiation of darapLadIb TherapY (STABILITY) trial.
Methods: 10,634 of 15,828 study participants completed the Montreal Cognitive Assessment (MoCA) test a mean of 3.17±0.37 years after randomisation to darapladib or placebo. The odds ratios (OR) for MCI (MoCA score <26 out of 30) versus normal cognitive function (MoCA score ≥26) were determined for clinical and demographic factors assessed at baseline using a multivariable model.
Results: The median age was 64 (IQR 59, 70) years and 82% were men. MoCA was <26 in 4,578 (43%) subjects. In the multivariable model older age, lower educational achievement, geographic region and country income level were each associated with MCI (P<0.0001). MCI was also more common in patients with a history of hypertension (OR 1.12, 95% Confidence Interval [CI] 1.02, 1.23), diabetes mellitus (OR 1.11, 95% CI 1.01, 1.21), LDL cholesterol >2.58mmol/L (OR 1.11, 95% CI 1.01, 1.23), HDL cholesterol <1.03mmol/L (OR 1.12, 95% CI 1.02, 1.23), <2.5 hours moderate intensity exercise each week (OR 1.15, 95% CI 1.06, 1.27), renal dysfunction (eGFR <60 mL/min, OR 1.10, 95% CI 1.00, 1.21) and history of stroke (OR 1.42, 95% CI 1.19, 1.70). Randomisation to darapladib or placebo, sex, obesity, current smoking, history of myocardial infarction, coronary artery bypass surgery, multi-vessel coronary artery disease and poly-vascular disease were not independently associated with MCI.
Conclusion: MCI is common in patients with stable CHD and associated with several cardiovascular risk factors, some of which are modifiable. These observations suggest that interventions which improve cardiovascular risk factors could, over the longer term, decrease the likelihood of developing cognitive impairment.
Acknowledgement/Funding: The STABILITY study was funded by GlaxoSmithKline

P6229 | BEDSIDE
Effect of ivabradine on heart rate variability in patients with stable coronary artery disease

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Background: Ivabradine is a specific heart-rate lowering agent with anti-anginal properties and is commonly used in patients with stable coronary artery disease (CAD). Heart rate variability (HRV) reflects autonomic nervous system activity and predicts outcome. It is not known whether ivabradine modulates HRV in these patients.
Purpose: We aimed to evaluate the effect of ivabradine on HRV in patients with stable CAD.
Methods: We included 36 patients (61±13 years, 75% women) with stable CAD, on maximal tolerated beta blocker therapy, and in sinus rhythm >65bpm. Ivabradine (5mg bid) was initiated and uptitrated to 7.5mg bid, if tolerated. Prior to treatmet initiation and after 3 months, a 24h Holter was recorded.
Results: Diabetes mellitus, arterial hypertension, and heart failure were known for 58%, 89% and 27% of patients, respectively. All patients were treated with >50% of beta blocker target dose. Ivabradine decreased heart rate in most patients and improved time domain HRV parameters – see table. It increased average 24h high frequency power (p=0.006), but had no significant influence on low frequency power.

HRV parameters

Variable	Before treatment	After treatment	p value
HR	78±1 bpm	68±1 bpm	≤0.001
SDNN	125±4 ms	140±5 ms	0.003
SDNNi	47±2 ms	54±3 ms	0.01
rMSSD	33±3 ms	39±4 ms	0.01
pNN50	8±1%	10±2%	0.005
LF	450±48 ms^2	649±122 ms^2	0.2
HF	238±41 ms^2	382±1 ms^2	0.006

All results are presented as mean ± standard error of mean. HR, heart rate; SDNN, standard deviation (SD) of all normal to normal (NN) intervals; SDNNi, mean of the SD of all NN intervals for all 5-min segments of the entire recording; SDANN, SD of the averages of NN intervals in all 5-min segments of the entire recording; rMSSD, the square root of the mean squared differences of successive NN intervals; pNN50, the proportion of the number of successive interval differences greater than 50 ms to the total number of NN intervals; LF, low frequency power; HF, high frequency power.

Conclusion: Ivabradine, on top of maximal tolerated beta blockers, improves HRV in patients with stable CAD.
Acknowledgement/Funding: The study was partially funded by Servier.

P6230 | BEDSIDE
Circulating high-sensitivity cardiac troponin T is a strong predictor of coronary atherosclerotic burden independently from the presence of inducible ischemia

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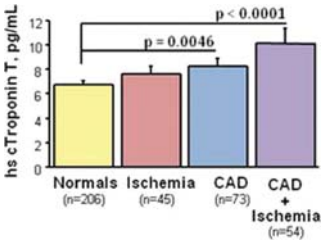
Background: Circulating levels of high-sensitivity cardiac troponin T (hs-cTnT) are predictors of coronary artery disease (CAD) and long term prognosis in patients with stable angina.
Purpose: We aimed to assess whether inducible myocardial ischemia is the major determinant of circulating hs-cTnT levels in these patients.
Methods: Hs-cTnT was measured in 378 patients (60.1±0.5 years, 229 males) with stable angina and unknown CAD enrolled in the Evaluation of Integrated

Cardiac Imaging (EVINCI) European study. All patients underwent stress imaging (nuclear perfusion imaging or echocardiography or cardiac magnetic resonance) to detect inducible myocardial ischemia, and coronary computed tomography angiography (CCTA) to assess the presence of CAD (>50% stenosis of at least one major coronary vessel). Moreover, an individual CTA score, expressing the coronary atherosclerotic burden, was calculated combining extent, severity, composition, and location of plaques.
Results: Patients were subdivided according to the absence/presence of CAD and ischemia. Hs-cTnT concentrations were significantly increased in patients with CAD with or without inducible ischemia (Figure). CTA score progressively increased from the first to the last group (6.3±0.5 to 23.3±1.3, P<0.0001 for trend). In a multivariate model, plasma hs-TnT was an independent predictor of the CTA score, even after adjustment for age, sex, risk factors and presence of ischemia (coefficient 0.71, SE 0.1, p<0.0001).



hs-cTnT according to CAD/ischemia

Conclusions: Circulating hs cTnT is a strong predictor of coronary atherosclerotic burden also in the absence of inducible ischemia. These results suggest alternative mechanisms linking coronary atherosclerosis with release of hs-cTnT in patients with stable CAD.

ANGINA PECTORIS STABLE II

P6231 | BEDSIDE
Occurrence and in-hospital mortality of vasospastic angina pectoris in Finland

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Background: Epidemiology of vasospastic angina pectoris (AP) has been studied mainly in Japan while information on western populations is limited.
Purpose: To study occurrence and in-hospital mortality of vasospastic AP in general population of Finland.
Methods: Occurrence and mortality of admissions caused by vasospastic AP in Finland were studied using a retrospective nationwide, population-based (n=39,191,852 person-years) registry of hospital admissions in patients aged ≥18 years. Data were collected from all 22 Finnish hospitals with coronary angiolaboratory from May 2000 to October 2009. Incidence was calculated by using age and sex matched population data of mainland Finland.
Results: The study period included 1786 vasospastic AP admissions. Vasospastic AP patient was more likely to be male (59.5%; CI 55.9–63.1%) than female (40.5%; CI 37.6–43.6%) with age-adjusted RR of 1.55 (CI 1.03–2.33, p=0.035) for male sex. Female patients were significantly older than male patients (67.6±12.2 vs. 64.9±11.0 years, <0.0001). Standardized incidence rate for vasospastic AP caused admission was 3.77 (CI 3.58–3.97)/100,000 person-years overall, 5.05 (CI 4.74–5.38)/100,000 among men and 2.74 (CI 2.52–2.98)/100,000 among women. Total incidence increased steadily with age in population aged 40- 75 years followed by gradual decrease in population aged older than 85 years. Slope of increase in incidence with aging was steeper among men, while peak in incidence lasted longer in women. Incidence rate ratio for vasospastic AP caused admission was 1.77 (CI 1.41–2.22) among men compared to women (p<0.0001). Vasospastic AP caused 1.3% of all cardiovascular admissions among adults aged 45–60 years, but the proportion decreased gradually to 0.1% among nonagenarians. Total in-hospital mortality for vasospastic AP was 1.6% (CI 1.0–2.3%). Mortality increased with age, but was not associated with sex.
Conclusion: Men have a higher risk for vasospastic AP caused admissions compared to women, but the observed sex-bias was smaller than in previous Japanese reports. Age-distribution of vasospastic AP patients in Finland was similar to that reported previously for Japan. In-hospital mortality for vasospastic AP is low.
Acknowledgement/Funding: Finnish Cardiac Society, Clinical Research Foundation of the Turku University Hospital

P6232 | BEDSIDE
Increased level of circulating glutamate and cystine in patients with coronary artery spasm

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Background: Glutathione (GSH), an important antioxidant restoring intracellular redox imbalance, is reported to attenuate coronary vasoconstriction to acetylcholine in patients with coronary spastic angina. GSH synthesis is dependent on the availability of the amino acid precursors such as glutamate, glycine, and cysteine. Because cystine levels are generally higher than cysteine levels in extracellular fluids, mechanisms for cystine uptake are also crucial for GSH biosynthesis. Cystine is taken up by the specific cystine/glutamate transport system (xc- transports), in association with the export of the same amount of glutamate. Extracellular glutamate competitively inhibits import of cystine. This could raise the possibility that potential role of plasma glutamate in coronary vasospasm might be modulated by plasma cystine level.
Aims: The aim of the study was to examine this possibility in clinical settings.
Methods: We evaluated consecutive 39 patients with chest pain at rest, who had not coronary stenosis nor structure heart disease. Coronary spasm provocation tests were performed by stepwise intracoronary acetylcholine administration (20 to 50 μg for right, 50 to 100 μg for left). Patients were categorized as test-positive if they developed angina with ECG changes accompanied with coronary vasospasm, defined as the transient or near total (>90%) occlusion. Blood samples were collected from aortic root to measure glutamate levels before procedure.
Results: Twenty-five patients were test-positive (spasm group) and 14 were negative (control group). Cystine levels in spasm group (32.5±10.3 nmol/ml) were significantly higher (p=0.018) than control (24.8±9.7 nmol/ml). Glutamate levels in spasm group (61.0±22.0 nmol/ml) were higher than control (48.1±23.1 nmol/ml), but did not reach statistical significance (p=0.06). To investigate influence of smoking, we divided both groups into current or ex-smokers (n=17) and non-smokers. Glutamate levels in non-smokers of control group (35.8±9.9 nmol/ml) were significantly lower (p<0.05) than other 3 groups (61.4±18.0 nmol/ml for non-smoker/spasm, 70.2±24.0 nmol/ml for smoker/control, 60.7±26.6 nmol/ml for smoker/spasm). Despite high glutamate levels in smoker of both groups, cystine levels were significantly higher in spasm group than that of control (34.7±12.5 nmol/ml v.s. 22.1±8.3 nmol/ml; p<0.05).
Conclusions: Increased level of plasma glutamate may play an important role in the pathogenesis of coronary artery spasm when associated with high cystine level.

P6233 | BEDSIDE
The predictive value of stress echocardiography. A real life study from a tertiary center

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Introduction: Stress echocardiography (SE) is a useful tool to diagnose coronary artery disease and guide patient management. In this study we aim to re-assess its predictive value with regard to patient outcomes
Methods: 912 consecutive patients who underwent SE (dobutamine or exercise) within a calendar year were included in the registry. All demographic data and the result of the SE were entered prospectively in electronic patient records. Follow-up data with regards to MACCE (cardiovascular mortality, cerebrovascular accident, documented myocardial infarction and any repeat revascularization) were recorded for a period of 12 months following the SE
Results: 27 patients had a non-diagnostic test and 17 did not have full demographic and follow-up data. For the remaining 868, the mean age was 61.07±12.26 years and 49.9% were male. In univariate analysis, male gender [Hazard Ratio (HR):3.66, 95% CI: 1.36–9.85; p=0.010), previous history of coronary artery disease (CAD) (HR: 4.07, 95% CI: 1.72–9.59; p=0.001) and the positive result of the test (HR: 5.15, 95% CI: 1.91–13.86; p=0.001) were correlated to MACCE. Hypertension (HR: 2.03, 95% CI: 0.75–5.47; p=0.161) was close to significant correlation with outcome. In a multi-variable model only the positive result of SE was found to be significantly related to MACCE (HR: 3.67, 95% CI: 1.32–10.21; p=0.013). Other known risk factors tested (age, diabetes, smoking, hyperlipidaemia and family history of CAD) did not show correlation with MACCE.

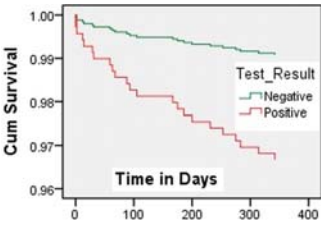

Fig. 1. MACCE survival curves

Conclusion: Our study shows that stress echocardiography is not only a useful diagnostic tool but also a strong predictor of patients' outcome. A positive stress echo result was the only predictor of 12-month MACCE. Patients with a positive test have a 3.7 -times higher risk of adverse outcome compared to those with a negative SE

P6234 | SPOTLIGHT
Clinical efficacy of a device to narrow the coronary sinus for the treatment of refractory angina a single center real-world experience

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Objective: The purpose of this study was to assess the clinical efficacy of the a device to narrow the Coronary Sinus (CS), the Reducerin a "real world" cohort of patients with refractory angina with no option for conventional revascularization methods.
Background: The CS Reducer is a new method to treat patients with refractory angina pectoris not eligible for conventional revascularization methods. The first-in-man experience with the CS Reducer in 15 untreatable chronic refractory angina patients showed feasibility of this technique and angina improvement in 80% of the patients. Recently, a randomized –sham-controlled trial in 104 "selected" patients with refractory angina confirmed the safety and efficacy of the Reducer as compared to placebo with clear benefits in terms of angina improvement. The device received CE-mark in 2013 and from 2014 CS Reducer procedures are carried out in our institute as a part of clinical care.
Methods: This is a single center retrospective registry to assess outcomes of the CS Reducer in "unselected" patients with refractory angina. Patients were treated if they showed any objective evidence of myocardial ischemia and no option for conventional revascularization. The primary end point of this study was angina improvement according to the Canadian Cardiovascular Society (CCS) classification.
Results: Twenty-three patients (74% male, mean age 69±9 years) with medically refractory angina (87% previous coronary artery bypass surgery, 48% previous myocardial infarction, 74% previous PCI, 52% diabetes mellitus) and no conventional revascularization options underwent CS Reducer implantation. Procedural success (defined as the successful placement of the device in the CS without any periprocedural adverse events) was 100%. After a median follow-up of 6 [IQR: 4–11] months there was a significant improvement in CCS class (baseline 3.35±0.49 versus 2.13±0.92 at follow-up, P=<0.001). The majority of patients (78%) experienced an improvement of clinical symptoms: 9 (39%) by 1 CCS class, 8 (35%) by 2 CCS classes and 1 (4%) by 3 CCS classes. There were 5 (22%) patients with no clinical CCS changes.
Conclusion: In this single center "real-world" experience, the CS Reducer demonstrated high efficacy in the treatment of refractory angina at mid-term follow-up.

P6235 | BEDSIDE
Nationwide trends in revascularization in patients referred to coronary angiography for stable angina

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Background: The current knowledge of nationwide trends in patients undergoing first coronary angiography (CAG) for stable angina is limited
Purpose: To describe changes over time in demographics and 30-days revascularization in patients undergoing first CAG due to stable angina and no prior events of ischemic heart disease.
Methods: Cross-linking nationwide registries, including data from the Danish Heart Registry, we identified a national sample aged ≥15 years in the time span between 2000 and 2011. Descriptive analyses were employed. The annual number of procedures (CAG, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) was adjusted for the national population growth in Denmark. Multivariate cox regression model was used to establish predictors of 30-days revascularization (PCI or CABG).
Results: Included were 21,127 patients who underwent first time CAG for stable angina. During the study period the average age in males and females increased from 60.0 [95% confidence interval (CI): 58.8–61.3] and 59.8 (95% CI: 59.3–61.3), respectively, to 62.4 (95% CI: 61.9–63.0) and 64.1 (95% CI: 63.4–64.7) years, respectively. Males constituted the majority (56.9%) of the study population. Compared to other national birth places, Danish born (89.1%) served the largest group. The adjusted annual number of CAG increased from 11.1 to 56.6 procedures per 100,000 inhabitants in males. The corresponding increase in females was from 6.3 to 39.2 procedures per 100,000 inhabitants. Similarly we observed an increase in 30-days revascularization in both genders: males 3.7–20.7 annual procedures per 100,000 inhabitants and females 1.0–7.3 annual procedures per 100,000 inhabitants. In multivariate analyses, age [hazard ratio (HR) 0.99; 95 CI: 0.99–0.99], female gender (HR: 0.94; 95% CI: 0.89–0.99), and treatment with either nitrates (HR: 0.90; 95% CI: 0.85–0.96), renin-angiotensin system inhibitors (HR: 0.93; 95% CI: 0.87–0.98), beta-blockers (HR: 0.93; 95% CI: 0.88–0.99)) or statin (HR: 0.90; 95% CI: 0.85–0.96) prior admission were associated with lower likelihood of 30-days revascularization.
Conclusion: Compared to their counterparts, women referred to CAG for stable angina were older and underwent less frequently CAG and subsequently 30-days revascularization. Furthermore, age and use of anti-ischemic drugs or drugs for event prevention were associated with lower likelihood of revascularization.

P6236 | BEDSIDE
Comparison of NICE and ESC risk scores for diagnosing stable coronary artery disease; is there a real-world consensus? A tertiary centre experience

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Purpose: The use of pre-test probability (PTP) risk scores is recommended by the European Society of Cardiology (ESC) and UK National Institute for Health and Care Excellence (NICE) guidelines on stable chest pain, to guide the choice of investigation. It is not known whether the two risk scores are equally predictive of coronary artery disease (CAD). We compared the two risk scores in patients who underwent stress echocardiography (SE) in a large UK tertiary centre
Methods: We investigated 912 consecutive patients referred for SE from January to December 2012. Presenting symptoms of chest pain were categorised as typical angina, atypical angina and non-cardiac chest pain. Age, gender and risk factors for CAD were recorded. The PTP risk score according to ESC and NICE Guidelines was calculated for each patient as was the recommended investigation.
Results: Out of 912 patients, 26 did not report symptoms and were referred for SE for other indications and were excluded. Mean age was 61.0±12.3 years. The mean NICE PTP risk score was higher compared to ESC score (61.7±29.8% vs 41.1% ± 23.0%; p<0.001). The recommended management by NICE and ESC guidelines was recorded for each patient and categorized in three groups (Table 1). They were compared to each other using Cohen's kappa, which showed only slight agreement (k = 0.05). Comparison of NICE vs ESC guidance for patients with low risk score for CAD, who do not need further investigation was 8.2% vs 12.8%; for patients in whom both guidelines recommend non-invasive tests was 36.5% vs 84.8% and for those in whom both guidelines recommend invasive tests was 55.3% vs ESC 2.4%.

Management according to ESC PTP score	Management according to NICE PTP score			
	No test	Non-invasive test	Invasive test	Total
No test	47	67	0	114 (12.8%)
Non-invasive test	26	256	469	751 (84.8%)
Invasive test	0	0	21	21 (2.4%)
Total	73 (8.2%)	323 (36.5%)	490 (55.3%)	886

PTP, pre-test probability.

Conclusion: This study has shown that the two risk scores have a systematic difference with NICE risk score overestimating risk compared to ESC risk score and hence the NICE guidelines lead to many more patients recommended to have an invasive strategy compared to ESC.

P6237 | BEDSIDE
Angiographic Gensini score predicts coronary plaque burden and components assessed by iMap-intravascular ultrasound in patients with stable angina pectoris

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Background: Gensini score (GS) is a simple and widely used angiographic tool for evaluating the severity of coronary artery disease (CAD). However, the angiographical assessment of CAD burden is challenged by under- or overestimation of atherosclerotic narrowing and diffuseness, and there are disparities between lesion severity determined by angiography and true atherosclerotic burden.
Purpose: The aim of this study was to determine whether GS can predict coronary plaque burden and its components evaluated by iMap-intravascular ultrasound (iMap-IVUS) system in patients with stable angina pectoris (SAP).
Methods: We enrolled 154 patients with SAP who underwent percutaneous coronary intervention (PCI) following iMap-IVUS analysis to culprit lesions. GS was calculated based on the coronary angiographic findings before PCI. Patients were divided into the following two groups according to median GS value: low-GS (n=78, score ≤34.5) and high-GS (n=76, score >34.5). Volumetric grayscale- and iMap-IVUS analysis was performed across the entire lesion segment. Plaque components were classified by iMap-IVUS as fibrotic, lipidic, necrotic and calcified, and each volume [fibrotic volume (FV), lipidic volume (LV), necrotic volume (NV) and calcified volume (CV), respectively] was reported as a percentage of the total plaque volume.
Results: Compared with patients with low-GS, those with high-GS had significantly greater plaque volume (103±52 vs. 86±43 mm^3, p=0.020), increased %plaque volume (69±10 vs. 64±10%, p<0.001), higher %NV (36±13 vs. 31±13%, p=0.016), and lower %FV (47±13 vs. 53±15%, p=0.025). The %LV and %CV values did not significantly differ between the groups. The GS correlated positively with plaque volume (r=0.28, p<0.001), %plaque volume (r=0.36, p<0.001), %NV (r=0.21, p=0.011), and inversely with %FV (r=–0.20, p=0.011). In linear regression analysis, the presence of high-GS was significant factor associated with %NV (standardized coefficient β = 0.17, p=0.037) and %FV (β = –0.17, p=0.041) after adjustment for age, hypertension, hypercholesterolemia, diabetes, estimated glomerular filtration rate, and statin use.
Conclusion: High-GS was associated with increased plaque burden with greater %NV and smaller %FV. These findings suggest that GS can serve as a predictor of coronary plaque burden and its components.

P6238 | BEDSIDE
Impact of moderate vasomotor response to acetylcholine provocation test on long-term prognosis

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Background: Acetylcholine provocation test (Ach-test) has been performed for the diagnosis of vasospastic angina (VSA). However we experience the cases showing moderate spasm without reaching a definite diagnosis of VSA, whose clinical significance has not been elucidated. The aim of this study was to assess the impact of moderate coronary vasomotor responses to Ach-test on long-term prognosis.
Methods: A total of 283 consecutive patients who underwent Ach-test for suspected VSA were retrospectively investigated. The degree of coronary spasm was evaluated by epicardial coronary artery diameter reduction compared with the relaxed state achieved with the intracoronary administration of Isosorbide dinitrate. Patients were divided into 3 groups according to the diameter reduction during Ach-test: severe spasm (SS) showing $\geqq$75% diameter reduction; moderate spasm (MS) showing $\geqq$50% diameter reduction; or the others (N) regardless of the symptoms and ECG changes. Major adverse cardiac events (MACE) included cardiac death, myocardial infarction, coronary revascularization, fatal arrhythmia, and congestive heart failure. MACE rate was compared among the 3 groups.
Results: We excluded the patients with catheter-induced spasm (n=6). Therefore, 277 patients with median follow-up of 4.7 years were investigated: 85 were categorized in SS; 91 were in MS; and 101 were in N. For the treatment of coronary spasm, calcium channel blockers and long acting nitrate were used more frequently in SS and MS compared with N, whereas there was no significant difference in terms of medication between SS and MS. In Kaplan-Meier analysis, the incidences of MACE in the SS, MS, and N were 9.4%, 7.7%, and 1.0% respectively (P=0.028). Cox regression analysis revealed that the degree of spasm by Ach-test remained an independent predictor of MACE even after adjustment with other confounders (HR: 2.32, 95% CI: 1.03–5.30, P=0.043).
Conclusions: Patients with moderate spasm by Ach-test had a comparable cardiac event rate with those with severe spasm, which is significantly worse than those with normal vasomotor response. Moderate spasm should be identified as a risk group requiring an aggressive treatment strategy.

P6239 | BEDSIDE
Ultrasensitive troponin assay predicts cardiac stress and diastolic function

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Aims: Novel ultrasensitive troponin-I assay comprises a feasible alternative approach to monitor cardiac stress. However, physiological and clinical relevance of hs-TNI values in the normal range remains incompletely examined.
Methods: Four hundred patients undergoing myocardial perfusion scintigram were recruited and adenosine-assisted coronary flow reserve (CFR) and cardiac stress-echocardiography test performed. Ultrasensitive Troponin-I assay using microparticle-based immunoassays and single molecule counting technology was used to measure troponin-I levels. (LLoQ of 0.4 pg/mL, compared to typical hospital lab tests with a LLoQ at 100pg/mL). Correlation analysis was done among patients with TNI levels below 4.6 pg/ml (normal range).
Results: TNI levels were strongly related to systolic volume ($p<0.0001$, r=0.4) and ejection fraction ($p<0.0001$, r=–0.37). Further, TNI levels were correlated to coronary flow reserve ($p<0.001$, r=–0.19) as well as stress diastolic function ($p<0.0001$, r=–0.27). In a multivariate analysis adjusting for hypertension, age and EF both CFR and hyperemic diastolic relaxation velocity remained independently associated with hs-TNI levels.
Conclusion: TNI as measured using this ultrasensitive assay predicts microvascular function, systolic and diastolic function in CV patients.

ANGINA PECTORIS STABLE III

P6240 | BEDSIDE
Comparison of coronary artery disease consortium 1, 2 and duke clinical score to predict obstructive coronary disease by coronary angiography

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Introduction: The first step in evaluating a patient with suspected coronary artery disease (CAD) is the determination of the pretest probability. The european society of cardiology guidelines recommends the use of CAD consortium 1 score (CAD1), that is a modified version of Diamond and Forrester model, which does not include modifiable cardiovascular risk factors. On the contrary, the CAD consortium 2 score (CAD2) and the Duke clinical score (DCS) includes those risk factors.
Purpose: Our aim was to compare the accuracy of those scores in the prediction of CAD in a population referred to invasive coronary angiography.
Methods: We included all patients referred to invasive coronary angiography for suspected CAD between January 2008 and December 2012 (n=2234). The pretest likelihood of CAD was estimated using CAD1, CAD2 and DCS. The presence CAD was defined as stenosis of more than 50% in at least one major epicardial vessel. The performance of those scores was evaluated by the area under the receiver operating characteristic curve.
Results: The observed mean age was 63.7 years and 32.5% were females. The majority (66.9%) was referred for typical angina (13.7% with atypical angina). The prevalence of CAD was 58.5% and the estimated prevalence was 71.1% (DCS), 63.5% (CAD1) and 41.5% (CAD2).
In patients with CAD the pretest likelihood was estimated above 85% in 54.3% using DCS, 21.1% using CAD1 and 1.4% by CAD2. On the other side, in patients without CAD the pretest likelihood was below 15% in 9.9% of cases estimated by DCS, 3.8% using CAD1 and 27.8% by CAD2.
The area under the curve was 0.685 for DCS, 0.664 of CAD1 and 0.683 for CAD2, with a statistical significant difference between CAD1 and the other two ($p<0.001$). The net reclassification improvement was 20% for DCS, related to adequate reclassification of 38.4% patients with CAD to a higher risk category, and 5% for CAD2, at the cost of adequate reclassification of 69.7% of patients without CAD to a lower risk category.
Conclusion: The estimation of likelihood pretest of CAD using scores that include modifiable cardiovascular risk factors (CAD2 and DCS) seems to improve the accuracy in comparison to CAD1. Our results suggest that, in this population, DCS may better identify patients at higher risk and CAD2 may better predict those at lower risk for CAD.

P6241 | BEDSIDE
Translating clinical trial results into clinical practice for patients with diabetes and multivessel coronary artery disease in British Columbia: A population-based study

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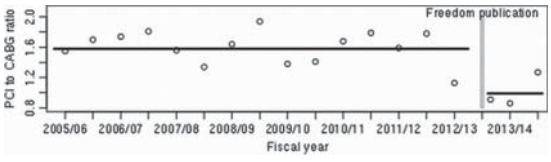
Background: Randomised Clinical Trials are the main tool used by health scientists to test and evaluate interventions. The Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, published in Nov/2012 demonstrated superiority of coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) in pts with diabetes (DM) and multivessel coronary artery disease (CAD). We assessed the impact of the FREEDOM trial results in British Columbia, Canada (BC).
Methods: We identified all BC pts with DM in the provincial cardiac registry, from 04/2005 to 03/2014, undergoing PCI or CABG for multivessel CAD at sites capable of perfoming both PCI & CABG. Patients were selected using the FREEDOM trial inclusion/exclusion criteria. A ratio (PCI:CABG) was calculated with 95% confidence interval (CI)for the time periods pre & post-publication of the FREEDOM trial.
Results: A total of 6008 revascularization procedures made up the final group with 60% undergoing PCI. The pre & post-publication cohorts consisted of n=5193 (86%) & n=815 (14%) respectively. Cohorts were well matched for age, sex, CAD risk factors, LVEF, renal insufficiency, indication and urgency of revascularization. The PCI to CABG ratio during the pre & post-publication time periods was 1.58; 95% CI, (1.49–1.67) and 0.99; 95% CI, (0.85–1.13) respectively. The figure below shows the PCI:CABG ratio by 6 month intervals.



Conclusion: In this first "real world" experience of revascularization in DM pts with multivessel CAD post-FREEDOM, there has been a marked increase in the proportion of pts undergoing CABG in BC. The result of the FREEDOM trial has led to significant changes in practice. These findings will have significant resource allocation implications.

P6242 | BEDSIDE

Assessment of the relationship between serum visfatin levels and presence and extension of the coronary slow flow phenomenon

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Background: The coronary slow flow (CSF) phenomenon is a delayed antegrade progression of contrast agent to the distal branch of a coronary artery in the absence of obstructive coronary artery disease (CAD). Levels of visfatin, a novel adipocytokine, are reported to be increased in atherosclerosis, obesity, and type 2 diabetes.
Purpose: The aim of the present study was to investigate the relation between CSF and visfatin in patients who underwent elective coronary angiography for suspected CAD.
Methods: A total of 140 participants were recruited and were divided into two groups according to their coronary flow rates: 90 patients with isolated CSF and 50 control participants with normal coronary flow. Coronary flow was quantified by thrombolysis in myocardial infarction (TIMI) frame count (TFC).
Results: Serum visfatin levels were higher in the CSF group compared with the controls (3.29±1.11 vs. 2.70±1.08 ng/mL, p=0.003). A significant correlation was found between TFC and visfatin (r=0.535,p<0.001). The area under the receiver operating characteristic curve was 0.720 (95% confidence interval, 0.622–0.817,p<0.001) for visfatin in the diagnosis of CSF. If a value of 2.59 ng/mL was used as cutoff, higher levels of visfatin could predict the presence of CSF with 78.9% sensitivity and 64.0% specificity (Figure).

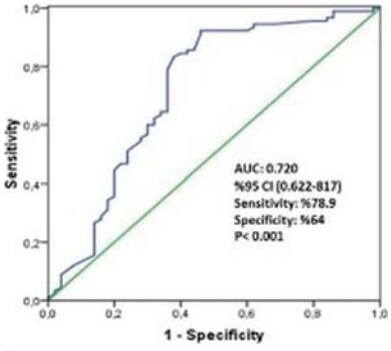

Figure 1

Conclusion: This is the first study to demonstrate the significant association between increased serum visfatin levels and the presence and extent of CSF. We conclude that visfatin levels might be a useful biomarker for predicting CSF in patients who undergo diagnostic coronary angiography.

P6243 | BEDSIDE

Inflammatory mediators TIMP-1 and MMP-8 as prognostic markers for mortality in cardiac patients and TIMP-1 as indication of a vulnerable coronary plaque

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Introduction: In coronary artery disease (CAD) rupture of an atherosclerotic coronary plaque and ensuing thrombosis of an epicardial coronary artery cannot be predicted by coronary angiogram (CA), since a vulnerable plaque may not present as a significant stenosis in CA. Hence, a marker of intracoronary vulnerability is desired.
Purpose: We hypothesised that inflammatory mediators matrix metalloproteinase 8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) would be of prognostic value in CAD.
Methods: Serum samples were obtained in conjunction with coronary angiogram (CA) in 1627 successive patients scheduled for elective CA on clinical basis. Concentrations of MMP-8 and TIMP-1 were measured using enzyme-linked immunosorbent assay (ELISA). CA verified CAD in 974 patients, and no significant coronary stenosis in 653 patients (no-CAD). Patients were followed on average 7 years for mortality.
Results: In the CAD patient group 198 (20%) patients died during follow up. TIMP-1 and MMP-8 were significantly higher in the patients who died, than those who survived the follow up-period (169±70 ng/ml and 64±94 ng/ml vs. 140±44 ng/ml and 44±52 ng/ml, respectively, p<0,001). In the no-CAD patient group 61 (9%) patients died during follow up. MMP-8 was significantly higher in those who died vs. those who survived the follow up-period (74±83 ng/ml vs 44±45 ng/ml, respectively, p<0.001), whereas TIMP-1 showed no difference between the groups (154±64 ng/ml vs 146±42 ng/ml, respectively, p=0,535).
Conclusion: Inflammatory marker TIMP-1 is a prognostic marker of long term survival in patients with CAD. MMP-8 is a prognostic marker of death, irrespective

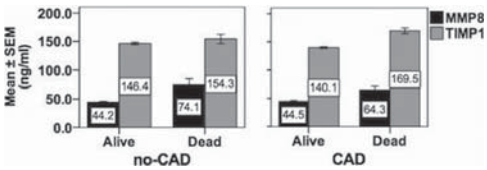

Figure 1

of coronary status. TIMP-1 may, thus reflect a vulnerable plaque situation, and call for more intensive treatment in patients with CAD.
Acknowledgement/Funding: Finnish-Norwegian Medical Foundation

P6244 | BEDSIDE

Incremental value of B-type natriuretic peptide for detection and risk reclassification of obstructive coronary artery disease on computed tomography angiography

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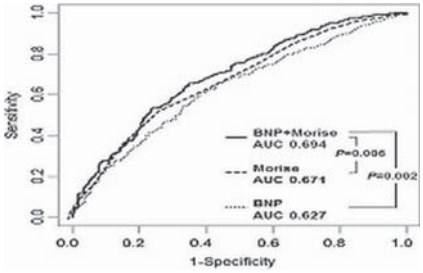
Background: B-type natriuretic peptide (BNP) is well known to increase as a result of left ventricular systolic dysfunction and is a useful diagnostic marker for heart failure. Whether BNP is associated with obstructive coronary artery disease (CAD) on computed tomography angiography (CTA) is unknown.
Methods and results: A consecutive 944 patients with suspected CAD underwent 64-slice CTA in our institution between 2008 April and 2013 October. Obstructive CAD was defined as ≥50% luminal narrowing. We divided the patients into 4 groups according to BNP quartile (Q1, <10.8 pg/ml; Q2, 10.8–21.8 pg/ml; Q3, >21.8–41.1 pg/ml; Q4, >41.1 pg/ml). The presence of any plaques was detected in 579 patients (61.0%), and obstructive CAD was found in 275 (28.6%) patients. In multivariate logistic analysis, BNP Q3 and Q4 were associated with obstructive CAD, as compared with Q1 (Q3; odds ratio [OR], 2.02; 95% confidence interval [CI], 1.16–3.53; P=0.013 and Q4; OR, 2.66; 95% CI, 1.53–4.63; P<0.001). Analyzing the incremental value of the Morise pre-test score and BNP for predicting obstructive CAD, the predictive value of the Morise pre-test score (area under the curve [AUC], 0.671) could be increased by BNP (AUC 0.694 for the combined model; P=0.006). Addition of BNP to a model containing the Morise pre-test score resulted in continuous net reclassification improvement of 0.30 (95% CI, 0.17–0.44; P<0.001) for the prediction of obstructive CAD.



AUC for detecting obstructive CAD

Conclusions: BNP might provide an incremental improvement in the detection of obstructive CAD on CTA when combined with a conventional cardiovascular risk score.

P6245 | BEDSIDE

Ivabradine reduces post-ischemic stunning in patients with exercise-inducible ischemia assessed by longitudinal strain

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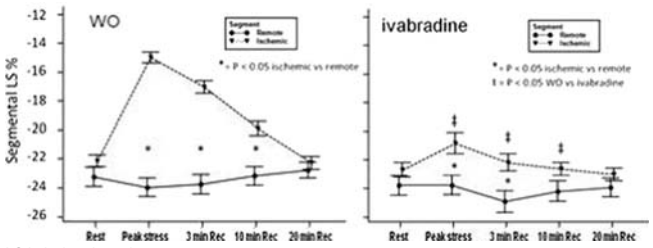
Background: Ivabradine is an effective treatment for stable coronary artery disease (CAD) and heart failure. Experiments in a canine model have shown that ivabradine reduces both acute left ventricular (LV) dysfunction (DYS) and post-ischemic stunning (PIS). Aim of this study was to investigate the effect of ivabradine on LV-DYS and PIS in patients with CAD.
Methods: We studied 15 patients (66±7 years) with exercise inducible ischemia, ejection fraction >40% and heart rate (HR) >70 bpm. After pharmacologic washout (WO), echocardiography was performed at rest, at peak treadmill exercise and during recovery until return to baseline. After 2 weeks of ivabradine (7.5 mg bid) stress echocardiography was repeated at the same workload achieved during WO. Peak global and segmental (ischemic vs. remote normal segments) LV longitudinal strain (LS) were assessed by 2D speckle tracking analysis.
Results: At WO LS was significantly impaired in ischemic segments compared to remote at peak stress and for several minutes during recovery. In contrast, after ivabradine no significant change in LS was observed in ischemic segments either at peak or during recovery (Figure). Similarly, after treatment global LS at peak

stress was significantly improved (–20% vs –22%; p=0.03). Blood pressure was unchanged after ivabradine whilst HR was reduced both at rest and at peak stress (both p<0.05).



LS in ischemic and remote segments

Conclusion: Ivabradine reduces acute LV-DYS and PIS in patients with exercise-inducible ischemia. We hypothesize that this mechanisms might contribute to reduce chronic LV-DYS in patients with CAD treated with ivabradine. In this setting the drug might limit the development of hibernating myocardium (i.e. chronically dysfunctional, but viable tissue) which is believed to result from repeated episodes of ischemia and stunning.

Acknowledgement/Funding: Partly supported by an unresctricted grant of Servier International

P6246 | BEDSIDE
Prevalence and prognostic significance of preprocedural high-sensitivity cardiac troponin elevation among patients with stable coronary artery disease undergoing percutaneous coronary intervention

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Background: High-sensitivity cardiac troponin assays enable the accurate and rapid diagnosis of myocardial infarction (MI) among patients with suspected acute coronary syndromes. The prevalence and prognostic significance of pre-procedural high-sensitivity cTnT elevation among patients with stable coronary artery disease (CAD) scheduled to undergo PCI is unknown.
Purpose: The aim of the present study was to determine the prevalence of pre-procedural hs-cTnT elevation in unselected patients undergoing PCI for stable or silent angina, and to investigate the association between elevated hs-cTnT levels prior to the procedure and one year clinical outcomes.
Methods: Between March 2009 and November 2013, 8605 consecutive patients undergoing PCI were prospectively included in the Bern PCI Registry (NCT02241291) and followed for one year. The Roche hs-cTnT assay was introduced in August 2011. The following 3 inclusion criteria were applied for the present study: 1. Stable CAD or silent ischemia. 2. CKMB level <1 of the upper limit of normal (=ULN, 0.014 mcg/L) before PCI. 3. Availability of hs-cTnT levels before PCI. We compared all cause mortality between patients with versus without increase in hs-cTNT (>ULN) before PCI and assessed whether hs-cTNT is a predictor of mortality after correction for age, gender, smoking, diabetes and renal function.
Results: Among 1721 patients fulfilling these criteria, 436 patients (25.3%) had baseline hs-cTnT level >1 ULN and 1285 (74.7%) patients had baseline hs-cTnT level ≤1ULN. Patients presenting with elevated hs-cTnT levels were older, more frequently men, diabetic, and had more often renal failure. At 1 year, patients with preprocedural hs-cTnT >ULN had significantly increased all-cause (7.6% vs. 1.5%, HR 5.37, 95% CI 3.02–9.57, p<0.001) and cardiac mortality (3.2% vs. 0.7%, HR 4.35, 95% CI 1.86–10.17, p=0.001). hs-cTnT remained an independent predictor of mortality at one year (adjusted HR 2.08, 95% CI 1.00–4.30, p=0.049) after correction for baseline demographic and cardiovascular risk factors.
Conclusion: Baseline elevation of hs-cTnT concerns 1/4 of patients undergoing PCI for stable CAD and independently predicts all-cause mortality. Routine assessment of hs-cTnT prior to PCI in patients with stable CAD or silent ischemia identifies a population at increased risk for adverse clinical outcomes, which may have important implications for long-term secondary prevention.

P6247 | BEDSIDE
Poor performance of guidelines endorsed CAD prediction tool results in overdiagnosis of CAD risk in patients investigated for chest pain. A single centre experience in a large cohort of patients

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Background: An optimal investigation strategy for patients with suspected AP remains elusive. UK guidelines (NICE 2010) use an historical prediction model to estimate the CAD likelihood using symptom characteristics and risk factors profile. The prediction models in use may grossly overestimate CAD prevalence in today patients.
Purpose: Prospective study to assess the actual versus predicted CAD prevalence in CP patients, as documented by either angiographic obstructive CAD or a positive functional test.
Methods: We reviewed 964 consecutive CP clinic patients (age: 57±13 years). Using the NICE model, patients were assigned to an estimated CAD likelihood group: <10% (Gr. A), 10–29% (Gr. B), 30–60% (Gr. C) and >60% (Gr. D). Discharge or referral to Ca scoring, functional testing or angiography were decided upon based on the expected CAD likelihood, as per a nationally endorsed algorithm.
Results: 515 pts. (53%) had non-anginal CP, 239 pts. (25%) had atypical AP and 210 (22%) had typical AP. 208 pts. (21%) were assigned to group A, 202 pts. (21%) to group B, 238 pts. to group C (25%) and 316 pts. (33%) to group D. 324 patients (34%) were discharged and 640 pts. (66%) were further investigated for possible CAD. Investigations results are available for 536/640 patients (84%). The actual prevalence of positive CAD findings as compared with the expected one is detailed in table 1.

Table 1

Predicted prevalence	Actual no. of CAD pts.	Actual CAD prevalence (%)	p
Group A: <10% (n=46)	4	8.6	ns
Group B: 10–29% (n=111)	12	10.8	0.05
Group C: 30–60% (n=159)	33	20.7	<0.01
Group D: >60% (n=220)	63	28.6	<0.01

For the whole sample the actual prevalence of CAD was only 112/536 (20.8%) vs. an expected one of 285/536 (53.1%), p<0.01
Conclusions: 1) The CAD prevalence in patients referred for suspected AP is significantly lower than expected by using accepted historical models.
2) The model is accurate for low risk patients but it increasingly overestimates the actual prevalence as the predicted probability increases.
3) The use of historical CAD prediction models may result in overuse of costly diagnostic strategies in patients perceived to be at ≥ moderate risk of CAD.
4) The results emphasise the need to develop new/updated prediction models.

P6248 | BEDSIDE
Soluble vascular endothelial growth factor receptor-1 levels in serum collected from arterial catheter sheath are inversely associated with cardiovascular events in combination with the SYNTAX score

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Background: Vascular endothelial growth factor (VEGF) plays a role in endothelial integrity. The soluble VEGF receptor-1 (sVEGFR-1) is an endogenous inhibitor of VEGF. The association between circulating sVEGFR-1 levels and cardiovascular events has been controversial, and it may depend on how to collect blood samples.
Methods and results: We performed a prospective cohort study involving 417 inpatients who attended for elective coronary angiography (CAG) for the first time. Blood samples were collected from the arterial catheter sheath at the beginning of CAG. Serum levels of high-sensitivity C-reactive protein (hsCRP), VEGF, and sVEGFR-1 were measured. The SYNTAX score of angiographic complexity and severity of coronary artery disease was evaluated. Patients were followed up over 1 year. The primary outcome was major adverse cardiac events (MACEs). The median follow-up was 360 (IQR, 26–360) days. During the follow-up period, a total of 149 patients (35.7%) developed MACEs. Patients were divided into two groups based on the median of each biomarker. In Kaplan-Meier analyses, low-sVEGFR-1 (P=0.0011 by log-rank test), but not high-hsCRP or high-VEGF, was significantly associated with the risk of MACEs. Multivariate Cox proportional hazard analyses revealed that the SYNTAX score (hazard ratio [HR], 2.1 per 1-SD increase; 95% confidence interval [CI], 1.8–2.3; P<0.0001) was positively, and levels of sVEGFR-1 (HR, 0.19 per 1-SD increase; 95% CI, 0.05–0.54; P=0.0001), but not hsCRP or VEGF, were inversely, and significantly associated with MACEs after adjustment for established risk factors. Finally, we performed multivariate Cox proportional hazard analysis including data on age, gender, systolic blood pressure, low-density-lipoprotein cholesterol, high-density-lipoprotein cholesterol, diabetes, history of smoking, the SYNTAX score, and sVEGFR-1 levels. Notably, the SYNTAX score (HR, 1.99; 95% CI, 1.76–2.26; P<0.0001) and the sVEGFR-1 level (HR, 0.28; 95% CI, 0.07–0.76; P=0.004), but not other factors, were independently associated with MACEs.
Conclusions: The sVEGFR-1 level in serum, collected from arterial catheter sheath at the beginning of CAG, may serve as an inverse predictor of MACEs in combination with the SYNTAX score.

P6249 | BEDSIDE
Correlation of rise in high sensitive troponins following positive exercise testing with underling coronary artery disease

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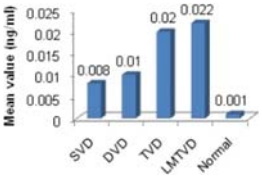
Background: Cardiac troponins are sensitive markers of acute myocyte injury. Recent studies with high sensitive cardiac troponins (hs-TnT) assays have shown prognostic value even in chronic stable angina. It seems plausible that subjects

with reversible myocardial ischemia during exercise stress testing have a release of hsTnT that is greater than the release seen in subjects with positive stress test but without ischemia.
Purpose: The objectives of the study were to correlate the rise of circulating hsTnT post exercise treadmill testing with underlying coronary artery disease (CAD) presence & severity.
Methods: 99 subjects of suspected stable angina with positive exercise TMT test were enrolled. Blood samples was obtained before the TMT and again 20 hr after peak exercise and samples were analyzed for troponins using a high sensitive assay.Coronary anatomy was determined by invasive coronary angiography.
Results: There was significant increase in mean hsTnT levels following a positive exercise TMT (0.009±0.012 ng/ml, p=0.0001).The rise in hsTnT levels were significant only in patients obstructive CAD versus those with normal coronaries (p=0.0001). The elevation in hsTnT in subjects with single vessel, double vessel, triple vessel & left main-triple vessel CAD were 0.008±0.007 ng/ ml, 0.010±0.012 ng/ml, 0.020±0.015ng/ml, 0.22±0.015 ng/ml respectively.Males had more hsTnT rise (p=0.003). Smoking, diabetes and hypertension did not affect the troponin rise.



Mean tropinin rise and severity of CAD

Conclusion: In patients of stable angina, the rise in hsTnT from baseline after a positive stress test predicts the presence underlying of coronary artery disease and that the degree of rise correlates with the severity of disease conversely. Absence of elevation in hsTnT may indicate a normal anatomy despite a positive stress test.

INFLAMMATION AND IMMUNITY I

P6250 | BEDSIDE
Monocyte chemoattractantprotein-1 (MCP-1) as an independent predictor of coronary artery ectasia

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Inotroduction: Coronary artery ectasia (CAE) is an infrequent finding that confers an adverse prognosis. Nonetheless, its pathophysiology is poorly understood, although several theories have been suggested, including inflammation.
Purpose: To assess a possible association of several biomarkers related to inflammation, atherothrombosis and myocardial damage with the presence of CAE.
Methods: We studied 270 patients with coronary disease that had an acute coronary syndrome (ACS) 6 months before and underwent coronary angiography (CA).Clinical variables were recorded and plasma levels of the following biomarkers were determined: monocyte chemoattractantprotein-1 (MCP-1), soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK), galectin-3, neutrophil gelatinase associated lipocalin (NGAL), N-terminal fragment of brain natriuretic peptide (NT-proBNP) and high-sensitivity C-reactive protein. All CA were reviewed by two experienced interventional cardiologists and were diagnosed with CAE or not, according to published criteria. All variables were analyzed with binary logistic regression, taking the presence of CAE as dependent variable. Thereafter, we constructed a multivariate model including all variables with level of significance $p<0.2$ and then, we removed all variables with $p>0.2$. The final model included all the significant variables, whose effect is presented as odds ratio (OR) for CAE with its 95% confidence interval (95% CI).
Results: Twenty-three (8.5%) patients had CAE. They were more frequently male (91 vs 64%), had more hyperlipidemia (83 vs 47%), larger body-mass index (30.8 vs 28.4) and higher triglyceride (155 vs 112 mg/dL), low-density lipoprotein (93 vs 79 mg/dL) and MCP-1 (206 vs 152 pg/mL) plasma levels. We did not found any other significant difference between groups. At multivariate regression analysis, MCP-1 was the strongest predictor of CAE (OR=1.55 for each increase of 50 pg/mL [95% CI: 1.19–2.00; p=0.001]) along with male sex (OR=6.34, 95% CI: 1.31–30.75, p=0.005), hyperlipidemia (OR=6.3, 95% CI: 1.74–22.79; p=0.001) and NT-proBNP (OR=0.89 for each increase of 100 pg/mL, 95% CI: 0.76–1.00; p=0.045).
Conclusion: This is the first report of an independent association between MCP-1 plasma levels and CAE. Further studies are needed to assess a potential role of this pro-inflammatory molecule in the development of CAE.

P6251 | BEDSIDE
Allergic inflammation is associated with coronary instability and a worse clinical outcome after acute myocardial infarction

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Background: Plaque rupture with activation of inflammatory cells and thrombus formation is the most frequent mechanism causing acute coronary syndromes (ACS). However, the role of allergic inflammation in ACS has not been clearly defined so far.
Purpose: The aim of this study was to assess eosinophil and basophil activation in ACS and the prognostic role of eosinophil cationic protein (ECP) in ST elevation myocardial infarction (STEMI).
Methods: In a cross-sectional study, we prospectively enrolled 51 patients undergoing percutaneous coronary intervention (PCI) [60.8% patients with ACS and 39.2% with stable angina (SA)]. Flow cytometry analysis assessed CD66b, CD69 and CD203c median fluorescence intensity expression. In a longitudinal study, 181 patients presenting with STEMI, undergoing primary PCI, were prospectively enrolled with a follow-up of 24 months. The endpoints of the study were the composite of cardiac death, recurrent myocardial infarction (MI), and target lesion revascularization (TLR), all defined as major adverse cardiac events (MACEs).
Results: Eosinophil activation (CD66b) was similar in patients with ACS and SA [6.61 (4.91–7.72) vs 6.62 (5.27–8.73), p=0.63], while eosinophil degranulation (CD69) and basophil activation (CD203c) were higher in ACS patients compared to SA patients, [1.38 (1.16–1.52) vs 1.17 (1–1.31), p=0.01], [0.97 (0.89–1.11) vs 0.92 (0.87–0.95), p=0.03], respectively. ECP serum levels were significantly higher in STEMI patients with MACEs as compared to those without [21.1 (10.37–25.65) vs 7.83 (3.37–12.8) μg/l, p=0.01] and in patients with thrombus score>3 compared with those with thrombus score ≤3 [15 (9.88–24.7) vs 5.21 (3.46–22.96) μg/l, p=0.006]. ECP serum levels predicted occurrence of MACEs during follow-up (OR=1.041, 95% CI 1.012–1.071, p=0.005), while CRP serum levels showed a borderline statistical significance (OR=0.904, 95% CI 0.806–1.014, p=0.085).
Conclusions: These findings are the first demonstration of in vivo eosinophil degranulation and basophil activation during ACS and of the prognostic role of ECP after STEMI.

P6252 | BENCH
Functional mannan-binding lectin deficiency is not associated with improved outcome in comatose survivors of out-of-hospital cardiac arrest

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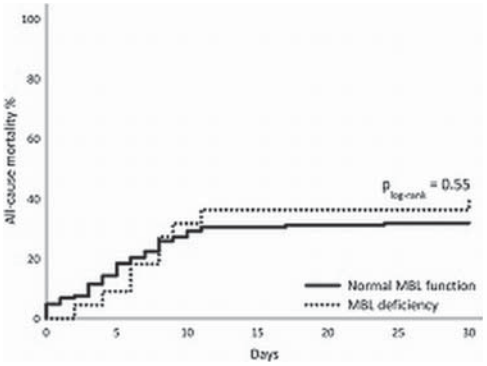
Introduction: The mannan-binding lectin (MBL) complement pathway may play a role in the systemic ischemia and reperfusion injury in post-cardiac arrest syndrome (PCAS). Functional MBL deficiency has been associated with favorable outcome in stroke patients, however the importance of MBL deficiency in PCAS patients is not known.
Methods: In a single center post-hoc analysis of the Target Temperature Management (TTM) trial, we studied MBL levels in 169 consecutive patients randomly assigned to TTM at 33°C or 36°C for 24 hours. At baseline and 24, 48 and 72 hours we measured MBL concentrations. MBL deficiency was defined as plasma levels ≤100 ng MBL/ml at baseline. Primary outcome was 180 days mortality and secondary outcome was favorable neurological outcome assessed by Cerebral Performance Category (CPC1–2) and modified Rankin Scale (mRS0–3).
Results: MBL deficiency was found in 22 (13%) patients. Age, sex, initial rhythm, time to ROSC or lactate levels at admission was not significantly different between MBL sufficient and MBL deficient patients. There was no overall difference in MBL levels between the two temperature groups (p=0.67).
Patients with MBL deficiency carried a 30-day mortality of 41% compared to 32% in MBL sufficient patient, p=0.55 (Figure) with no significant difference in neu-



Mortality curves for MBL deficiency

rological outcome assessed by CPC (p=0.69) and mRS (p=0.91). MBL level at baseline was not associated with neurological outcome, CPC (OR=0.94 (95% CI: 0.7–1.3), p=0.71) or mRS (OR=0.98 (95% CI: 0.7–1.3), p=0.88) when adjusting for potential confounders.
Conclusions: In PCAS patients, MBL deficiency was not associated with lower mortality or improved neurological outcome. In MBL sufficient patients, baseline MBL levels was not associated with neurological outcome.

P6253 | BEDSIDE
Leukocyte characteristics improve prediction of mortality after coronary angiography

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Background: Inflammation and leukocyte infiltration are hallmarks of atherosclerosis. Leukocyte characteristics are routinely analyzed in clinical laboratories and thus readily available. In this study we hypothesized that these characteristics associate with coronary artery disease (CAD) severity and mortality in coronary angiography patients.
Methods: Patients suspected of CAD undergoing coronary angiography (n=1,114) were enrolled in the UCORBIO cohort and included in the current study. Leukocyte properties were assessed in blood drawn directly prior to angiography. Angiographic CAD severity was quantified by SYNTAX score where possible (n=617). Multivariable linear regression was performed to assess the association of leukocyte markers with SYNTAX score. Multivariable Cox regression analysis was used to test the association of leukocyte markers with all-cause and cardiovascular mortality and the additive value of leukocyte markers was analyzed by assessing the improvement of the basic Cox model. Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) analyses were additionally performed.
Results: Leukocyte markers associated significantly with SYNTAX score. Monocyte-to-lymphocyte ratio (MLR) showed the strongest predictive value (HR 1.43 [1.23–1.68], p<0.001) for all-cause and cardiovascular mortality (HR 1.54 [1.22–1.95], p=0.001). Furthermore, higher variation in neutrophil complexity had additive value on top of the SYNTAX score for prediction of all-cause mortality (HR 1.58 [1.15–2.17], p=0.006). The IDI (0.05 [0.01–0.10], p=0.007) AND NRI (0.23 [0.07–0.41], p=0.02) of MLR were substantial and significant, confirming its clinical usefulness in mortality prediction.
Conclusion: Leukocyte characteristics, especially MLR, are strongly associated with mortality in patients undergoing coronary angiography. Readily available leukocyte characteristics from routine hematology analyzers thus may serve as clinically applicable biomarkers for mortality risk prediction in angiography patients.

P6254 | BEDSIDE
Prognostic significance of carotid artery inflammation in patients with coronary artery disease

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Background: Carotid atherosclerosis is a major cause of stroke. Inflammation is associated with the progression and destabilization of atherosclerotic plaques in both coronary and carotid arteries, leading to cardiovascular events. Microwave radiometry (MWR) allows the rapid, in vivo, noninvasive assessment of the internal temperature of carotid arteries, reflecting local inflammation.
Aim: The aim of the present study was to evaluate the prognostic role of carotid atherosclerotic plaque temperatures in patients with documented coronary artery disease (CAD).
Methods: Consecutive patients with significant CAD (≥50% stenosis in at least one major epicardial vessel) were included in the study. Both carotid arteries of all patients were evaluated by 1) carotid ultrasound and 2) microwave radiometry (MWR). Maximum carotid plaque thickness was assessed in all carotids during the ultrasound study. Temperature difference (ΔT) by MWR was assigned as maximal temperature along the carotid artery minus minimum. ΔT ≥0.90°C was assigned as high ΔT. Major cardiovascular event (MACE) was defined as death, stroke, myocardial infarction or revascularization. All patients were followed-up clinically for one year.
Results: In total 154 patients with documented CAD were included in the study. Twenty five patients (16.2%) had high ΔT temperatures bilaterally. MACE was 28% in the group with bilateral high ΔT and 4.7% in non-high ΔT group (p<0.001). By multivariate logistic regression analysis, ΔT was an independent predictor for MACE, when adjusted for sex, age contemporary risk factors, number of vessels with significant stenosis and maximum carotid plaque thickness (OR: 15.76, 95% CI 2.88–86.30, p=0.001). In Kaplan-Meier plots patients with bilateral high ΔT showed higher event and mortality rates, compared with patients in non-high ΔT group (log-rank p=0.001 for both comparisons).
Conclusion: Bilateral high carotid artery temperatures are associated with increased one-year rates of cardiovascular events in patients with CAD. A long term study is warranted to establish the prognostic impact of MWR in this high-risk population.

P6255 | BEDSIDE
Monocyte subset distribution in patients with stable atherosclerosis and elevated levels of lipoprotein(a)

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Purpose: Lipoprotein(a) is a pro-atherogenic plasma lipoprotein currently established as an independent risk factor for the development of atherosclerotic disease and as a predictor for acute thrombotic complications. Today, atherosclerosis is considered to be an inflammatory disease of the vessel wall in which monocytes and monocyte-derived macrophages are crucially involved. Circulating monocytes can be divided according to their surface expression pattern of CD14 and CD16 into at least three subsets with distinct inflammatory and atherogenic potential. Therefore, the aim of this study was to examine whether elevated levels of Lp(a) are associated with changes in monocyte subset distribution.
Methods: We included 90 patients with stable coronary artery disease (CAD). Lp(a) was measured and monocyte subsets were identified as classical monocytes (CD14++CD16-; CM), intermediate monocytes (CD14++CD16+; IM) and non-classical monocytes (CD14+CD16++; NCM) by flow cytometry.
Results: In patients with elevated levels of Lp(a) (>50mg/dL), monocyte subset distribution was skewed towards an increase in the proportion of IM (7.0±3.8% vs. 5.2±3.0%; p=0.026), while CM (82.6±6.5% vs. 82.0±6.8%; p=0.73) and NCM (10.5±5.3 vs. 12.8±6.0; p=0.10) remained unchanged. This association was independent of clinical risk factors, choice of statin treatment regime and inflammatory markers.
Conclusion: In conclusion, we provide a new link between elevated levels of Lp(a) and a proatherogenic distribution of monocyte subtypes in patients with stable atherosclerotic disease.

P6256 | BEDSIDE
Comparison between change of lipid profiles and on-treatment C-reactive protein in patients treated statin monotherapies after the first year of onset of acute coronary syndrome

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Backgroud: Previous research about stable coronary artery disease reported that on-treatment CRP level after statin treatment associated with clinical outcomes. However, details of on-treatment CRP level after statin treatment for patients with acute coronary syndrome (ACS) were uncertain. The aim of study was to evaluate efficacy for lipid profiles and inflammation among different statin monotherapies for one year in ACS patients.
Methods and results: From January 2012 to December 2014, consecutive 352 ACS patients who were admitted our hospital were enrolled. Excluding patients without statin monotherapies and with data deficiency, 125 patients (male 80.6%, 64.6±10.7 years) were analyzed on-treatment CRP level and lipid profiles after a year treatment. Patients treated with Atorvastatin and Rosuvastatin were significantly lower prevalence of residual inflammation (follow-up CRP >1.0mg/L) and tend to be lower % change of LDL-C than patients treated with other statins (Fluvastatin, Pitavastatin or Pravastatin) (Table).

Lipid profiles and on-treatment CRP

	Rosuvastatin 2.5 or 5 mg/day (n=56)	Atorvastatin 10 mg/day (n=46)	Other statins (n=24)	P value
Baseline LDL-C	128 [104, 158]	121 [104, 142]	100.0 [89, 116]	0.003
Follow-up LDL-C	79 [65, 102]	78 [67, 95]	78 [66, 86]	0.764
% Change of LDL-C	–35.4 [–48.1, –20.8]	–33.6 [–48.5, –18.0]	–25.2 [–31.6, –16.5]	0.052
Baseline HDL-C	46 [39, 52]	42 [37, 48]	46 [39, 61]	0.592
Follow-up HDL-C	46 [39, 52]	42 [37, 48]	46 [39, 61]	0.113
% Change of HDL-C	–5.0 [–16.4, 6.1]	–4.4 [–16.0, 5.4]	–1.4 [–11.4, 14.3]	0.419
Baseline TG	100 [75, 160]	123 [77, 165]	104 [63, 168]	0.800
Follow-up TG	114 [83, 221]	127 [96, 172]	100 [65, 123]	0.043
% Change of TG	16.1 [–23.9, 72.8]	28.6 [–12.8, 73.3]	1.0 [–47.4, 41.4]	0.283
Incidence of high on-treatment CRP level	26.8%	28.3%	54.2%	

CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride. Values were reported as median [interquartile range]. Other statins included Fluvastatin 10 or 20 mg/day, Pitavastatin 1 or 2 mg/day or Pravastatin 10 mg/day. High on-treatment CRP level was defined as above 1.0 mg/L of CRP in patients with statin monotherapy.

Conclusion: Our result suggested that a year of Atorvastatin or Rosuvastatin

monotherapies had a potential to improve inflammation in ACS patients comparing with other statin monotherapies.

P6257 | BEDSIDE
Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes

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Objective: The Syntax score (SXscore) is an anatomic scoring system based on the coronary angiography (CA), which not only quantifies lesion severity and complexity, but also predicts poor cardiovascular outcomes including mortality in patients with acute coronary sydromes (ACS). Recent studies have shown that platelet-to-lymphocyte ratio (PLR) is associated with worse outcomes in many cardiovascular diseases.
Purpose: We sought to investigate the association of PLR with severity and complexity of coronary atherosclerosis as assessed by the SXscore in patients with ACS undergoing urgent CA.
Methods: A total of 1016 patients with ACS undergoing urgent CA were included into the study between August 2012 and March 2014. Admission PLR values were calculated before CA. The SXscore was determined from baseline CA. The patients were divided into two groups as low SXscore ($\leq$22) and intermediate-high SXscore ($\geq$23).
Results: The PLR was significantly higher in patient with intermediate-high SXscore compared with low SXscore ($P<0.001$). In-hospital mortality was significantly higher in high PLR and intermediate-high SXscore groups. In multivariate analysis, the independent predictors of intermediate-high SXscore were PLR (OR: 1.018, 95% CI: 1.013–1.023, $P<0.001$) together with left ventricular ejection fraction (OR: 0.935, 95% CI: 0.910–0.960, $P<0.001$), and age (OR: 1.029, 95% CI: 1.029–1.054, P=0.02). An PLR $\geq$116 had a 71% sensitivity and 66% specificity in predicting intermediate-high SXscore.
Conclusion: The PLR at admission is significantly associated with the severity and complexity of coronary atherosclerosis in patients with ACS. Increased PLR is an independent predictor of higher SXscore in patients with ACS underwent urgent CA.

P6258 | BEDSIDE
Elevated antiendothelial antibodies are associated with improved survival in patients undergoing coronary angiography

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Background: Antiendothelial antibodies are associated with allograft rejection after heart transplantation. However, their significance in native hearts is unknown. The purpose of this study was to evaluate the correlation of the levels of these antibodies with clinical and laboratory characteristics and mortality.
Patients and methods: This was a single center prospective study; 857 consecutive patients undergoing coronary angiography were enrolled. The levels of antiendothelial antibodies were determined by ELISA. Based on the median value (0.85684), level of 1.0 optical density units was used to define elevated values. The mean follow up was 871 days.
Results: Of total 857 patients, 412 had elevated levels of antiendothelial antibodies (group 1) and 588 had normal levels (group 2). Both groups did not differ in age, gender, or presence of diabetes. Patients from group one had higher total cholesterol (171. 7 vs 161.7 mg/dl, p=0.0019), HBA1c (8.7% vs 6.6%, p=0.028), and lower LVEF (50.5% vs 48.1%, p=0.002). They were more likely to have elevated troponin levels (40.6% vs 28.1%, p=0.003). Abnormal renal function as determined by elevated creatinine levels (more than 1.1 mg/dl) was less frequent in patients in group 1 (19.8% vs 26.1%, p=0.018). These patients were more likely to have normal coronary arteries on angiography (22.5% vs 19.7%, p=0.001) and less likely to have calcified lesions (19.7% vs 27.6%, p=0.027). Patients with higher levels of the antiendothelial antibodies had lower mortality (11.2% vs 16%, p=0.026).

Antiendothelial antibodies and mortality

	Group 1	Group 2	P value
No. of patients	412	588	
Total cholesterol	171.7 mg/dl	161.7 mg/dl	0.0019
HBA1c	8.7%	6.6%	0.028
Creatinine >1.1 mg/dl	26.1%	19.8%	0.018
Normal coronary angiogram	22.5%	19.7%	0.001
Mortality	11.2%	16%	0.026

Group 1: elevated levels of antiendothelial antibodies; Group 2: normal levels of antiendothelial antibodies.

Conclusions: Despite association with elevated troponin and HBA1c levels and reduced LV function, higher levels of the antiendothelial antibodies are associated with lower prevalence of coronary disease and improved survival in patients undergoing coronary angiography.

INFLAMMATION AND IMMUNITY II

P6259 | BEDSIDE
Plasma chemerin is elevated in type 2 diabetes, is associated with impaired kidney function and is predictive for cardiovascular events

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Background and introduction: Chemerin has been implicated in autocrine/paracrine signaling for adipocyte differentiation and also stimulation of lipolysis. Whether chemerin is predictive for cardiovascular events is still unclear.
Purpose: The purpose of our study was to investigate the association of chemerin with cardiovascular event risk.
Methods: We measured plasma chemerin levels in 495 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD.
Results: Chemerin was higher in patients with type 2 diabetes mellitus (T2DM, n=111) than in non-diabetic subjects (192±73 vs. 170±65 ng/ml, p=0.001). Further, chemerin was significantly and independently associated with the glomerular filtration rate (GFR) in analysis of covariance using age, sex, and BMI as covariates (F=49.6, $p<0.001$). Prospectively, we recorded 107 cardiovascular events over 3.5 years. Chemerin both univariately and after multivariate adjustment including baseline GFR significantly predicted cardiovascular events, with hazard ratios of 1.83 [95% CI 1.19–2.83], p=0.006 and 1.67 [1.05–2.67], p=0.030 for the top tertile of chemerin versus the first and second tertiles, respectively. A cardiometabo-chip-analysis revealed an association of two nearby located SNPs in TP53BP1 and CAPN3 rs2444030 nominal p-value=5.2 e-9, and rs3098423 nominal p-value=9.6 e-8) with chemerin concentration. Haplotype analysis for these two SNPs revealed a significantly impaired GFR associated with the fully mutated haplotype compared to all other haplotypes (OR=0.63, p=0.006).
Conclusion: We conclude that high chemerin is characteristic of T2DM, is associated with impaired kidney function, and is predictive for cardiovascular events.

P6260 | BENCH
Recombinant human placental growth factor 2 treatment for ischemic cardiomyopathy in atherosclerotic mice

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Aim: We evaluated whether systemic infusion of recombinant human placental growth factor 2 (rhPlGF2) improves myocardial neovascularization and left ventricular (LV) function in a murine model of advanced atherosclerosis and chronic myocardial infarction (MI) without enhancing plaque vulnerability.
Methods: ApoE–/– mice were fed a high cholesterol diet and MI was induced 4 weeks (w) later using 60 min LAD occlusion followed by reperfusion. After 8 w, we assessed LV ejection fraction (EF) using echocardiography and randomized mice to receive rhPlGF2 (450μg/kg/day, n=20) or PBS (n=20) via osmotic minipumps for 28 days. Echocardiography and histological analyses were performed at 12 and 20 w.
Results: Infusion of rhPlGF2 increased PlGF plasma levels for 3 w up to ~1600-fold without side effects. In rhPlGF2-treated mice, capillary and arteriolar density was significantly higher in ischemic myocardium (2813±212 capillaries/mm^2 at 12 w vs 2144±478 in PBS, $P<0.05$; 125±18 arterioles/mm^2 at 20 w vs 77±13 in PBS, P=0.001); EF improved from 36.5±5.9% to 49.4±12.5% attributable to reduced LV end-systolic and end-diastolic volumes (8.7±2.6 to 7.7±2.8 ml/m^2). RhPlGF2 did not affect total cholesterol, high sensitive CRP, interleukin-6 or interleukin-10 levels (figure). RhPlGF2 did not increase cardiac troponin I levels, MI size, plaque area in the aortic arch, or the degree of fibrosis, calcification, capillary or arteriolar density or MAC3+ cell infiltration in plaques and ischemic myocardium at 12 and 20 w.

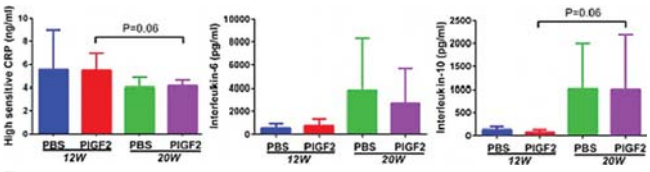

Figure 1

Conclusion: Systemic rhPlGF2 infusion improves LV neovascularization, contractile function and prevents post-MI adverse remodeling without increasing atherosclerotic plaque vulnerability and inflammatory responses. RhPlGF2 may represent a promising and safe therapy for ischemic cardiomyopathy.

P6261 | BENCH
Galectin-2 polarizes macrophages into an non-arteriogenic phenotype

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Background: The carbohydrate-binding lectin Galectin-2 (Gal-2) is expressed by monocytic cells and is known to mediate immune responses and associated with impaired collateral artery growth (arteriogenesis) in patients with coronary artery disease. Furthermore, systemic treatment with Gal-2 significantly decreases perfusion restoration after femoral artery ligation in mice and lowers the quantity of perivascular macrophages, suggesting Gal-2 alters arteriogenesis by modulating macrophage behavior. Interestingly, macrophages are known to polarize (M1/M2 phenotype), changing their arteriogenic capabilities.
Purpose: Determining the effect of galectin-2 on macrophage polarization in mice.
Methods: 20 mice were allocated into two equal groups and treated twice daily with intraperitoneal injections of either 10 mg galectin-2 (R&D Systems) or a placebo. Two days after start of treatment, the left femoral artery was permanently ligated. One week after operation, left adductor muscles were collected and stained immunohistochemically for smooth muscle actin, F4/80 (to identify macrophages), CD40 (M1-macrophages) and Mannose receptor (MR; M2-macrophages). The ratio between perivascular CD40+ to F4/80+ or MR+ to F4/80+ cells was calculated to quantify macrophage skewing to either the M1 phenotype (CD40+:F4/80+) or the pro-arteriogenic M2 phenotype (MR+:F4/80+). In vitro isolated and cultured human monocytes were incubated with interferon-gamma or interleukin-4 to polarize them into a resp. M1 or M2 phenotype, after which cells were incubated with Gal-2 for 24 hours. After incubation protein levels of CD40 and MR were analysed for both subsets by flow cytometry.
Results: In vivo, systemic treatment with galectin-2 significantly increases the perivascular M1-macrophage fraction (CD40+:F4/80+) (0.26±0.061 vs 0.029±0.061, $p<0.01$) and decreases the M2-macrophage fraction (MR+:F4/80+) (0.29±0.12 vs 0.75±0.072, $p<0.01$). In vitro, incubation with galectin-2 significantly reduces MR expression and increases CD40 expression ($p<0.05$), indicating a shift away from the pro-arteriogenic phenotype.
Conclusion: Galectin-2 polarizes macrophages into a M1-phenotype which is associated with impaired arteriogenesis.

P6262 | BEDSIDE
Prevalence at computed coronary tomography of non-calcified plaques in asymptomatic hiv patients treated with haart: a meta-analysis

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Introduction: Asymptomatic patients with human immunodeficiency virus (HIV) infection are at increased risk of vascular disease. Whether asymptomatic HIV patients have increased prevalence or structural differences in coronary artery plaques is not clear.
Methods: Pubmed, Cochrane and Google Scholar were searched for articles evaluating asymptomatic HIV patients evaluated with coronary computed tomography. The prevalence of coronary stenosis (defined as >30% and >50%), of calcified coronary plaques (CCP) viewed as more "stable" plaques, and of non-calcified coronary plaques (NCP) viewed as more "vulnerable" plaques were the end points of interest.
Results: 9 studies with 1229 HIV patients and 1029 controls were included. No significant differences were detected about baseline cardiovascular risk profile. The prevalence of significant coronary stenosis >30% or >50% did not differ between HIV+ and HIV– patients (42% [37–44] and 46% [35–52] with an Odds Ratio [OR] of 1.38 [0.86–2.20] for >30% stenosis) and (15% [9–21] and 14% [7–22] with an OR of 1.11 [0.81–1.52]), respectively. The prevalence of calcified lesions CCP (31% [24–32] and 21% [14–30] with an OR of 1.17 [0.63–2.16]) also did not differ among HIV+ and HIV– patients. On the contrary rates of NCP were >3-fold higher in HIV-positive patients [58% (48–60) and 17% (14–27) with an OR of 3.26 (1–30–8.18)], with an inverse relationship with CD4 cell count at meta-regression (Beta –0.20 [–0.35–0.18], p 0.04).
Conclusion: Asymptomatic HIV patients present a similar burden of coronary stenosis or calcified coronary artery plaques but significantly higher rates of non-calcific coronary plaques at computed tomography. The association between HIV infection, reduced CD4 cell counts and higher prevalence on non-calcific coronary artery plaques may shed light into the pathogenesis in HIV-associated coronary artery disease, stressing the importance of primary prevention in this population.

P6263 | BENCH
Cooperative effect of palmitic acid and minimally oxidized LDL on macrophage activation via MAPK-dependent manner

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Background: Free saturated fatty acids and early oxidized LDL have been nominated as emerging risk for atherosclerosis. Although a few studies reported plausible pathway by which they act, data on their additive effect is very limited.
Purpose: To examine whether palmitic acid and minimally oxidized LDL (mmLDL) have cooperative proinflammatory effect and what the mechanism is.
Methods: J774 macrophage cells were exposed to palmitic acid, mmLDL, and lipopolysaccharide alone and in combination. The effect eicosapentaenoic acid (EPA), a polyunsaturated fatty acid, was also evaluated. ELISA assay was performed to check the secretion of chemokines including CXCL2 and TNFalpha. Western blot was used to estimate the effect on the phosphorylation of inflammatory proteins. Microarray test is being conducted to evaluate gene regulation.
Results: We found that palmitic acid and mmLDL cooperatively activated macrophages to release proinflammatory chemokines CXCL2 and TNFalpha. Palmitic acid and mmLDL induced only a limited response of macrophages. We showed that phosphorylation of ERK and p38 was enhanced by combined treatment compared to the treatment of palmitic acid or mmLDL alone (Figure). Meanwhile, EPA revealed marked inhibitory effect on chemokine secretion and the activation of inflammatory proteins. Microarray result is going to be presented in the congress.

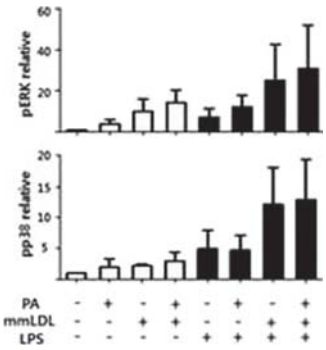

Figure 1

Conclusion: These results provide evidence for cooperative effect of palmitic acid and mmLDL on the macrophage inflammatory response. Our findings suggest how these two, when present simultaneously, escalate the risk of vascular inflammation.
Acknowledgement/Funding: 2012R1A4A1029061 and the Creative Allied Project (CAP) grant

P6264 | BEDSIDE
Inflammatory markers MMP-8 and TIMP-1 identify vulnerable coronary artery plaque in acute cardiac situation

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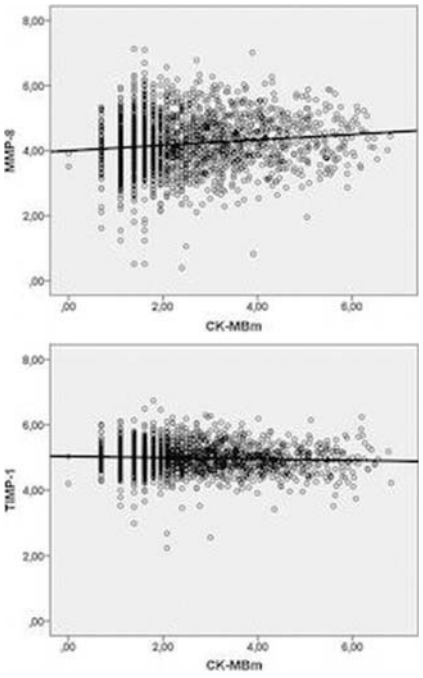
Introduction: In acute coronary syndrome (ACS) inflammation and rupture of an atherosclerotic coronary plaque lead to intracoronary thrombosis and myocardial injury, and calls for immediate intervention.
Takotsubo cardiomyopathy (TTC) mimics ACS with similar symptoms and findings, but without obstructive coronary disease. Electrocardiogram (ECG) and myocardial enzymes are, however, abnormal and unable to distinguish between ACS and TTC.
Purpose: We hypothesised that inflammatory markers matrix metalloproteinase 8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) would: 1) discriminate between intracoronary inflammation and non-atherothrombotic induced myocardial injury and 2) show a different concentration profile from the traditional markers troponin T (TnT) and creatine kinase MB mass (CK-MBm) in different types of myocardial injury.
Methods: Blood samples were obtained in conjunction with CA from 2072 ACS and 45 TTC patients. MMP-8 and TIMP-1 concentrations were measured along with TnT and CK-MBm.
Results: Serum TnT (1.1±2.7 μg/L vs. 0.4±0,4 μg/L, p=0.001), CK-MBm (34.7± 78.1 μg/L vs. 15.6±19.9 μg/L, p=0.001), MMP-8 (93.5±95.0 ng/mL vs. 74.2±74.4 ng/mL, p=0.047) and TIMP-1 (160.0±70.6 ng/mL vs. 126.0±51.8 ng/mL, p=0.001) were higher in ACS than TTC. The MMP-8 and TIMP-1, however, had only weak or no correlation with TnT and CK-Mbm (Figure 1).
Conclusion: Novel markers of myocardial injury MMP-8 and TIMP-1 correlate weakly with the injury size. Such markers, however, reflect coronary plaque inflammation and rupture – thus helping to distinguish TTC from ACS.



Abstract P6264 –Figure 1

P6265 | BEDSIDE
Similarities in impairment of endothelial glycocalyx between psoriasis and coronary artery disease: the role of oxidative stress and inflammation

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Background: Endothelial glycocalyx is a determinant of vascular integrity, however its relation with inflammation and oxidative stress in psoriasis patients has not been widely validated. We investigated the presence of reduced endothelial glycocalyx thickness in psoriasis, in comparison with coronary artery disease (CAD) patients
Methods: We compared 114 patients with psoriasis (age: 50±12 yrs, PASI disease activity score: 11.8±8) with 59 patients with angiographically documented CAD and 40 normal controls. We measured a) perfused boundary region (PBR) of the sublingual arterial microvessels (5–25 micron) using Sideview Darkfield imaging. The PBR in microvessels is the cell-poor layer which results from the phase separation between the flowing red blood cells (RBC) and plasma. The PBR includes the most luminal part of glycocalyx that does allow cell penetration. Increased PBR is considered an accurate index of reduced endothelial glucocalyx thickness because of a deeper RBC penetration in the glycocalyx b) inflammation and oxidative stress markers including interleukins-6 (IL-6-pg/ml and malondialdehyde (MDA-nM/L), tumor necrosis factor (TNFa-pg/ml), -10 (IL-10-pg/ml), -12 (IL-12- pg/ml) and -17 (IL-17-pg/ml).
Results: Psoriasis patients had similar PBR, IL-6 and MDA values with CAD patients ($p>0.05$) but higher values of these markers than normals ($p<0.05$) after adjustment for atherosclerotic risk factors [PBR: 2.05±0.2 vs. 2.01±0.3 vs. 1.77±0.14, IL-6-pg/ml (median values): 2.26 vs. 2.2 vs. 1.7, MDA-nM/L (median values): 1.68 vs. 1.76 vs. 1.01, $p<0.05$ for all comparisons]. Increased PBR, indicating reduced endothelial glycocalyx thickness was associated with increased IL-6 (r=0.36, P=0.03), IL-10 (r=0.45, P=0.03), IL-12 (r=0.51, P=0.01), IL-17 (r=0.36, P=0.03) and TNFa/IL-10 (r=0.60, P=0.005) in psoriasis patients.
Conclusion: Impaired endothelial glycocalyx integrity is associated with increased inflammation and oxidative stress burden in psoriasis patients. Psoriasis and CAD patients present similar impairment of endothelial glycocalyx, possibly because of similar underlying inflammatory and oxidative stress processes.

P6266 | BEDSIDE
Respiratory infection following acute myocardial infarction is an independent predictor of in-hospital cardiovascular mortality

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Background: Respiratory infection (RI) has been established as a trigger for the development of acute myocardial infarction (AMI). However, data on prognostic implications of RI complicating hospital admissions for AMI is still scarce.
Purpose: Evaluate the prognostic impact of RI in patients admitted for acute myocardial infarction.
Methods: We retrospectively analyzed 1907 patients who were admitted to our coronary care unit with AMI. Respiratory infection was defined as the presence of clinical, analytical and radiologic data suggestive of respiratory infection. Clinical and laboratory features, treatment and adverse events were compared in each group of patients. The primary endpoint was in-hospital cardiovascular (CV) death.
Results: Patients with RI were older (69±14 vs 64±13 years, $p<0.001$) and had increased prevalence of diabetes (37.61 vs 27.21%, p=0.015). On admission, they more frequently presented with ST-segment elevation myocardial infarction (56.4 vs 45.6%, p=0.022), Killip class>1 (58.12 vs 16.65%, $p<0.001$), higher troponin I (35.6 vs 23.2ng/mL, $p<0.001$), proBNP (6302 vs 2737pg/mL, $p<0.001$), C reactive protein (47.8 vs 14.37mg/L, $p<0.001$) and neutrophil count (10683 vs 7816 cells/μL, $p<0.001$), lower haemoglobin (13.26 vs 13.87 g/dL, p=0.005), eGFR MDRD (73.0 vs 84.49mL/min/1.73m^2, $p<0.001$), systolic (121 vs 132mmHg, $p<0.001$) and diastolic blood pressure (73 vs 79mmHg, $p<0.001$). Individuals with RI required more often ventilatory (16.67 vs 0.95%, $p<0.001$), aminergic (31.6 vs 4.3%, $p<0.001$) and transfusional (14.29 vs 1.34%, $p<0.001$) support and intra-aortic balloon pump (15.4 vs 1.79%, $p<0.001$). During hospitalization they had higher incidence of malignant arrhythmias (17.0 vs 4.3%, $p<0.001$), ischemic stroke (3.4 vs 1.2 vs 0.7%, p=0.002), reinfarction (5.1 vs 2.1%, p=0.036), heart failure symptoms (81.2 vs 25.1%, $p<0.001$), and IR was also associated with an increased incidence of major adverse cardiovascular events at follow-up (stroke, acute coronary syndrome, death) (43.3 vs 29.8%, p=0.005). Compared with non-infected patients, RI had 6.12 times higher in-hospital CV mortality [OR 6.12; 95% CI (3.34–11.21)]; $p<0.001$]. In multivariate analysis, adjusting for significant predictors of CV mortality (age, gender, SBP, eGFR, proBNP, Killip class and haemoglobin), RI remained as an independent predictor of in-hospital CV mortality [infected vs non-infected, OR adjusted 3.93; 95% CI (1.704–9.074); p=0.001].
Conclusion: Respiratory infection is an independent predictor of in-hospital CV mortality in patients admitted for AMI.

P6267 | BEDSIDE
Evaluation of neutrophil/lymphocyte and platelet/lymphocyte ratios in the extent of coronary artery calcification among clinically stable patients

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Introduction: It is well established that stable coronary atherosclerotic disease (CAD) is related to a chronic low-grade subclinical inflammation. Among markers of inflammation, increasing importance has been given to neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), simple methods for assessment of inflammatory status. However, the association of those hematological indices of inflammation and coronary atherosclerotic burden has been little studied.
Objective: To investigate the association between NLR and PLR and the extent of coronary artery calcification in clinically stable patients.
Methods: Consecutive stable patients underwent collection of blood cell count and evaluation of the coronary artery calcium score (CAC) by CT scan without contrast, as a noninvasive method of CAD risk stratification. Age, sex, NLR and PLR were evaluated at different levels of CAC. Statistical tests included chi-square, linear regression and logistic regression.
Results: Patients with stable CAD (n=136, age 60.0±13.0 years and 63.2% men) were evaluated and categorized into 4 groups according to the CAC score (Agatston), and the evaluation of age, sex (male), NLR and PLR in each group were determined: CAC = 0 (n=52, 53.1±14.3 years, 52%, 2.1±1.2; 120.1±43.8), CAC 1–100 (n=35, 61.1±8.6 years, 55%, 2.1±1.1; 117.3±44.8), CAC 101–400 (n=21, 62.2±9.4 years, 63%, 2.6±1.4, 142.0±61.1), CAC >400 (n=28, 68.8±10.8 years, 65%, 3.9±2.4, 202.6±93.6). CAC >400 correlates with higher ages ($p<0.0001$), NLR (p=0.001) and PLR (p=0.0006) compared to lower CAC categories. Linear regression demonstrated positive association between log CAC and NLR ($p<0.0001$, r^2 = 12.4%), as well as log CAC and PLR ($p<0.0001$, r^2 = 14.9%). Multivariate logistic regression analysis showed that, with the exception of PLR (OR 1.31 [0.83–2.07], p=0.2454), gender (male/female), age (decades), and NLR are independently associated with CAC >100, (OR [CI], p-value): 0.36 (0.14–0.90, p=0.0292), 2.25 (1.52–3.33, p=0.0001) and 2.08 (1.27–3.41, p=0.0035), respectively.
Conclusion: In this study, among clinically stable patients, there is an independent association of NLR and CAD extent (assessed by CAC score). However, PLR has proved to be an inefficient inflammation marker for the prediction of severity of CAD.

P6268 | **BEDSIDE**

Role of macrophage migration inhibitory factor (MIF) and its endogenous inhibitor Gremlin-1 in intracoronary thrombi of patients with acute myocardial infarction

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Background: Macrophage migration inhibitory factor (MIF) is involved in atherosclerotic plaque progression and instability leading to intracoronary thrombosis. Gremlin-1 (Grem1), a member of the DAN/Cerberus-protein family, has been recently identified as endogenous inhibitor of MIF. Intracoronary thrombi are a main cause of acute myocardial infarction in patients with coronary artery disease. The thrombus leading to an acute vessel occlusion consists of plateles and other blood cells, such as monocytes, macrophages, and CD34+ peripheral stem cells. There is evidence that arterial thrombi may influence the development of neointima after coronary stenting. However, the underlying pathophysiological role of arterial thrombi during and after acute myocardial infarction remains unclear. Therefore we analyzed the histology of and the expression of MIF and Grem1 in intracoronary thrombi.
Methods and results: We analysed the cellular constituents of 25 thrombi aspirated from coronary lesions with a thrombectomy device in 25 patients who underwent emergent coronary intervention for the treatment of acute (<24 h) or recent (24 to72 h) ST-segment elevation myocardial infarction. Immunohistological analysis of aspirated thrombotic materials revealed a high expression amount of Grem1 and MIF in the platelet rich areas of the thrombi, as determined by immunostaining for CD42b, and in regions with a high amount of inflammatory cells such as monocytes and macrophages, as determined by immunostaining for CD14 and CD68. Grem1 was also expressed in fibroblasts within the arterial thrombi, as detected with S100B immunostaining.
Parts of intracoronary thrombi were brought in tissue culture and grown over 15 days. Between day 4 and day 7 cells grew out from the main thrombus and formed colonies of fibroblasts and cells positive for endothelial cell markers. Expression of Grem1 and MIF could be detected within these colonies on day 15 of tissue culture, analyzed by FACS.
Conclusion: These findings suggest a potential role of Grem1 and MIF during intracoronary thrombus formation. Grem1 and MIF might furthermore be involved in processes of regeneration after acute plaque rupture. However, further in vitro studies are necessary to elucidate these interactions more in detail.

P6269 | **SPOTLIGHT**

Three-year results of stenting of bifurcation stenoses of the left main coronary artery: data of intravascular ultrasound study

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Aim: Using objective methods of intravascular imaging to evaluate the results of bifurcation stenting stenosis of the left main coronary artery.
Methods: Three-year results of endovascular treatment of patients with true bifurcation stenosis of the left main coronary artery were evaluated in 94 patients, of whom 48 patients were using one stent technology “provisional-T”, and while 46 were stented “two stent” techniques. All interventions were conduded by final dilation by “kissing-balloon” high pressure balloons and under IVUS guidence. Long-term results were assessed by following criteria: frequency of cardiovascular complications (death, myocardial infarction, re-intervention), IVUS data (residual area of vessel lumen in the proximal segment of left main, zone of bifurcation, the ostia of anterior descending artery and circumflex artery). Decrease in diameter in remaining lumen >70% coas considered as criteria for restenosis.
Results: Survival amongest patients in late period was 97,9%, 2 patients died from non-cardial causes. The frequency of cardiac events in both groups was 8.3 and 4.3%, respectively (p 0,05). Restenosis rate according to IVUS in the body trunk of the left coronary artery and anterior descending artery Stavila 0%. Restenosis of the circumflex artery to IVUS was found to be 14,5% and 4.3% of cases (p 0,001). Repeated revascularization was needed in 4.2% of patients from group 1 and 2.2% in patients of group 2 (p 0,05). Stent thrombosis was not detected in either group. The average residual area of the lumen of the left coronary artery in the proximal part, after “T-provisional” was stenting 7,89+0,03, and after a full bifurcation stenting of 8.0+0.02 mm^2 (p 0,05), at the ostia of the circumflex artery 5,62+0,12 and 5,98+0,01 mm^2 (p 0,05), at the ostia of the anterior descending artery 6,62+0,03 and 6.78+0,04 mm^2. These results did not significantly differ compared to the same 12 months of observation.
Conclusion: The study demonstrates that the use of objective methods of visualization of coronary arteries in patients with bifurcation stenosis of left coronary artery as a method of monitoring the results of stenting, as well as adequate final dilation “kissing balloons” high pressure leads to low frequency of cardiovascular complications and restenosis in long-term period,that have a positive impact on the prognosis of such patients.

ANGINA PECTORIS STABLE IV

P6270 | **BEDSIDE**

The effect of ivabradine on silent ambulatory myocardial ischemia

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Background: Heart rate (HR) reduction is a powerful method used to reduce myocardial oxygen demand thus reducing the frequency and duration of angina in chronic ischemic heart disease (CIHD). Ivabradine selectively inhibits the Na+/K+ current (If current) in pacemaker cells of the sinoatrial node thus reduces the slope of diastolic depolarization resulting in slower HR without causing other side effect on myocardial contractility or AV conduction. Treating silent myocardial ischemia has a prognostic effect and may improve long term mortality of (CIHD). The effect of Ivabradine on angina frequency was already studied but its effect on silent ambulatory myocardial ischemia (SAMI) has not been reported yet. In this study we report the effect of ivabradine on (SAMI)
Methods: We enrolled 50 patients with proven stable coronary artery disease (CAD) and at least one episode of ST-segment depression on ambulatory ECG monitoring. All of them were receiving optimal therapy for CIHD. 25 patients were randomized to receive Ivabradine 7.5mg bid. And the other 25 patients received placebo. Ambulatory monitoring was repeated after 4 to 6 months of therapy. The two groups were comparable with respect to baseline characteristics, number of episodes of ST-segment depression, and baseline serum cholesterol levels. Holters were read by a blinded cardiologist.
Results: The Ivabradine group had lower mean HR at study end and experienced a significant reduction in the number of episodes of ST-segment depression compared with the placebo group. ST-segment depression was completely resolved in 9 of 25 patients (36%) in the Ivabradine group versus 3 of 25 (12%) in the placebo group. The Ivabradine group exhibited a highly significant reduction (SAMI) ($P<0.001$). By logistic regression, treatment with Ivabradine was an independent predictor of (SAMI) resolution.
Conclusions: Further lowering of HR with Ivabradine can result in reduction or resolution of (SAMI) recorded as episodes of ST-segment depression in ambulatory monitoring of the ECG. A larger study is required to cofirm this theory and to see the effect of SAMI reduction on long term mortality of CIHD.

P6271 | **BEDSIDE**

Different vasoreactivity of left internal thoracic artery bypass grafts and left anterior descending coronary arteries to acetylcholine in patients with stable angina and no relevant stenosis

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Background: Coronary angiography is often performed in patients with recurrent or ongoing angina pectoris after successful coronary artery bypass grafting (CABG) in search of progression of atherosclerosis. However, in many of these patients no relevant stenosis can be detected. We speculate that abnormal coronary vasomotion (i.e. large vessel or microvascular spasm) represents an alternative explanation for angina in these patients.
Methods: From 1451 patients with angiographically unobstructed coronaries (no stenosis >50%) who underwent intracoronary acetylcholine provocation testing (ACH-test) between 2012 and 2014 at our institution we consecutively recruited 40 patients (29 male (73%), mean age 70±10 years) who fulfilled the following inclusion criteria: previous CABG including left internal thoracic artery (LITA) bypass on the left anterior descending (LAD) coronary artery, ongoing/recurrent angina pectoris (25% with effort angina, 33% with resting angina, 42% with a mixed presentation), no significant (<50%) coronary artery or bypass stenosis. In all patients the provocation test with acetylcholine was performed via the LITA bypass and the degree of vasoconstriction was measured separately in the LITA and LAD with quantitative coronary angiography software.
Results: In eighteen patients (45%) the ACH-test elicited epicardial spasm in the LAD distal to the anastomosis (≥75% diameter reduction with reproduction of the patient’s symptoms) and microvascular spasm (reproduction of symptoms, ischemic ECG-changes and no epicardial spasm) was seen in 13 additional patients (32%). The ACH-test was uneventful in the remaining 9 patients (23%). Interestingly, acetylcholine did not elicit any relevant vasoconstriction in the LITA bypasses (mean diameter reduction 6.6±6%) whereas mean vasoconstriction in the LAD was 49.0±34% on QCA ($p<0.01$).
Conclusion: Coronary vasomotor abnormalities (epicardial and microvascular spasm) are frequently found as the cause of angina pectoris in patients with previous CABG but no relevant stenosis. Vasoreactivity to acetylcholine is markedly different between LITA bypasses and native LAD arteries with vasoconstriction almost exclusively occurring in the LAD. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treatment.

P6272 | BEDSIDE

Associations of ankle-brachial index with the severity and characteristics of coronary atherosclerosis in patients with stable angina pectoris: assessment by Gensini score, IVUS, and OCT

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Background: Ankle-brachial index (ABI) is a non-invasive method to assess the patency of the lower extremity artery and to screen for the presence of peripheral arterial disease (PAD). Low ABI levels have been reported to be associated with cardiovascular mortality. However, the relationship between ABI and severity of coronary artery disease has not been sufficiently elucidated.
Purpose: The aim of this study was to investigate the association of ABI with the severity and characteristics of coronary atherosclerosis as assessed by Gensini score, iMap-intravascular ultrasound (iMap-IVUS), and optical coherence tomography (OCT) in patients with stable angina pectoris (SAP).
Methods: We enrolled 130 patients with SAP who underwent percutaneous coronary intervention following iMap-IVUS and OCT to culprit lesions. The ABI of bilateral lower extremities were measured, and their mean values were calculated in each patient. The PAD was defined as the ABI value <0.90. Gensini score was used as the parameter of angiographic severity of coronary atherosclerosis. Culprit plaque components were classified by iMap-IVUS as fibrotic, lipidic, necrotic and calcified, and each area (FA, LA, NA and CA, respectively) was reported as a percentage of the total plaque area. Thickness of fibrous cap overlying a lipid core in culprit plaque was measured in its thinnest part by OCT.
Results: We identified 22 and 108 patients with and without PAD, respectively. Patients with PAD had significantly higher prevalence of multivessel diseases (64 vs. 36%, p=0.016) and higher Gensini scores than those without PAD (61.7±45.2 vs. 41.9±38.3, p=0.043). Culprit plaques in patients with PAD had significantly greater %NA (50±12 vs. 38±17%, p=0.016), smaller %FA (32±9% vs. 46±18%, p=0.007), and thinner fibrous cap thickness (91±71 vs. 166±151 μm, p=0.007) than in those without PAD. In linear regression analysis, a mean ABI was significant factor associated with Gensini score (standardized coefficient β = –0.31, p=0.008), %NA (β = –0.37, p=0.018), and %FA (β = 0.38, p=0.013) after adjustment for age, hypertension, hypercholesterolemia, diabetes, cigarette smoking, estimated glomerular filtration rate, and statin use.
Conclusions: The lower ABI value was related to higher Gensini score and plaque with greater %NA, smaller %FA, and thinner fibrous cap. These findings suggest that ABI can serve as a predictor of the severity and characteristics of coronary atherosclerosis.

P6273 | BEDSIDE

Fractional flow reserve after percutaneous coronary intervention was strongly associated with better long-term clinical outcome in stable coronary artery disease

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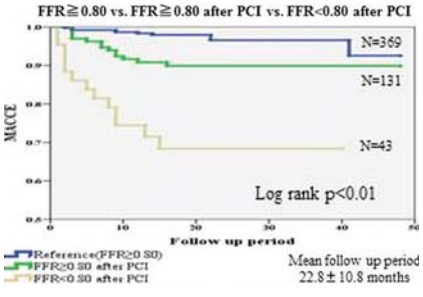
Background: Past reports showed that fractional flow reserve (FFR) >0.90 or 0.96 after percutaneous coronary intervention (PCI) was associated with better prognosis. However, there were few patients that FFR after PCI was >0.90 or 0.96. It is unknown whether FFR≥0.80 after PCI has impact on long-term clinical outcome.
Methods: We investigated 549 lesions (415 patients with stable coronary artery disease) in our hospitals between April 2011 and August 2014. 374 lesions (68.1%) were deferred PCI because of FFR≥0.80. 175 lesions (31.9%) with FFR<0.80 were performed PCI guided by FFR and optical coherence tomography (OCT) or Intravascular ultrasound (IVUS). Basically, the end point of PCI was defined as FFR≥0.80. However, there were 42 lesions of FFR<0.80 after PCI at at the operator's direction. FFR value was checked after intracoronary administration of papaverin (left;12–20mg, right;8–16mg) or intravenous administration of adenosine (180μg) to induce maximal hyperemia. Follow-up was performed to document the occurrence of major adverse cardiac event (MACE): cardiac death, myocardial infarction, or target vessel failure (Median follow-up period: 22.8±10.8months). We compared frequency of MACE among three groups (FFR≥0.80 after PCI (N=133), FFR<0.80 (N=42) after PCI, and PCI defer group (N=374)). Moreover, we investigated predictors of MACE among three groups.



Results: The frequency of MACE in FFR<0.80 after PCI was significantly higher than that in FFR≥0.80 after PCI (p<0.01, shown in figure).
Conclusion: We should aim FFR≥0.80 after PCI to improve long-term clinical outcome.

P6274 | BEDSIDE

Association of platelet to lymphocyte ratio with inflammation and severity of coronary atherosclerosis in patients with stable coronary artery disease: a single center large scale study

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Objective: Atherosclerotic coronary artery disease (CAD) is known as a complex and chronic inflammatory disease. The platelet to lymphocyte ratio (PLR) has recently been emerged as a new potential inflammatory biomarker. Hence, we aimed to assess the relationship between PLR and the extent/severity of CAD by using Gensini score in association with the inflammatory marker including C-reactive protein in patients with stable CAD.
Methods: Angiographic data of 1615 patients were analyzed retrospectively in this study. Patients were categorized according to Gensini scores as no CAD (control), mild CAD and severe CAD groups. Independent predictors of the severe CAD were determined by logistic regression analysis.
Results: PLR in the control group were significantly lower than those of the other groups (Figure). After multivariate logistic regression analysis PLR [Odds ratio: 1.228 (1.106–1.362), p<0.001] was found as independent predictor for the severe CAD. Furthermore, there was a significant positive correlation between PLR and the severity of CAD determined by Gensini score (r=0.260, p<0.001) and inflammatory marker like CRP (r=0.162, p<0.001).

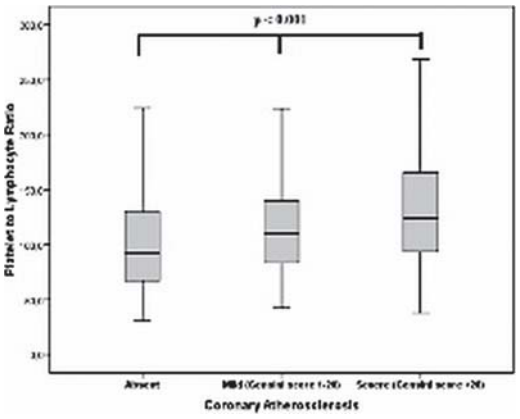

Figure 1

Conclusion: PLR was independently and positively associated with the severity of coronary atherosclerosis in patients with stable CAD. In addition, PLR was positively correlated with CRP as a reliable indicator of inflammation. These results suggest that PLR is an easily available and cheap inflammatory indicator, so that PLR can be used in prediction of the severity of coronary atherosclerosis.

P6275 | BEDSIDE

The acute and chronic effects of ivabradine on the parameters of central aortic pressure in patients with stable coronary artery disease

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Background: Data from small studies in healthy humans show that heart rate (HR) increase induced by vasoactive drugs or pacing is associated with a reduction in augmentation index (AIx) and even central diastolic pressure. However, it remains unclear if parameters of central aortic pressure (CAP) such as AIx, AIx normalized for HR of 75 bpm (AIx@75), and augmented pressure (AP) increase during HR-lowering therapy in patients (pts) with coronary artery disease (CAD). The aim of our study was to investigate the acute and chronic effects of If inhibitor Ivabradine on the parameters of CAP in pts with CAD.
Methods: 30 pts with proven CAD, stable angina (2.3±0.4 CCS), mean baseline HR of 76.0±1.4 bpm and peripheral systolic/diastolic blood pressure (SBP/DBP) of 111.9±1.2/70.3±1.1 mm Hg were enrolled in this study. The parameters of CAP were quantified noninvasively using applanation tonometry of the radial artery. Measurements were made at baseline, 3 hours after the intake of 5 mg Ivabradine and then after 1 and 2 months of Ivabradine therapy (mean dose 11.5±0.7 mg/day). All pts received guideline-based therapy (including beta-blocker bisoprolol 5 mg/day), which remained unchanged.
Results: A single dose of Ivabradine and then 1 and 2 months treatment with Ivabradine resulted in a pronounced HR reduction (–10.8%, p<0.01; –17.5%, p<0.001; and –22.1%, p<0.001, respectively). No significant changes in aortic SBP and AP were noted during the acute test: 103.9±1.2 mm Hg vs. 101.8±1.2 mm Hg and 7.6±0.9 mm Hg vs. 7.4±0.9 mm Hg, respectively. After 1 and 2

months of Ivabradine therapy these parameters remained unchanged: aortic SBP (102.1±1.1 mm Hg and 101.6±1.1 mm Hg) and AP (7.8±0.9 mm Hg and 7.9±0.7 mm Hg). AIx did not significantly change: 22.7±2.4% at baseline vs. 21.8±2.6%, 23.4±2.6%, and 23.9±2.1% after the acute test, and 1 and 2 months of therapy, respectively. But AIx@75 decreased significantly from 23.4±2.1% (baseline) to 19.1±2.4% (acute test, $p<0.05$), 17.6±2.6% (1 month, $p<0.02$) and 16.7±2.1% (2 months, $p<0.01$).
Conclusion: HR reduction with Ivabradine does not worsen the parameters of CAP in pts with CAD. It may be considered as a positive characteristic of this agent. Further studies are needed to investigate long-term effects of Ivabradine on the parameters of CAP.

P6276 | BEDSIDE
Efficacy of everolimus-eluting stent implantation in patients with small coronary (<2.5 mm) arteries: outcomes of 4-year clinical follow-up

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Background: Previous studies have demonstrated that patients with small coronary artery lesions (SCAL) are at increased risk for late cardiac events after percutaneous coronary intervention (PCI). It remains uncertain whether second-generation drug-eluting stents have an advantage first-generation drug-eluting stents (DES) in patients with SCAL. This study aimed to evaluate the long-term efficacy of everolimus-eluting stent (EES) and sirolimus-eluting stents (SES) on SCAL.
Methods and results: Consecutive 390 patients with 432 SCAL, who were treated with EES (187patients, 212 lesions) and SES (203 patients, 220 lesions) were enrolled. SCAL was defined the lesions with reference vessel diameter (RVD) <2.5 mm. Within ten months angiographic follow-up results and 4-year clinical follow-up outcomes were compared between EES and SES groups. The prevalence of diabetes was higher and the stent length was longer (23.0±7.0 vs. 20.1±6.8, $p<0.05$) in EES group than in SES group. Initial success rate was similar in both groups. There was no difference in 4-year %binary restenosis, TLR (3.1 vs. 5.1%), and MACE (4.0%vs 8.9%) rates between 2 groups. This similar major adverse cardiovascular events rate remained after adjustment. However, the rate of stent thrombosis was 0% in the EES group and 3.2% in the SES group (p=0.10).
Conclusions: EES demonstrated comparable clinical outcomes to those of SES in SCAL. The absence of stent thrombosis among patients treated with EES suggests a good safety profile for this second-generation drug-eluting stent, which should be carefully studied in a larger series of patients with SCAL.

P6277 | BEDSIDE
Ivabradine reduces symptoms and improves quality of life in patients with stable angina and diabetes mellitus

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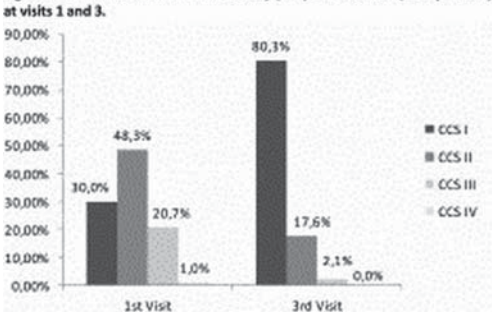
Introduction: Diabetic patients present extensive and rapidly progressive coronary artery disease (CAD), as well as a propensity to higher angina burden.
Purpose: To evaluate the antianginal efficacy of ivabradine co-administered with a β-blocker and its impact on quality of life (QOL). To record compliance with treatment, during 4-months' therapy in patients with CAD and a history of diabetes mellitus (DM).
Methods: This is a post hoc analysis (739 patients with DM) of a Pan-Hellenic, prospective, non-interventional study including 2403 patients with CAD and stable angina. Patient follow-up was performed at baseline, at 1 and 4 months after inclusion. Patients' QOL was assessed by means of the EQ-5D questionnaire.
Results: Of 739 CAD patients, 19 (2.6%) prematurely discontinued treatment. Addition of ivabradine decreased the % of patients with heart rate (HR) >80 bpm from 47% (1st visit) to 1% (3rd visit) (mean decrease −17.8 bpm). Patients with ≥2 angina attacks decreased from 57.6% at baseline to 14.1% (2nd visit) and 5.5% at study completion ($P<0.001$). Consumption of nitroglycerin decreased from 1.7±2.2 times/week (1st visit) to 0.4±0.9 (2nd visit) and 0.2±0.5 times/week (3rd visit) ($P<0.001$). 2.1% of patients presented angina Canadian Cardiovascular Society class III-IV at study completion vs. 21.7% at baseline ($P<0.001$). QOL was improved; 25% more patients reported being autonomous in self-care, 73% and 53% more patients had no difficulties in their usual activities or mobility respectively, 56% more patients reported no stress, while the number of patients reporting no pain was tripled at study completion compared with baseline ($P<0.001$).

Figure 1: Canadian Cardiovascular Society (CCS) classification (% of patients) at visits 1 and 3.



Conclusions: Ivabradine showed a significant antianginal efficacy, reflected in improved quality of life of diabetic patients with stable angina.
Acknowledgement/Funding: SERVIER HELLAS

P6278 | BEDSIDE
Percutaneous coronary intervention for restenosis with stent fracture after drug-eluting stent implantation compared between first and new drug-eluting stents

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Background: Stent fracture (SF) is related to restenosis after drug-eluting stent (DES) implantation. Although SF is a rare complication in the era of new generation DES, the results of percutaneous coronary intervention (PCI) for restenosis with SF after DES implantation remain unclear.
Purpose: To compare the results of PCI for restenosis with SF after DES implantation between first and new generation DESs.
Methods: From November 2002 to December 2013, 10437 patients with 17798 lesions underwent DES implantation successfully. Of these, 14412 lesions were angiographically followed up after 6 to 8 months (midterm f/u), and 10999 lesions were followed up 12 months after midterm f/u. Restenosis with SF was defined as a restenosis lesion within 5 mm from a SF site. SF occurred in 602 (4.2%) of the 14412 lesions, and restenosis with SF occurred in 214 lesions, in which target lesion revascularization was performed on 209 lesions. First generation DES was defined as sirolimus- and paclitaxel-eluting stents, and new generation DES as everolimus- and biolimus-eluting stents. The final analysis was performed in 194 lesions, excluding those treated with other types of DES.
Results: As shown in the table, the incidence of SF at midterm f/u was significantly lower in new generation DES than in first generation DES, but the incidence of re-restenosis showed no significant difference between the two groups.

	First generation DES	New generation DES	p
N	149	35	
Stent fracture	4.98% (444/8917)	2.11% (140/6624)	<0.001
Midterm follow up	88.6% (132/149)	91.4% (32/35)	
Re-restenosis	42.4% (56/132)	50% (16/32)	0.552
Re-TLR	33.3% (44/132)	37.5% (12/32)	0.681

DES, drug-eluting stent; TLR, target lesion revascularization.

Conclusion: Even with the use of new generation DES, the results of PCI for restenosis with SF after DES implantation have not been improved and the incidence of re-restenosis was still high.

P6279 | BEDSIDE
Blood bioactive sphingolipids and activity of sphingomyelinases in patients with multivessel coronary artery disease

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Ceramide (Cer) and sphngosine-1-phosphate (S1P) are principal bioactive sphingolipids. In the heart, Cer induces apoptosis of cardiomyocytes whereas S1P exerts cardioprotective action during ischemia, ischemia/reperfusion, ischemic pre- and postconditioning. There is a bulk of evidence that the two compounds are also involved in the process of atherosclerosis. Cer was shown to be produced in the atherosclerotic plaque and in the plasma by the enzyme secretory acid sphingomyelinase (ASmase). The compound augments development of atherosclerosis. Plasma S1P is connected mostly to HDL and exerts anti-atherogenic action. Metabolism of plasma Cer and S1P is altered in patients with acute coronary syndrome. No data are available on metabolism of blood sphingolipids in advanced atherosclerosis.
The aim of the present study was to investigate the level of different bioactive sphingolipids in plasma, erythrocytes and platelets in patients witch multivessel coronary artery disease. 20 healthy control subjects (C) – mean age 63 y. and 32 patients (P) – mean age 65 y. with multivessel coronary artery disease (confirmed angiographically) participated in the study. Blood samples were taken from the antecubital vein and separated in three fractions: plasma, erythrocytes and platelets. The following sphingolipids were quantified in each blood fraction by means of high pressure gas-liquid chromatography: Cer, S1P, sphingosine (SO), sphinganine (SA) and sphinganine-1-phosphate (SA1P). In plasma, the activity of ASmase was measured by isotopic method.
Results: The plasma concentration of S1P (P-146.48±42.6pmol/ml, C-197.1±58.3, p=0.002) and SA1P (P-20.8±6.6 pmol/ml, C-28.0±6.7, p=0.001) was reduced in the group of patients. The concentration of other sphingolipoids was stable. The content of the of examined sphingolipids in erythrocytes was simi-

lar in the two groups of subjects. In platelets, the content of SO (P-238.1±57.9 pmol/mg protein, C-109.9±43.5 p=0.01) and SA (P-50.3±3.8 pmol/mg protein, C –22.1±4.2,p=0.003) in P was markedly elevated as compared to the respective values in C. Plasma activity of ASmase was: C- 1.706±0.62, P – 2,124±0.67 nmol/h/ml (p=0.029).
Conclusions: 1. Anti-atherogenic potential of plasma is reduced in patients with multivessel coronary artery disease.
2. The activity of pro-atherogenic secretory acid sphingomyelinase increases in the disease.
3. The disease affects metabolism of sphinganine (a precursor of ceramide) and sphingosine (product of ceramide catabolism) in the platelets.
4. The disease does not affect the content of examined sphingolipids in erythrocytes.

ANGINA PECTORIS STABLE V

P6280 | BEDSIDE
Effect of allopurinol on serum uric acid and platelet aggregation in patients with essential arterial hypertension

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Background: High serum uric acid (SUA) level promotes platelet (PLT) aggregation (Agg), essential in cardiovascular disease (CVD) development and progression. Allopurinol (ALLO) has beneficial effects in CVD, but its acting mechanisms are not well known and a possible effect on PLT function has not been studied.
Purpose: The aim of the study was to assess the effects of ALLO on PLT Agg in relationship with its lowering SUA effect in patients (pts) with essential arterial hypertension (AH).
Methods: In 70 pts with essential AH (grade 2–26.15%, grade 3–61.53%), mean age 62.34±11.89 years, 53.84% women, optimally treated according to 2013 ESH/ESC Guidelines, 31 receiving acetylsalicylic acid (ASA), with mean blood pressure 133.87±11.89/80.53±7.79 mmHg on 24 hour ambulatory monitoring, in 37 pts (ALLO+ group) ALLO 300 mg/day was randomly administered, irrespective of SUA level. In all pts (ALLO+/ALLO- group) we determined PLT Agg to adenosine diphosphate (ADP) and collagen by the light transmission aggregometry of PLT rich plasma, SUA level and PLT count at baseline and after one month of treatment. Statistical analysis was performed.
Results: At baseline SUA level (p=0.22), PLT count (p=0.10) and PLT Agg to ADP (p=0.19) and collagen (p=0.23) were similar in both groups. In ALLO+ there was a significant decrease in ADP Agg (%) from 76.89±15.98 to 38.43±23.87 (p=0.0009), in collagen Agg (%) from 87.02±14.49 to 71.27±20.82 (p=0.0002) and in SUA (mg/dl) from 5.62±1.91 to 3.35±1.49 (p=0.0003), but the PLT number (/mm^3) did not change from 223702±5901 to 223081±66811 (p=0.48). Pts receiving ASA had a lower collagen Agg at baseline and in ALLO+ the decrease in collagen Agg was more important in pts who did not receive ASA (p=0.0004) than in those receiving ASA (p=0.003). In ALLO+ the decrease in PLT Agg was not correlated to the decrease of SUA, neither for ADP Agg (r=–0.25, p=0.35), nor for collagen Agg (r=–0.15, p=0.59). In ALLO- there were no significant changes in PLT Agg to ADP (p=0.06) or collagen (p=0.34), SUA (p=0.49) or PLT (p=0.34).
Conclusion: ALLO has an antiaggregant effect by inhibition of PLT Agg to ADP and collagen, irrespective of its SUA lowering effect and does not affect PLT production and survival.

P6281 | BEDSIDE
The Difference between Ergonovine and Acetylcholine in the Changes of Reactive Oxygen Metabolites during Intracoronary Spasm Provocation Test in Patients with Vasospastic Angina

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Background: We reported that direct measurement of diacron reactive oxygen metabolites (dROMs) levels in the coronary sinus during the acetylcholine (ACh) provocation test for diagnosis of vasospatic angina was useful to evaluate reactive oxygen species (ROS) in the coronary circulation. However, the changes of the dROMs test in the intracoronary ergonovine provocation test for diagnosis of vasospatic angina remain unknown.
Methods: We directly measured the serum dROMs in the coronary sinus by using the dROMs test in 32 patients with chest pain and normal coronary arteriograms who underwent the intracoronary ergonovine (n=16) or ACh provocation test (n=16).
Results: Ergonovine provocation test was positive in 12/16. The provocation positive group had significantly higher dROMs levels after ergonovine administration (233±69 vs. 255±56 CARR U, P<0.05) than baseline, suggesting the myocardial ischemia after the induction of coronary artery spasm in the provocation positive group induced ROS formation. In the provocation negative group no significant difference of dROMs levels was observed between baseline and after ergonovine administration. On the other hands, ACh provocation test was positive in 9/16. The ACh provocation negative group had significantly lower dROMs levels after ACh administration than baseline (191±53 vs. 233±52 CARR U, P<0.01). No significant difference of dROMs levels was observed between baseline and after ACh administration in the ACh provocation positive group. The dROMs levels after ACh administration might be affected by the antioxidant activity of the released NO from the endothelial cells.
Conclusion: The changes of dROMs levels in the coronary sinus vein during the intracoronary ergonovine spasm provocation test in patients with rest angina were quite different from the ACh provocation test.

P6282 | BEDSIDE
Impact of diabetes mellitus for angiographical mid-term outcome in new generation drug eluting stent

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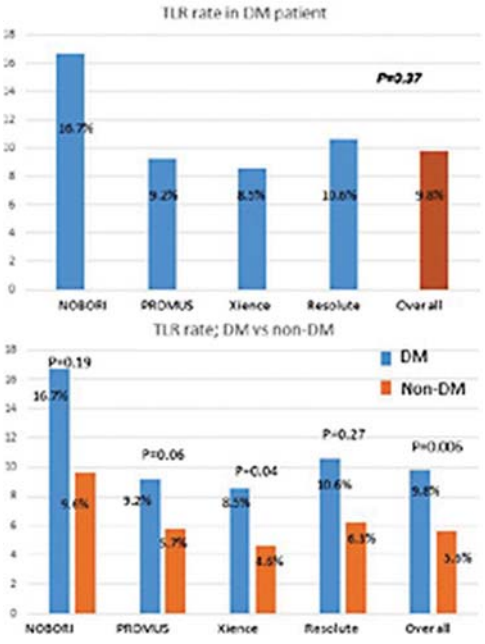
Background: New generation drug eluting stent (DES) showed better outcomes compared to 1st generation DES. However, it is not clear about the relationship between angiographical outcomes and diabetes mellitus (DM) in new generation DES.
Purpose: We performed this study to investigate the association between angiographical mid-term outcomes after new generation DES implantation and lesions in patients with DM/non-DM.
Methods: We compared the mid-term (9–12 months) angiographical outcomes among 4 new generation DES (Nobori; Biolimus-eluting stet: BES, Promus: Everolimus-eluting stent:EES-P, Xience; EES-V, Resolute; Zotarolimus-eluting stent: ZES). In addition, we compared the angiographical outcomes of each DESs between patient with DM and non DM.
Results: We treated 3745 lesions in 2027 patients between February 2010 and April 2014 with new generation DES in our centers. Hybrid stenting lesions were not included. Within them, angiographic follow up was performed 2680 lesions (BES: 215 lesions, EES-P: 1136 lesions, EES-V: 1087 lesions, ZES: 242 lesions) in 1595 patients. Lesion characteristics were not well matched among those 4 groups. In DM patients, lesions with BES revealed significantly higher restenosis rate compared to other kinds of DES. However, target lesion revascularization (TLR) rate were similar among 4 groups. Although restenosis rate was higher in BES, EES-P and EES-V in lesions with DM patients compare to non-DM patients, that in ZES was similar. Similarly, TLR rate in ZES was similar between lesions with DM and non-DM (Figure).



Conclusion: ZES showed similar restenosis and TLR rate compare to EES-P and EES-V in lesions with DM patients. And there was no significant difference about restenosis and TLR rate between DM and non-DM patients.

P6283 | BEDSIDE
Dose-dependent effect of aspirin on the level of sphingolipids in human blood

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Introduction: Acetylsalicylic acid (ASA) is antiplatelet drug which is commonly used in secondary prevention in ischemic heart disease and cerebrovascular events and in newly diagnosed myocardial infarction. Plasma sphingosine-1-phosphate (S1P) plays important cardioprotective role during ischemia, is-

chemia/reperfusion, ischemic-pre- and postconditioning. The aim of this study was to examine effect of ASA on the level of selected sphingolipid intermediates in plasma, erythrocytes and plates.
Methods: 42 healthy volunteers (both sexes, aged 23–24 years) participated in the study. They were divided into two groups: I ASA was given orally,75 mg once daily, for one week (n-25 11 males, 14 females); II. subjects received one dose 300 mg of the drug (n=17, 7 males, 10 females). In both groups the blood was taken before the teratment and 4h after the last dose of ASA. The following sfhingolipid intermediates were quantified using high-pressure liquid chromatography: sphinganine, sphingosine, S1P, sphinganine-1-phosphate (SA1P) and ceramide.
Results: Statistical comparisons were made by using the paired samples t test; $P<0.05$. There were no significant differences in erythrocyte and platelet count or hemoglobin concentration between the experimental groups. It was found that lower dose of ASA increased of S1P and erythrocytes (by 23 and 37% respectively) having no effect on plasma and platelet sphingolipid levels. Higher dose of the drug significantly reduced S1P and SA1P concentration in the plasma (by 16 and 10% respectively); the concentration of sphingosine and sphinganine remaind stable. There was also a trend towards an increase in plasma ceramide level (by 16%), but it did not reach statistical significance. We conclude that ASA interferes with sphingolipid metabolism in blood and that this effect depends on a dose of the drug. Since S1P is a potent cardioprotectant, the reduction in its plasma concentration after the loading dose of ASA could be undesired side effect of the drug.

P6284 | BEDSIDE
Mechanisms of ischemic preconditioning in coronary artery disease by arterial compliance and heart rate variability

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Background: Ischemic preconditioning (IP) seems to be universal protective method for patients with cardiovascular diseases. We propose that the effects of IP could be based positive effect on arterial compliance and heart rate variability (HRV).
Aim: Study of IP impact on pulse wave amplitude (PWA) and velocity (PWV), pulsoxymetry and heart rate variability (HRV) in CHD patients.
Methods: The randomized controlled crossover design study with active control in 25 stable patients with CHD and in control group (n=11) was performed. The PWA, PWV and HRV (AtCor, Australia) were estimated before and after IP (blood pressure + 50 mm Hg) versus sham IP (diastolic IP) according to randomization. The next day the same patients were investigated before and after on the contrary from the from former test sham IP/IP.
Results: IP did not change heart rate in both groups (Table); peripheral and central systolic and diastolic blood pressure decreased ($p<0.01$) but not in control (p=0.89); IP in compare to sham significally improved some HRV parameters (Triangular index, SDNN) and had the same tendency in rest of them but not in control.

IP in patients with CHD

Parameter	CHD group (n=25)		Control group (n=11)
	Δ(IP +50 mm Hg)	Δ(sham IP)	Δ(IP +50 mm Hg)
HR, beat/min	5.5	2.5	5.89
SBP, mm Hg	16.5**	12.9*	3.9
DBP, mm Hg	3.98	3.3*	1.4
Aortic syst BP, mm Hg	15.6*	12.1*	2.9
Aortic syst pulse pressure, mm Hg	13.6*	3.2*	–0.3
Augmentation pressure, mm Hg	3.07*	1.59*	–1.5
PWV, m/sec	0.34	–0.69	–0.2
Triangular index	–3.38*	–1,06	–0.37
SDNN index	–14.99*	–30.11	–3.23

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV, forced expiratory volume; AP, augmentation pressure; PWV, pulse wave velocity. *$p<0.05$.

Conclusions: IP showed positive effect on cardiovascular system decreased permanently high systolic and pulse pressure also in aorta and increased triangular index and some HRV parameters that may partly explain its positive effect in CHD patients.

P6285 | BEDSIDE
Prolonged chest symptoms in patients with vasospastic angina: what does this mean?

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Background: Clinicians often encounter patients with vasospastic angina (VSA) who have chest symptoms for a prolonged duration. However, the characteristics of such patients remain unclear. Therefore, we analysed the clinical characteristics of such patients.
Methods: We enrolled 122 patients with VSA, which was diagnosed by the spasm provocation test using acetylcholine (ACh). Medical interviews of all patients were conducted, and the maximum duration of chest symptoms and the presence of cold sweats were checked. In addition, we analysed the incidence of variant angina (VA), which was defined as angina with ST-segment elevation on electrocardiography during the attacks. The patients were divided into the two groups according to the duration of maximal chest symptoms: normal group (N, <15 min) and prolonged group (P, >15 min). During the spasm provocation test, the incidence of multi-vessel spasm, the findings induced by a low dose of ACh, total occlusion due to spasm, use of nitroglycerine (NTG) for relief of spasm during the provocation test, were investigated in the two groups.
Results: There were 96 patients in Group N and 26 patients in Group P (21%). The patients' characteristics did not differ between the two groups. The presence of cold sweats was more frequently observed in Group P (15% vs. 1% in Group N, $p<0.001$), and VA tended to be more frequently observed in Group P (4% vs. 0% in Group N, p=0.0537). NTG use for relieving severe spasm during the provocation test was more frequently observed in Group P (56% vs. 37% in Group N, $p<0.05$), whereas the incidence of multi-vessel spasm (P: 70% vs. N: 69%), positive provocation by a low dose of ACh (P: 32% vs. N: 20%) and total occlusion due to spasm (P: 12% vs. N: 11%) were not different in the two groups.
Conclusions: These findings suggest that VSA patients with prolonged chest symptoms may comprise one-fifth of all VSA patients. Such patients may have more severe characteristics of VSA.

P6286 | BEDSIDE
Comparison between plain old balloon angioplasty and drug-eluting stent implantation for the treatment of stent fracture

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Objectives: The aim of this study was to evaluate clinical outcomes after percutaneous coronary intervention (PCI) for stent fracture (SF).
Background: SF has been reported as a predictor of in-stent restenosis (ISR) and stent thrombosis (ST).
Methods: Between January 2009 and December 2012, consecutive SF cases treated with either drug-eluting stent (DES) or plain old balloon angioplasty (POBA) were retrospectively enrolled in this study. The study endpoints were all-cause death, cardiac death, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), ST, re-stent fracture (re-SF) and major adverse cardiac events (MACE) defined as the composite of cardiac death, MI and TLR.
Results: Of 135 SF cases, 67 (49.6%) cases were treated with DES, whereas 68 (50.4%) cases with POBA. Median follow-up period was 1401 (IQR: 967 to 1771) days. The estimated MACE rate at 3 years was significantly lower in the DES group as compared with the POBA group largely driven by less TLR (25.7% vs. 55.8%, $p<0.001$). Moreover, 1-year landmark analysis after PCI for SF revealed that MACE continued to occur even after 1 year irrespective of the treatment option (p=0.47). On multivariable Cox regression analysis, POBA and large post-procedure angle (Δ) defined as the degree difference between the end systolic and diastolic angle were identified as independent predictors for TLR.
Conclusions: DES implantation for SF is associated with lower TLR as compared with POBA possibly due to a smaller post-procedural angle (Δ). MACE, mainly driven by TLR, continued to increase even after 1 year irrespective of treatment option.

P6287 | BEDSIDE
Long-term clinical outcome of angiotensin-converting enzyme inhibitor versus angiotensin II receptor blocker in patients with acute myocardial infarction undergoing percutaneous coronary intervention

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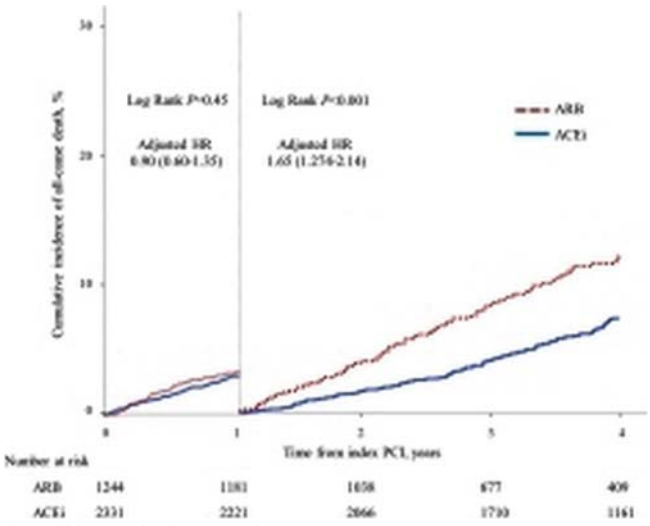
Background: Current guidelines recommend that angiotensin-converting enzyme inhibitor (ACEi) should be used as the first choice for post myocardial infarction (MI) treatment and angiotensin II receptor blocker (ARB) should be considered in patients who are intolerant to ACEi. Although 2 large randomized clinical trials were published at the early 2000s, there have been a little data about head-to-head comparisons at percutaneous coronary intervention (PCI) era.
Methods: We consecutively enrolled AMI patients who underwent PCI in the COREA-AMI (COnvergent REgistry of cAtholic and chonnAm university for AMI) from January 2004 to December 2009. Of 4,748 AMI patients, 2,332 and 1,245 patients were treated with ACEi and ARB at discharge, respectively. The primary endpoint was the incidence rates of all-cause death.
Results: Median follow-up duration was 43.8 months. In overall population, long-term survival was superior in ACEi group (201 death, 10.1%) as compared with ARB group (150 death, 15.2%) ($p<0.01$). In multivariable Cox regression, adjusted HR is 1.37 (95% CI 1.10 to 1.70, $p<0.01$). Overall findings were consistent in propensity matched population. In subgroup analyses, there were significant interaction between preserved (HR 1.07, 95% CI 0.81 to 1.46, p=0.69) and decreased renal function (HR 1.78, 95% CI 1.22 to 2.60, $p<0.01$, p for interaction p=0.04) and between STEMI (HR 1.00, 95% CI 0.71 to 1.40, p=0.98) and NSTEMI (HR 1.78, 95% CI 1.26 to 2.50, $p<0.01$, p for interaction 0.019).
Conclusion: Long-term survival of ACEi was significantly superior than ARB in patients with AMI treated with PCI. ACEi should be remained as the first-choice



Kaplan-Meier curve for all-cause death

of treatment in AMI patients and ARB might be used as alternative with careful consideration of renal function or clinical diagnosis.

P6288 | BEDSIDE
Association of neutrophils to lymphocytes ratio, carotid atherosclerosis, and coronary artery disease in patients with chest pain

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Background: Inflammation plays a role in the pathogenesis of systemic atherosclerosis, and neutrophils and lymphocytes ratio (NLR) have been studied as new predictors of cardiovascular risk. This study aimed to investigate the relationships between NLR and the parameters of carotid atherosclerosis in the common carotid artery (CCA) in patients with suspected coronary artery disease (CAD).
Methods: Carotid artery US was performed in 839 patients with suspected CAD, and mean IMT, total plaque area (TPA), and inflammatory markers including NLR, platelet to lymphocyte ratio (PLR) and high-sensitive C-reactive protein (hs-CRP) were measured. Inflammatory parameters were analyzed according to the presence of CAD (>50% in diameter stenosis) and the carotid atherosclerosis (defined as an increased IMT ≥0.9 mm or with a plaque).
Results: Compared to patients without CAD (n=592), patients with CAD (n=247) showed significantly higher NLR (2.19±1.94 vs. 2.79±2.96, p=0.003), PLR (104.1±44.5 vs. 117.7±91.8, p=0.027), mean CCA IMT (0.66±0.15 mm vs. 0.73±0.20, p<0.001) and TPA (0.13±0.24 vs. 0.29±0.62 cm^2, p<001). NLR showed significantly correlated with the presence of CAD (r=0.120, p<0.001) and carotid atherosclerosis (r=0.138, p<0.001). When the patients were classified into four groups based on the presence of CAD and carotid atherosclerosis, patients with CAD with carotid atherosclerosis showed the highest NLR (no CAD without carotid atherosclerosis; 1.82±0.91 vs. no CAD with carotid atherosclerosis; 2.63±2.62, vs. CAD without carotid atherosclerosis; 2.78±2.95 vs. CAD with carotid atherosclerosis; 2.84±3.03, p<0.001). On receiver operating characteristic analysis, NLR was found to have the largest area under the curve (AUC = 0.590, p<0.001 and AUC = 0.605, p<0.001, respectively) with an optimal NLR cut-off value of 1.98 (sensitivity 49%, specificity 65%) and 1.77 (sensitivity 62%, specificity 57%) for predicting the presence of carotid atherosclerosis and significant CAD.
Conclusion: In patients with chest pain, high NLR was significantly associated with the carotid atherosclerosis and CAD. These findings support the role of NLR as a simple inexpensive and readily available marker an index of atherosclerosis and serves as a predictor of significant coronary and carotid atherosclerosis.

P6289 | BEDSIDE
Single-night ventilation therapy for sleep disordered breathing is associated with a decrease in inflammatory markers in patients with heart diseases

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Purpose: Inflammatory markers (IM) have been shown to be higher in patients with heart failure (HF) and sleep disordered breathing (SDB) compared to HF patients without SDB. We investigated whether positive airway pressure (PAP) ventilation therapy reduces IM within one night of therapy.
Methods: Consecutive cardiac patients (coronary artery disease and/or heart failure) with documented moderate to severe SDB (full overnight polysomnography, PSG), were treated by PAP (continuous positive airway pressure, CPAP or adaptive servoventilation, ASV). Markers reflecting heart failure/structural heart disease (BNP, CK, CKMB, myoglobin), liver disease (ALT, AST), inflammation (high sensitive CRP, Fibrinogen, IL-6, lactate) and renal failure (creatinine) were taken the morning after diagnostic PSG and the morning after PAP therapy initiation.
Results: In 39 patients (77% male, 65±10 years, BMI 31±6 kg/m^2, 69% sinus rhythm, 62% Diabetes, 82% CAD, 10% NYHA III/IV) SDB was successfully treated by PAP, with a decrease in apnoea-hypopnoea index from 36±19/h to 11±10/h (p<0.001). This was associated with a significant decrease in CK (126±89 U/l vs. 111±67 U/l;p<0.001) and high sensitive CRP (0.48±0.70 mg/dl vs. 0.43±0.71 mg/dl; p=0.032) and a trend towards a decrease in BNP (181±213 pg/ml vs. 170±208 pg/ml; p=0.08) and troponin (0.024±0.075 pg/ml vs. 0.018±0.04 pg/ml: p=0.09)
Conclusion: Treatment of moderate to severe SDB with PAP therapy in cardiac patients results in a decrease of inflammatory markers and markers representing cardiac damage. This might be responsible for beneficial effects with long-term PAP therapy in such patients.

ADJUNCTIVE MEDICAL THERAPY

P6290 | BEDSIDE
Characterization of cardiovascular endpoints, impact of event adjudication and effects of darapladib in the STABILITY trial

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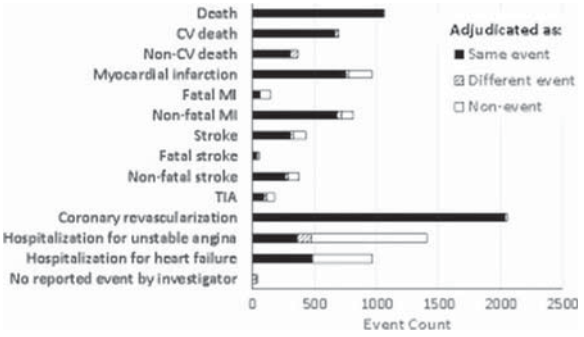
Background: In the STABILITY trial in 15828 pts with stable coronary heart disease darapladib did not reduce the primary outcome of MACE (cardiovascular death (CVD), myocardial infarction (MI) or stroke) vs placebo. Clinical Endpoint Classification (CEC) is a process for independent adjudication of investigator reported events aiming to provide a consistent blinded evaluation.
Methods: Investigators were instructed to report all suspected events. All events were reviewed by two independent reviewers according to a pre-specified process and endpoint definitions. We evaluated differences between reported and adjudicated rates of CV events, and whether these affected the final study results.
Results: In total, investigators reported 7096 events: 1064 deaths (696 CVD); 958 MI; 433 strokes; 182 TIA; 2052 coronary revascularisations; 1407 hospitalisations for unstable angina (UA) and 967 heart failures (HF). In total, 71.8% were adjudicated as the same event, 3.1% as a different and 25.1% as non-event. High concordance (>80%) was found for cause of death, non-fatal MI and coronary revascularisation and lower for hospitalisation for UA (75%) and HF (50%) (Fig). For the primary outcome, investigators reported 2086 events of which 82.5% were adjudicated as MACE. In addition 234 events were adjudicated to be MACE. The investigator reported results for the primary outcome on darapladib vs placebo HR 0.96 (95% CI 0.87–1.06) were consistent with the adjudicated HR 0.94 (95% CI 0.85–1.03).



Conclusions: Primary outcome results were consistent between investigator reported and CEC adjudicated events. Low concordance and greater heterogeneity occurred for UA and HF, highlighting the importance of a thorough CEC process with careful site instructions and adjudication to assure reliable high quality results.
Acknowledgement/Funding: The STABILITY study was funded by GlaxoSmithKline.

P6291 | BEDSIDE

Heart rate reduction by ivabradine for improvement of endhotelial function in patients with coronary artery disease: the randomized open-label RIVENDEL study

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Background: Data from experimental studies suggest that the I_f current-inhibitor ivabradine may reduce oxidative stress and improve endothelial function. However, no evidence is available on the effect of chronic therapy with ivabradine in patients with coronary artery disease (CAD) treated with percutaneous coronary angioplasty (PCI).
Purpose: We aimed to evluate the effect of ivabradine on endothelial function in patients with CAD after complete revascularization with PCI.
Methods: At least 30 days after complete revascularization with PCI, 70 patients were randomized (T1) to receive ivabradine 5 mg twice daily (ivabradine group, n=36) or to continue with standard medical therapy (control group, n=34). After 4 weeks (T2) ivabradine dose was adjusted up to 7.5 mg twice daily in patients with heart rate (HR) at rest >60 bpm, and thereafter continued for additional 4 weeks (T3). At all timings endothelial function was assessed by flow-mediated dilatation (FMD) and nitroglycerin-mediated dilatation (NMD).
Results: No significant differences were observed at T1 between ivabradine and control groups in terms of HR (68.0±6.4 vs. 67.6±6.4 bpm; p=0.803), FMD (8.7±4.9 vs. 8.0±5.5%; p=0.577) and NMD (12.7±6.7 vs. 13.3±6.2%; p=0.715). Over the study period, a significant reduction of HR (65.2±5.9 bpm at T2, 62.2±5.7 bpm at T3; p<0.001), and improvement of FMD (12.2±6.2% at T2, 15.0±7.7% at T3; p<0.001) and NMD (16.6±10.4% at T2, 17.7±10.8 at T3; p<0.001) was observed in the ivabradine group, while no significant changes were observed in the control group (p>0.5 for all parameters analysed). At T3, patients treated with ivabradine compared with those in the control group presented significantly lower HR (p=0.003) and higher FMD (p<0.001), while no significant difference was observed in terms of NMD (0.549). In the ivabradine group, a moderate negative correlation was observed between the HR variation and FMD variation from T1 to T3 (r=–0.448; p=0.006).
Conclusion: In patients with CAD undergoing complete revascularization with PCI, addition of ivabradine to standard medical therapy produces a significant improvement in endothelial function. This effect seems to be related to the HR reduction.

ECHO-VENTRICULAR FUNCTION AND MYOCARDIAL DISEASE

P6292 | BEDSIDE

Determinants of electrocardiographic parameters for the left ventricular mass index on echocardiography

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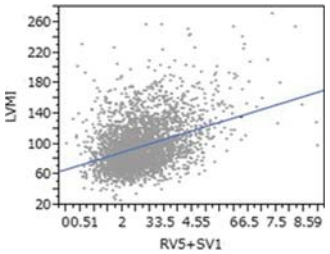
Background: Since the 1990's, numerous electrocardiographic criteria have been proposed for the detection of left ventricular hypertrophy (LVH) in Western countries. However, in Asian populations, the correlation between electrocardiogram (ECG)-determined LVH and LVH by echocardiography remains unclear.
Purpose: The aim of this study was to examine the electrocardiographic factors related to LVH in an Asian population.
Methods: We retrospectively analyzed the ECG and echocardiographic parameters, which were simultaneously acquired, in 3776 Japanese patients examined in our hospital during 2013. The left ventricular mass index (LVMI) was calculated according to the formula of Devereux.
Results: The simple linear regression analysis of the association between LVMI and ECG parameters, such as the summation of the amplitude of the R wave in V5 (RV5) and S wave of V1 (SV1), was significant; however, its correlation coefficient was low (r=0.3755, Figure). The QRS duration (p<0.0001); amplitude of the R wave in lead II (RII; p<0.0001), aVR lead (RaVR; p=0.0468), and aVL lead (RaVL: p=0.0025); RV5+SV1 (p<0.0001); age (p<0.0001); and sex (p<0.0001) were found to be determinant factors of LVMI in the generalized linear model using Poisson distribution. Receiver operating characteristics curve analyses, adjusted by age and sex, showed that the area under the curves were 0.744 in men and 0.787 in women when using the combined values of QRS duration, RII, RaVR, and RaVL for the prediction of the presence of more than 125 g/m^2 of LVMI.



Association with LVMI and RV5+SV1

Conclusions: ECG prediction of LVMI may be improved by using a more complicated model, and the use of such an approach is warranted to ensure further improvements in LVH detection.

P6293 | BEDSIDE

Left atrial ejection force as a quantitaive measure of left ventricular diastolic dysfunction measured by Doppler echocardiography

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Background: The value and clinical importance of Left atrial ejection force.
Aim: To assess the left atrial ejection force as a quantitative measure of left ventricular diastolic function compared to traditional Doppler and tissue Doppler measurements of diastolic function. Furthermore, the relationship between left atrial ejection force and LV end diastolic pressure was studied.
Patients and methods: We enrolled 120 patients presenting with different grades of LV Diastolic dysfunction (Grades I, Ia, II and III); allocating 30 patients to each group and 30 healthy subjects as a control group. A detailed transthoracic echocardiogram, including mitral flow velocities, tissue Doppler mitral annular velocities, and left atrial (LA) volume, was performed in both groups. LAEF was calculated using formula postulated by Manning et al. (LAEF = 1/3 x MVA x A^2). Correlations between variables were studied using "Pearson and Spearman's rho" test.
Results: In the test group, we found that Left atrial ejection force is a statistically significant quantitative measure of LV diastolic dysfunction. The %LAEF increases from Grade I (average 188.93% ± 40.12%) to become 239.70% ± 72.45% in grade Ia, then increasing further to 256.57% ± 45.92% in grade II and dramatically falling to 57.88% ± 32.49% in grade III Diastolic dysfunction. LAEF was increased in elderly patients, with a weak positive correlation between age and LAEF (r=0.27, p=0.003). A moderate negative correlation existed between different LV dimensions and %LAEF. Similarly, a moderate negative correlation existed between %LAEF and LAVI. (r=–0.342, p<0.0001). A good positive correlation existed between LAEF and IVRT, DT, A wave velocity and septal E' with a p value <0.0001 and r=0.449, 0.425, 0.53 and 0.457 respectively (p<0.0001).
Conclusion: Impaired diastolic function affects LA and increased LAEF is one of its manifestations. The initial rise in LAEF with the degree of diastolic dysfunction is due to the increase in LVEDP and thus a greater left atrial systolic force is needed, while the fall in LAEF in grade III may be explained by LA dilatation and failure. LAEF may also have diagnostic importance in diastolic dysfunction, but these findings should be confirmed by further studies.

P6294 | BEDSIDE

The association between semi-quantitative microalbuminuria, altered cardiac geometry, diastology and contractile mechanics in asymptomatic individuals

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Background: Microalbuminuriaas as an early sign of renal impairment may occur before overt reduction in renal filtration rate. The impact of proteinuria on cardiac geometry and associated cardiac mechanical changes remain largely unknown.
Methods: We consecutively examined 2D speckle-tracking in an asymptomatic cohort, with cardiac geometry, diastolic function, myocardial (LV) deformations and twist/torsion analyzed. We further categorized the study population into four groups based on urine dipstick results: ordered proteinuria amount: 0, 0.5, +1, +2 or +3).
Results: Totally 3,787 subjects had both urine dipstick and speckle-tracking results available (mean age 50.16±11.07 years, 67.7% female) with preserved LV ejection fraction. A trend toward greater LV wall thickness, higher LV mass index, impaired mitral annulus relaxation E', and larger LA volume index across 4 groups were observed (Table1, all trend p<0.001). We also noticed graded reduction of longitudinal (–20.29, –20.01, –19.91, –18.37%, adjusted β: –0.49, p<0.05) and circumferential strains (–24.12, –23.80, –23.82, –23.10%, trend p<0.05) though preserved LV ejection fraction across 4 groups.

Table 1

Variables	Group 1 n=3065	Group 2 n=486	Group 3 n=144	Group 4 n=92	Trend p value
Protein, urine test strip	0	0.5+	1+	2–3+	
Age, years	49.58±10.76	49.86±10.46	53.24±12.51	55.29±12.36	<0.001
NT-ProBNP, ng/ml	40.21±47.12	45.88±146.14	56.08±79.04	198.38±591.59	<0.001
LV mass index, g/m^2	75.32±13.87	76.42±13.83	79.25±15.93	83.19±18.54	<0.001
LV ejection fraction, %	66.87±4.57	66.55±4.51	66.16±5.04	66.23±5.12	<0.001
Lateral E', cm/sec	10.49±2.86	10.23±3.00	9.38±3.01	8.13±2.55	<0.001
Lateral S', cm/sec	9.29±2.34	9.12±2.24	8.78±2.04	8.04±2.01	<0.001
Global longitudinal strain, %	–20.29±1.93	–20.01±1.86	–19.91±1.95	–18.37±2.34	<0.001
Global circumferential strain, %	–21.37±3.60	–21.13±3.54	–21.25±3.58	–20.34±3.61	0.043
Twist, °	13.74±5.33	13.82±5.17	14.57±5.47	14.20±5.84	0.106
Torsion, °/cm	2.19±0.90	2.21±0.86	2.37±0.95	2.22±0.97	0.113

Conclusion: Microalbuminuria in asymptomatic population is associated with altered cardiac geometry accompanied by subclinical LV contractile disturbances

in terms of all strains. Our data suggested that proteinuria, even as minor degree, may be associated with detrimental effects on systolic function.

P6295 | BEDSIDE
Tissue mitral annular displacement - a novel technique for rapid quantitative assessment of global left ventricular systolic function based on speckle tracking algorithm

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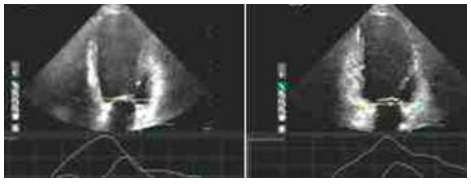
Background: TMAD (tissue mitral annular displacement) is a new technique for rapid quantitative assessment of global left ventricular function based on tracking of acoustic markers. It allows for the assessment of mitral annulus displacement relative to the apex, based on standard apical views.
Objective: To assess the feasibility and accuracy of measurements obtained with TMAD technique for the analysis of global left ventricular function using 3D ejection fraction (LVEF) measurements as a reference technique.
Methods: The study included 49 patients (33 men, mean age 65±10 years) with coronary artery disease, who underwent 2D and 3D transthoracic echocardiography with off-line measurement of LVEF using 3D datasets. Furthermore a TMAD algorithm was performed in all patients.
Results: TMAD analysis of one apical view took 10±4 seconds. Mean LVEF was 47,8±12,2%. Due to the suboptimal quality of the data, insufficient for tracking the acoustic markers by the TMAD algorithm, 5 patients were excluded. In the remaining 44 patients there was a statistically significant correlation between LVEF and the midpoint mitral annulus displacement towards the apex in the apical four chamber view ($r=0.57$, $p<0.0001$) and the percentage of the midpoint mitral annulus displacement ($r=0.63$, $p<0.0001$). A similar correlation was observed between midpoint mitral annulus displacement in the apical two chamber view ($r=0.6$, $p<0.0001$) and the percentage of the midpoint mitral annulus displacement ($r=0.65$, $p<0,0001$).



Conclusion: Measurement of midpoint mitral annulus displacement by TMAD technique is very rapid and provides satisfactory correlation with 3D LVEF measurements. This technique, however, requires echocardiographic recording of good quality.

P6296 | BEDSIDE
The prevalence of transient apical hypertrophy during recovery phase of takotsubo cardiomyopathy

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Background: Takotsubo cardiomyopathy (TTC) is characterized by a transient systolic dysfunction of the left ventricle. A few case was reported about left ventricular apical hypertrophy (APH) during recovery from TTC. The purpose of this study was to investigate the incidence of transient APH and the differences in clinical characteristics in TTC patients.
Methods: Sixty two TTC patients were enrolled in this study. Patients were divided into two groups as N -APH group which did not show APH like findings in the process of wall motion recovery and T-APH group which showed transient APH findings. Cardiac complications were defined as cardiac death, pump failure, sustained ventricular tachycardia or ventricular fibrillation and advanced atrioventricular block.
Results: Nineteen of 62 (30.6%) TTC patients demonstrated typical APH findings during recovery from wall motion abnormality. Finally, these APH findings disappeared and left ventricular morphology recovered to normal structure. There is no significant difference between two groups in clinical characteristics (table). Incidence of cardiac complication showed significantly lower in T-APH group than that in N-APH group ($P<0.05$, Table)

	N-APH (N=43)	T-APH (N=19)	P value
Age	78.3±10.2	75.6±12.8	NS
Female (%)	95.3	89.5	NS
Stress (%)	51.2	52.6	NS
Peak CK (IU/l)	278±496	216±233	NS
WBC (/μl)	9705±5526	7495±2566	NS
CRP (mg/dl)	3.70±6.44	2.06±2.67	NS
Time for wall motion recovery (day)	17.1±10.6	16.1±9.6	NS
Cardiac complication (%)	65.1 (N=28)	31.6 (N=6)	<0.05
Cardiac death	5	0	NS
Pump failure	27	6	<0.05

Conclusions: Transient left ventricular APH were observed in 30.6% in TCC patient by serial echocardiographic observation. Incidence of cardiac complications in T-APH group is significantly lower than that in N-APH group. Prevalence of T-APH in patients with TTC is higher than in previous reports.

P6297 | BEDSIDE
Wasted myocardial work in left ventricular dyssynchrony: a preliminary report of a novel principle to predict response to cardiac resynchronization therapy

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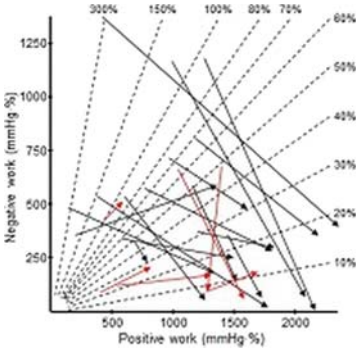
Background and aim: Cardiac resynchronisation therapy (CRT) in heart failure is limited by a large fraction of non-responders. We explore if degree of wasted left ventricular (LV) work identifies responders to CRT.
Methods: Twenty one patients who received CRT according to current guidelines were studied before and after an average of 8±2 months. By definition, segments which shorten in systole perform positive work, whereas segments which lengthen do negative work. Work was calculated from non-invasive LV pressure and strain by speckle tracking echocardiography. For each myocardial segment and for the entire LV wasted work fraction (WWF) was calculated as negative work in percentage of positive work. LV wall motion score index (WMSI) was assessed by echocardiography. Response to CRT was defined as ≥15% reduction in LV end-systolic volume (ESV).
Results: Responder rate to CRT was 71%. In responders WWF for septum was 117±102%, indicating more negative than positive work, and decreased to 14±12% ($p<0.01$) with CRT. In the LV free wall WWF was 19±16% and showed no significant change. Global WWF decreased from 36±21 to 19±10% ($p<0.01$) with CRT. In multiple linear regression analysis septal WWF and WMSI were the only significant predictors of ESV reduction (septal WWF: $\beta=0.14$, $p=0.01$; WMSI: $\beta=1.25$, $p=0.03$). Septal WWF together with WMSI showed AUC=0.86 (CI 0.71–1.0) for CRT response prediction.



Fig, 1 Individual data – percentage of wasted work is indicated in dashed lines. CRT responders (black arrows) showed a shift to more positive work with drop in the WWF. The non-responders (red arrows) showed no consistent shift.

Conclusions: In this pilot study septal WWF together with WMSI was a strong predictor of response to CRT. This novel principle should be studied in future larger studies.
Acknowledgement/Funding: This study was funded by a grant from the Norwegian Research Council to Oslo University Hospital's Center for Cardiological Innovation (CCI).

P6298 | BENCH
Myocardial stiffness as an important determinant of early systolic lengthening and post-systolic shortening

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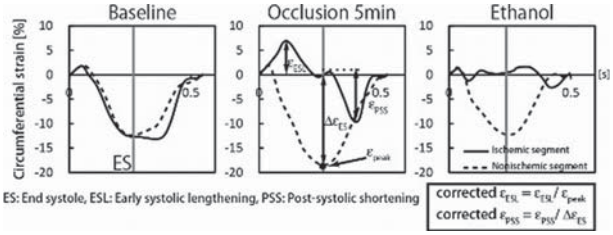
Background: Although early systolic lengthening (ESL) and post-systolic shortening (PSS) observed in the ischemic segment could be affected by the myocardial stiffness, there have been no reports to directly prove it.
Methods: In 6 open-chest dogs, left ventricular short-axis images were acquired at baseline, during left anterior descending coronary artery (LAD) occlusion and after intramyocardial injection of ethanol into the LAD territory to stiffen the myocardium in addition to ischemia. Circumferential strains were analyzed and the amplitude of ESL (ϵESL) and PSS (ϵPSS) were measured in each stage. To correct the effect of tension from the nonischemic segment, ϵESL was divided by the peak systolic strain (ϵpeak) in the nonischemic segment and ϵPSS was divided by the difference of strains at end systole between ischemic and nonischemic segments ($\Delta\epsilon$ES). The Young's modulus was measured at the ischemic and nonischemic myocardium from the excised heart with a digital force gauge.
Results: ϵpeak were almost similar during LAD occlusion and after ethanol injec-

tion. However, ESL and PSS significantly decreased after ethanol injection compared to during LAD occlusion (ϵESL, 6.8±2.7% vs. 0.28±0.30%, p<0.05; ϵPSS, −8.2±1.3% vs. −1.8±1.1%, p<0.05; corrected ϵESL, −0.54±0.37 vs. −0.24±0.11; corrected ϵPSS, 0.49±0.08 vs. 0.15±0.10, p<0.05) (figure). The Young's modulus of the myocardium in the LAD territory was higher than that of the nonischemic myocardium indicating that the myocardium became stiff by ethanol injection (0.07±0.02 vs. 0.28±0.13 N/cm^2, p<0.05).



Conclusion: ESL and PSS are affected not only by myocardial ischemia but also by myocardial stiffness. The feasibility of noninvasive assessment of myocardial stiffness in the ischemic segment using ESL and PSS should be investigated.

ECHO-IMAGING EVALUATION OF THE RIGHT VENTRICLE

P6299 | BEDSIDE
Validation of right ventricular volume derived from 3-dimensional speckle tracking echocardiography: application for adult congenital heart disease

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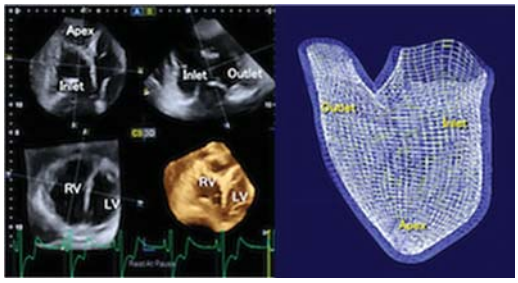
Newly developed 3D speckle tracking imaging (STI) system specialized for the right ventricle has been validated using sonomicrometry in experimental animal model, recently. Accordingly, the purpose of this study was to investigate the accuracy of the newly developed RV 3D echo STI in evaluating the chamber volume and ejection fraction (EF), in which cardiac magnetic resonance (cMR) was performed as the gold standard in various heart disease patients including adult congenital heart disease (ACHD).
Methods: Sixteen ACHD (7 ventricular septal defect, 6 tetralogy of Fallot, 2 pulmonary stenosis, 1 Ebstein) and 53 patients with other cardiovascular disease were included. In RV 3D echo STI, end-diastolic RV inlet, apex, and outlet endocardial borders were manually traced, then, end systolic volume (ESV) and EF were automatically calculated (Figure).
Results: Among total of 69 patients, 22 (32%) were excluded because of the inadequate echo image quality. In ACHD group, only 2 (12%) patients were excluded. Among remaining 47 patients, all RV subendocardial contour could be visualized in 22 (48%) patients. In remaining 25 patients, RV end diastolic volume, ESV, EF derived by 3Decho STI showed close relations with these by cMR (R2=0.91, 0.91, 0.67, all p<0.001, respectively), however, the bias and limits of agreement between two procedure −6ml (−43 to 30) in EDV, −2ml (−32 to 28) in ESV, and −3% (−15 to 10) in EF. Intra- and inter-analyzer reproducibility was 4.9±6.1% and 7.1±9.2% in RVEF for ACHD subgroup.



RV 3D speckle tracking echocardiography

Conclusion: While further technical progress should be required to overcome the limitation of the RV outlet assessment, RV 3D speckle tracking is the promising imaging modality in assessing RV volume and function with significant but small systemic underestimation.

P6300 | BEDSIDE
Pseudonormal right ventricular filling pattern reflects left ventricular systolic dysfunction and remodeling

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Background: Transtricuspid flow pattern is used to estimate right ventricular (RV) filling pressure, and high ratio of tricuspid inflow E velocity to tissue Doppler e' (E/e') is implicated as increased right atrial pressure. Left ventricular (LV) function may affect right heart function, but the relationship between LV function and RV filling pattern is not fully understood.
Methods: We retrospectively analyzed 915 patients who underwent echocardiography to assess cardiac function between January 2013 to March 2014 in our hospital. Transtricuspid early (E) and late (A) diastolic filling velocity ratio (E/A) and tricuspid E/e' ratio were measured. Patients were divided into two groups: non-pseudonormal (low tricuspid E/e' (<6), n=658) and pseudonormal (high tricuspid E/A (>0.8) with high tricuspid E/e' (≥6), n=257) RV filling groups.
Results: The pseudonormal RV filling group displayed lower LV ejection fraction (61 [52–65]% vs. 63 [57–68]%, P<0.01), lower LV systolic velocity (6.9 [5.7–8.2] cm/sec vs. 7.9 [6.4–9.5] cm/sec, P<0.01), and larger LV end-diastolic volume (89 [69–113] ml vs. 84 [68–104] ml, P<0.05) than non-pseudonormal RV filling group, suggesting that pseudonormal RV filling pattern reflected LV systolic dysfunction and remodeling. We next assessed the patients in the setting of elevated LV filling pressure. Out of 915 patients, 79 patients presented increased LV filling pressure pattern (mitral E/A>0.8 with mitral E/e'>15). Pseudonormal RV filling group (n=25) showed lower LV ejection fraction (52 [32–63]% vs. 63 [53–68]%, P<0.01) and larger LV end-diastolic diameter (51 [47–60] mm vs. 47 [40–55] mm, P<0.01) than non-pseudonormal RV filling group (n=54), indicating that RV filling pattern can stratify the category of the patients with elevated LV filling pressure pattern.
Conclusions: The transtricuspid flow pattern reflects LV condition, and useful for rigorous risk stratification of the patients with increased LV filling pressure.

P6301 | SPOTLIGHT
Impact of an expedition to 8000m peak on the right heart - the echocardiographic assessment of right ventricle structure, performance and mechanics after exposure to extreme altitude

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Introduction: Extreme mountaineering has aroused in a popularity last years. The chronic and acute exposure to altitude, even in healthy, prone individuals has an impact on the right heart but still little is known what happen after return from hypoxic condition. Therefore, we intended to evaluate right ventricle in alpinists after climbing eight thousands peak.
Methods: The echocardiographic examination was performed according to protocol, including 2D echocardiography, Doppler echocardiography, pulsed tissue Doppler imaging, and 2D speckle tracking echocardiography near the sea level in 11 subjects participating in an expedition to K2 or Broad Peak (BP) before and after altitude exposure.
Results: After the 6–8 weeks of residence above 2500 meters (m) aimed to climb K2 (8611m) or BP (8051m) right ventricle (RV) Tei index increased (0.5±0.1 after vs. 0.4±0.1 before; p=0.028) and RV free wall (RV FW) longitudinal systolic strain decreased (−23.1±2.7% after vs. −25.9±2.4% before; p=0.043). It was observed the decrease in peak systolic strain and strain rate in the basal (−24.4±4.4% after vs. −30.9±6.5% before; p=0.017 and −1.4±0.3 s^{-1} after vs. −1.8±0.3 s^{-1} before; p=0.017) and mid (−28.7±3.9% after vs. −34±3.3% before; p=0.028 and −1.5±0.2 s^{-1} after vs. −1.9±0.3 s^{-1} before; p=0.028) segments of the RV FW. A trend toward lower tricuspid annular plane systolic excursion, RV systolic excursion velocity, right ventricle ejection fraction and right ventricle fractional area change after expedition was found. The linear RV dimensions such as RV outflow track proximal and RV outflow track distal increased (accordingly: 31.3±4mm after vs. 29.2±3mm before; p=0.025 and 27±2.7mm after vs. 24.8±3mm before; p=0.012) and the ratio RV/LV was higher (0.8±0.1 after vs. 0.7±0.1 before; p=0.046). None of the subjects have high altitude pulmonary edema (HAPE) episode and pulmonary artery systolic pressure (PASP) remained unchanged.
Conclusions: In short time after return from exposure to extreme altitude such as climbing 8000m peak, in HAPE resistant individuals, RV dilatation and change in RV performance is observed, whereas PASP is normal. The Tei index and RV free wall longitudinal systolic strain are superior to other RV performance indices to detect changes in RV function after exposure to extreme hypoxic stress. Observed alterations in cardiac morphology and function seem to be the persistence of physiological adaptation to high altitude condition in healthy individuals. The RV performance evaluation should be a part of the sport qualification to altitude activities.

P6302 | BEDSIDE
Pre-operative right ventricular function predicts clinical outcome after prophylactic tricuspid ring implantation

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Background: Symptomatic patients with organic mitral regurgitation respond favourably to valve repair surgery which results in reduced left atrial pressure and pulmonary venous congestion, hence symptomatic improvement. However, the nature of the required open heart surgery is known to be associated with reduced right ventricular (RV) function and potential worsening of tricuspid regurgitation

(TR), a combination that clinically devalue an otherwise successful mitral valve surgery. Simultaneous tricuspid valve ring (TVR) implantation has been proposed as a potential preventive measure to such problem.
Objective: The aim of this study was to assess the effect of TVR implantation, at the same setting of mitral valve surgery for severe regurgitation, on RV structure and function.
Methods: We retrospectively analysed post-operative (mean 5.4 (2.5 SD) days) Doppler echocardiographic studies from 61 patients, mean age 66±12 years, 40 (65.6%) male, who underwent mitral valve repair surgery together with TVR insertion and compared them with pre-operative studies. RV inlet diameter, tricuspid annular peak systolic excursion (TAPSE) and myocardial velocities and deformation using TDI and speckle tracking techniques were all measured. TR was assessed by colour and continuous wave Doppler.
Results: Post-operatively, RV fraction area change increased ($p<0.03$), TAPSE reduced ($p<0.0001$), e' velocity did not change but a' velocity increased ($p<0.01$). RV global and free wall systolic strain reduced ($p<0.005$ for both) but early and late diastolic strain remained unchanged. Three patients deceased within 14 days, 10 developed heart failure and 13 had residual mild TR, after surgery.
Preoperative TAPSE ($p<0.05$) predicted death within 14 days post OP; Global Strain Rate S (p=0.013) predicted heart failure; and pulmonary hypertension predicted residual TR ($p<0.04$).
Conclusion: Although TVR results in significant reduction of TR, almost one fifth of patients remain with serious complications, even death. Comprehensive preoperative RV structure and function assessment should critically stratify patients according to expected benefit.

P6303 | BEDSIDE
Improvement of biventricular myocardial function in patients with cirrhosis following liver transplantation

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Background: Patients with cirrhosis have been shown to be associated with myocardial dysfunction. However, limited studies have evaluated cardiac function in patients with cirrhosis before and after liver transplantation.
Purpose: The aim of the study is to evaluate biventricular myocardial function before and after liver transplantation in patients with cirrhosis.
Methods: A total of 67 consecutive patients (mean age 54.9±7.7 years; 73.1% male) with cirrhosis referred for liver transplantation were recruited. Conventional and advanced 2-dimensional speckle tracking echocardiography were performed to assess for biventricular function. During the follow up period, a total of 41 patients underwent successful liver transplantation and the rest remains on the liver transplantation waiting list. A second echocardiography was performed in all patients within the following date (patients following liver transplantation: 18.2±6.6 months and patients who did not receive liver transplantation: 20.4±8.3 months).
Results: For patients who received liver transplantation, a reduction of left ventricular (LV) diastolic and systolic volume (71.3±16.9ml vs. 91.4±27.1ml and 25.2±7.7ml vs. 32.2±12.9ml, respectively; both $P<0.01$), a trend towards a lower LV mass (195.8±54.5g vs. 214.0±55.1g, P=0.05) and improved LV global longitudinal and circumferential strains (–20.8±2.0% vs. –18.5±2.6% and –18.7±2.3% vs. –16.5±2.4%, respectively; both $P<0.01$) were observed. In addition, these patients showed a reduction of right ventricular (RV) end diastolic and systolic area (12.4±2.2cm^2 vs. 13.6±3.7cm^2 and 5.5±1.2cm^2 vs. 6.2±2.1cm^2, respectively; both $P<0.05$), and improved RV strain (–23.2±2.5% vs. –21.0±4.8%, $P<0.01$) following liver transplantation. For patients who did not receive liver transplantation, both left and right heart dimension and function remained similar between first and second echocardiography.
Conclusion: The present study demonstrates that patients with cirrhosis had reduced biventricular chamber dimension and improved biventricular systolic function following liver transplantation. No such association was found in patients who did not receive liver transplantation. The present finding thus suggested that myocardial dysfunction in patients with cirrhosis could be reversed following successful liver transplantation.

P6304 | BEDSIDE
Right ventricular fractional area change obtained in different echocardiographic views. Comparison with right ventricular ejection fraction by cardiac magnetic resonance imaging

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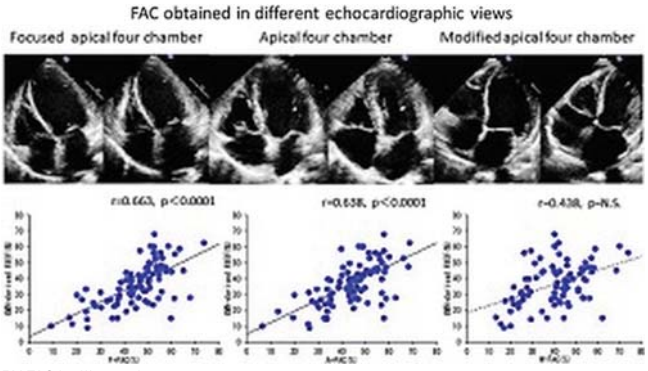
Background and purpose: Fractional area change (FAC) has been shown to correlate well with right ventricular (RV) ejection fraction (EF) by cardiac magnetic resonance (CMR). The guideline recommends that multiple echocardiographic views should be obtained to evaluate RV function. However, there is no clear recommendation which view should be used to evaluate RV FAC.
Methods: CMR and transthoracic echocardiography (TTE) were performed in 90 consecutive patients for evaluation of RV function. We measured tricuspid annular plain systolic excursion (TAPSE), FAC on apical four chamber view (A4CV) (A-FAC) and that of RV focused A4CV (F-FAC) and modified A4CV (M-FAC) and pulsed Doppler peak velocity at the tricuspid annulus (s') as an assessment of RV systolic function. The association between echocardiography-derived parameters of RV systolic function and CMR-derived measurement of RVEF and RV volume were evaluated.
Results: Both A-FAC and F-FAC measurement were fesible in 90 patients (100%) and M-FAC measurement was fesible in 84 patients (93%). End diastolic area (Area ED) (cm^2) of A-FAC and F-FAC showed correlation with CMR-derived end diastolic volume, respectively ($p<0.0001$, r=0.768 vs $P=<0.0001$, r=0.784). End systolic area (area ES) (cm^2) of A-FAC and F-FAC showed correlation with CMR-derived end systolic volume, respectively ($p<0.0001$, r=0.791 vs $p<0.0001$, r=0.820)
A-FAC and F-FAC has good correlation with CMR-derived RVEF ($p<0.0001$, r=0.638 vs $P=<0.0001$,r=0.663, respectively). M-FAC has no correlation with CMR-derived RVEF (p=N.S., r=0.438). There were no significant agreement between TAPSE, s' and CMR-derived RVEF in this study.



RV-FAC in dfferent views

Conclusion: Both A-FAC and F-FAC had good correlation with CMR-derived RVEF, and M-FAC didn't show correlation with CMR-derived RVEF. We should use F-FAC to evaluate FAC.

P6305 | BEDSIDE
Effect of CPAP therapy on right ventricular function by speckle tracking strain echocardiography in obstructive sleep apnea

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Background: Obstructive sleep apnea (OSA) is associated with right ventricular (RV) dysfunction and use of continuous positive airway pressure (CPAP) may improve RV function. 2D speckle tracking is a relatively new method for assessment of RV function and has recently been included in international guidelines for RV function assessment. We hypothesize that RV strain is more sensitive than conventional echo parameters in detecting early changes in RV function.
Purpose: To investigate the effect of OSA on right ventricular function and the impact of CPAP therapy.
Methods: We prospectively recruited 22 patients (18 male, mean age 53±9) with newly diagnosed with OSA (mean respiratory disturbance index (RDI) 29.8±21.5) and follow up for 1 month after initiation of CPAP therapy. Echocardiographic images were acquired with a modified apical 4 chamber view. RV global and free wall longitudinal strain by speckle tracking, tricuspid annular plane systolic excursion (TAPSE), and RV fractional area change (FAC) were measured. Offline strain analysis was performed by cardiologists off-site experienced in strain analysis and blinded to clinical data.
Results: At baseline, the mean RV global strain and free wall strain were –23.0±3% and –26.6±4.2% respectively, with TAPSE 2.21±0.2mm and FAC 34.5±8%. At one month after CPAP therapy, there were statistically significant improvements in both RV global (–24.8±3.2%, relative change 8.09%, p=0.012) and RV free wall strain (–30.8±4.1%, relative change 15.7%, $p<0.01$). There were no significant changes in TAPSE (2.24±2.9mm, p=0.54) and FAC (35.1±9.7%, p=0.83) post CPAP therapy.
Conclusion: Use of CPAP therapy improves RV function in subjects with OSA. RV global and free wall longitudinal strain are more sensitive in detecting subtle changes in RV function compared to conventional parameter of TAPSE and FAC.

P6306 | BEDSIDE

Right ventricular regional volume and systolic function in patients before and after percutaneous closure of atrial septal defect assessed by three-dimensional echocardiography

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Objective: To evaluate right ventricular (RV) regional volume and systolic function in patients with atrial septal defect (ASD) before and after percutaneous closure using real-time three-dimensional echocardiography (RT3DE).
Methods: RT3DE was performed in 86 patients with ASD the day before closure and within 24 hours afterwards to obtain RV regional end-diastolic volume (EDV), end-systolic volume (ESV), systolic volume (SV) and ejection fraction (EF) in three compartments (inflow, body and outflow). Two-dimensional and Doppler parameters including RV fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), pulmonary vascular resistance (PVR) and maximum diameter of ASD (ASD-D) were analyzed. Forty age and gender matched normal adults were included as controls.
Results: RT3DE images were successfully acquired and analyzed in 94% of all the subjects. When compared with controls, RV global and regional EDV, ESV and SV were significantly enlarged (all $P<0.001$) and EF was significantly decreased (all $P<0.001$) in pre-closure patients. Pre-closure TAPSE was higher while pre-closure FAC was lower (all $P<0.05$) than in controls. Post-closure patients showed reduced EDV, SV, EF, FAC and TAPSE than before closure (all $P<0.001$). But EDV and SV were larger while EF, TAPSE and FAC were lower in post-closure patients than in controls (all $P<0.05$). RV global and regional EDV, ESV and SV in pre-closure patients were significantly correlated with ASD-D (r=0.487–0.685, all $P<0.001$). RV global EF, regional EF in the inflow compartment, TAPSE and FAC were negatively correlated with PVR in patients before closure (r=–0.228 to –0.302, all $P<0.05$).
Conclusions: RV regional volume and systolic function decrease rapidly during the first 24 hours after percutaneous closure, but RV volume was still larger and systolic function was still lower than normal subjects. RV volume was positively correlated with RV pre-load, and RV regional systolic function in the inflow compartment was negatively correlated with RV after-load in patients with ASD.

P6307 | BEDSIDE

Differentiation of early arrhythmogenic right ventricular cardiomyopathy from right ventricular outflow tract ventricular tachycardia

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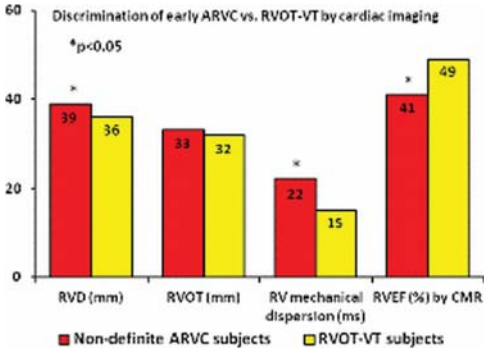
Introduction: Electrical disease precedes structural disease in arrhythmogenic right ventricular cardiomyopathy (ARVC) and ventricular tachycardia (VT) is often the first symptom. Differentiation of life threatening early ARVC from relatively benign right ventricular (RV) outflow tract VT (RVOT-VT) is challenging. Prognosis and treatment strategies differ substantially and correct diagnosis is important.
Purpose: We investigated if cardiac imaging can help to discriminate early ARVC from RVOT-VT.
Methods: We included 44 consecutive RVOT-VT patients (age 47±14 years) and 44 ARVC mutation carriers (age 39±17 years) with early ARVC disease, fulfilling non-definite diagnosis by Task Force criteria 2010. By echocardiography, we assessed RVOT and RV basal diameter (RVD), fractional area change (RVFAC) and LV ejection fraction (EF). By 2D speckle tracking strain echocardiography we assessed RV mechanical dispersion as standard deviation of time to peak longitudinal strain in 3 RV wall segments. By cardiac magnetic resonance imaging (CMR), we assessed RV ejection fraction (RVEF).
Results: RVD was larger (39±5mm vs. 36±4mm, p=0.02) and RV mechanical dispersion was more pronounced (22±15ms vs. 15±13ms, p=0.03) in ARVC compared to RVOT-VT subjects, but RVOT diameters did not differ (33±5mm vs. 32±4mm, p=0.36). RVEF by CMR was decreased in ARVC vs. RVOT-VT subjects (41±8% vs. 49±4%, $p<0.001$), while RV and LV function by echocardiography did not differ (RVFAC; 47±7% vs. 46±5%, p=0.96, LVEF; 58±4% vs. 57±5%, p=0.85, respectively).



Conclusions: Increased RVD, pronounced RV mechanical dispersion by echocardiography and reduced RV function by CMR discriminated early ARVC from RVOT-VT patients and may help correct diagnosis and treatment decisions.

P6308 | BEDSIDE

Assessment of right atrial and ventricular function by strain and strain rate imaging in patients with single ventricular physiology after cardiac progenitor cell therapy

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Background: The staged palliations for single ventricle lesions are not associated with cardiac function improvements directly in short-term. Recent clinical trials have suggested that cardiosphere-derived cell (CDC) infusion may enhance regional cardiac function in patients with heart diseases. Purpose- By using speckle-tracking echocardiography (UCG) and feature-tracking cardiac magnetic resonance imaging (cMRI), we sought to determine whether CDC therapy may improve myocardial strain and strain rate in patients with univentricular heart disease.
Methods: A total of 29 consecutive patients aged 2.7±1.4 years have enrolled the PERSEUS phase 2 randomized trial (NCT: NCT01829750) to receive intracoronary injection of CDCs after staged palliations in our institution. Twelve patients have received CDC infusion 1 month after surgery and 17 patients were assigned as controls with standard shunt procedure alone. Global and regional cardiac function were assessed by UCG and cMRI during follow-up of staged palliations and compared between 2 groups.
Results: CDC-treated patients showed significant increase in EF (44.8±8.7% at baseline vs. 50.3±9.0% at 3m, P=0.003), whereas control patients had no changes during the same follow-up interval. Compared with controls, CDC-treated patients showed reduced Tei index at 3 months follow-up (P=0.03). To validate these observations, right ventricular strain and strain rate were assessed by UCG and cMRI. We found that global longitudinal strain, circumferential strain, and radial strain were all significantly improved in CDC-treated group compared with baseline (Long: –18.8±5.6% at baseline vs. –22.1±4.5% at 3m, P=0.01; Circ: –4.7±1.8% at baseline vs. –6.7±2.5% at 3m, P=0.002; Rad: 3.8±1.4% at baseline vs. 4.8±1.4 at 3m, P=0.03). Increased right ventricular strain was closely associated with reduced circumferential strain rate in CDC-treated patients (–0.4±0.1 1/s at baseline vs. –0.5±0.1 1/s at 3m, P=0.005). In addition, CDC infusion significantly improved atrial function that was addressed by greater early diastolic strain rate (1.6±0.6 1/s at baseline vs. 2.0±0.6 1/s at 3m, P=0.03), increase in atrial fractional area change (29.7±9.0 at baseline vs. 35.0±6.7 at 3m, P=0.04), and reduced mitral flow velocity modified by early diastolic strain rate (P=0.005).
Conclusions: There is a significant favor of CDC therapy in patients with univentricular heart disease. Our results suggest that strain and strain rate parameters measured by UCG and cMRI closely reflect the regional improvements in both atrial and ventricular function after CDC infusion.
Acknowledgement/Funding: The Ministry of Health, Labour and Welfare

MISCELLANEOUS

P6309 | BEDSIDE

Pressure-volume relationship in the stress-echo lab: does (left ventricular end-diastolic) size matter?

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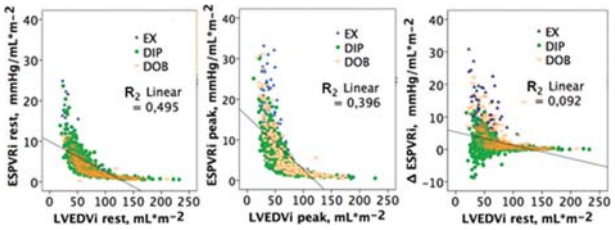
Background: The ΔESPVR is calculated as the variation between rest and peak stress End-Systolic Pressure-Volume Relation (ESPVR). ΔESPVR is an afterload independent index of left ventricular (LV) contractility which allows a more accurate prognostic stratification than ejection fraction in patients without inducible wall motion abnormalities. Whether and to what extent it depends upon LV end-diastolic volume (EDV) remains unclear.
Aim: To assess the dependence of ESPVR upon LVEDV during physical or pharmacological stress in patients with negative stress echo (SE) and all ranges of resting LV function.
Methods: We analyzed interpretable data obtained in 891 patients, (593 men, age 63±12 years) with ejection fraction 47±12%: 338 normal or near-normal or hypertensive; 229 were coronary artery disease; 324 were ischemic or non-ischemic dilated cardiomyopathy. They were studied with SE during exercise (n=172), dipyridamole (n=482) or dobutamine (n=237). The ESPVR was evaluated at rest and peak stress from raw measurement of systolic arterial pressure by cuff sphygmomanometer and EDV and ESV by biplane Simpson rule from 2D-echo.
Results: In the overall population, the relationship between ESPVR and LVEDV was present at rest (r2 = 0.5, p=0.00; Fig. left panel) and peak stress (r2 = 0.4, p=0.00; Fig. middle panel), but absent if only the ΔESPVR (Delta rest-stress ESPVR) was considered (r2 = 0.1, p = ns; Fig. right panel). The ΔESPVR value was

highest for normals or near-normals and hypertensives, and lowest for ischemic or non-ischemic dilated cardiomyopathy patients.



LVEDV does not affect the ΔESPVR

Conclusion: LV end-diastolic volume does not affect the rest-stress changes in ESPVR in either normal or abnormal left ventricles, during physical or pharmacological stress. The ΔESPVR is independent from the EDV.

P6310 | BEDSIDE
New echocardiographic parameters in the diagnosis of heart failure with preserved ejection fraction

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Background: Heart failure with preserved ejection fraction (HFpEF) is a serious clinical disease. Non-invasive diagnostics of this condition is still unsatisfactory. The aim of this work is to find new echocardiographic parameters, which could improve the current non-invasive diagnostics of HFpEF. The parametrs are the diastolic wall strain of posterior wall (DWS PW) and the vortex formation time (VFT).
Methods: The study includes 76 patients with exertional dyspnea having normal left ventricular ejection fraction and 19 healthy volunteers. All subjects underwent a spirometry examination, determination of plasma levels of NT-proBNP and transthoracic echocardiography. In addition to the standard parameters used in the diagnosis of HFpEF, DWS PW and VFT were assessed in all patients. The DWS PW is based on the linear elastic theory. The VFT is based on the parameters from transmitral Doppler left ventricular filling, end-diastolic left and end-systolic ventricular volumes and diameter of the mitral annulus in early diastole.
Results: HFpEF has been proved in 27 patients with dyspnea. Patients with HFpEF were compared to other subjects with dyspnea, where significantly different values were found: DWS PW (0.252±0.065 vs 0.340±0.066, $p<0.001$), E/e'(10.9±2.55 vs. 8.50±1.98, $p<0.001$), e' (7.00±1.47 cm/sec vs. 8.80±1.95 cm/s, $p<0.001$), LV mass index (110.40±27.98 g/m^2 vs. 82.30±116.00 g/m^2, $p<0.001$), NT-proBNP (366.3±301.3 pg/ml vs. 115.80±82.45 pg/ml), s' (peak mitral anular systolic velocity, 7.40±1.01 cm/sec vs. 8.80±1.49 cm/s, $p<0.001$) and VFT (2.80±0.93 vs. 4.1±1.4, $p<0.001$). There were no significant differences in these parameters among patients with noncardiac dyspnea and the control group. Multivariate analysis, which includes standard parameters for the diagnosis of HFpEF as well as new parameters, revealed, that NT-proBNP (Odds Ratio 1.236, 95% CI 1.071 to 1.426), LV mass index (Odds Ratio 1.945, 95% CI 1.164 to 3.250) and DWS PW (Odds Ratio 0.714, 95% CI from 0.569 to 0.896) independently predict the presence of HFpEF.
Conclusion: The new echocardiographic parameters DWS PW and VFT were significantly lower in patients with HFpEF. DWS PW appears to be an independent predictor of HFpEF presence.

P6311 | BEDSIDE
Improvements in ventriculo-arterial coupling and myocardial energetics under dobutamine stress are important determinants of cardiovascular outcome in patients with dilated cardiomyopathy

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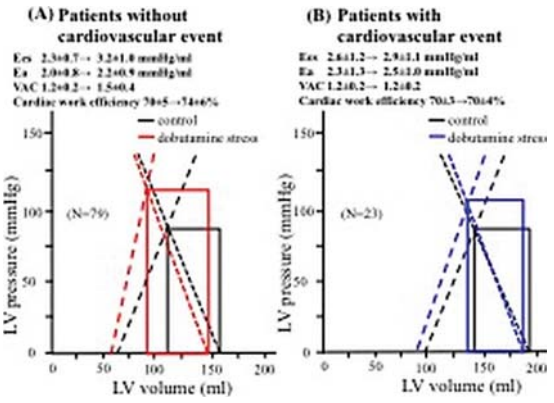
Background: Ventriculo-arterial coupling (VAC) is known to reflect the mechanoenegetic performance of the heart.
Purpose: The purpose of this study was to investigate the prognostic impact of the changes in VAC and cardiac work efficiency during dobutamine stress on the cardiovascular events in patients with dilated cardiomyopathy (DCM).
Methods: One hundred and two DCM patients with ejection fractions of 31±10% and 30 age- and gender-matched normal controls were recruited. Left ventricular (LV) end-systolic elastance (Ees) was measured by three-dimensional echocardiography using single-beat method under dobutamine stress (20μg/kg/min). Effective arterial elastane (Ea) was calculated as 0.9 systolic arterial pressure divided by stroke volume, and VAC was then calculated as the ratio of Ees/Ea. LV cardiac work efficiency was also defined as the ratio of external stroke work and pressure-volume area. Event-free survival was then tracked over 24 months.
Results: In patients with DCM, VAC (1.20±0.23 vs. 2.03±0.31, $p<0.001$) and cardiac work efficiency (70±4% vs. 80±2%) were significantly smaller than those of normal controls. During dobutamine stress, both VAC (from 1.20±0.23 to 1.52±0.41, $p<0.001$) and cardiac work efficiency (from 70±6% to 74±6%, $p<0.001$) were significantly improved in patients without cardiovascular events, whereas these responses were not observed in those with cardiovascular events (Figure). Multivariate Cox proportional-hazards analysis revealed the improvements in VAC as well as in cardiac work efficiency were the independent determinants of cardiovascular events (both $p<0.001$, respectively).



Conclusions: Improvements in ventriculo-arterial coupling and myocardial energetics under dobutamine stress were important determinants of cardiovascular outcome in patients with DCM.

P6312 | BEDSIDE
Association of periodontitis with subclinical myocardial dysfunction in patients with diabetes

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Introduction: In patients with type 2 diabetes mellitus (T2DM), the association between periodontitis and cardiovascular disease (CVD) is established recently. However, the association between periodontitis and subclinical cardiac dysfunction, especially exercise induced cardiac alterations in T2DM patients are not clear. In the present study, our goal was to investigate the relationship between periodontitis and subclinical cardiac dysfunction by 1) basic dental examination and 2) detailed cardiac assessment using resting and exercise echocardiography.
Methods: Fifty-two T2DM patients without histories of CVD were enrolled, and all received dental examination, resting and exercise transthoracic echocardiography. Echocardiographic images were analyzed in detail with the following parameters i) Left ventricular function evaluated (LVEF) by Simpson's method derived ejection fraction and speckle tracking derived global longitudinal strain (GLS), ii)diastolic function was assessed by tissue Doppler derived E' and E/E' ration. Dental measurement parameters include tooth loss number (TL) and probing depth (PD).
Results: The mean age of the recruited participant are 64.8±8.7, 50% of them are male. Even though LVEF didn't have significant relationship with dental parameters, TL was significantly correlated with resting (r=0.40, P=0.01) and exercise (r=0.44, 0.01) GLS, as well as E' after exercise (r=–0.38, $p<0.01$). PD had significant associations with resting (r=0.41, p=0.02) and exercise (r=0.52, $p<0.01$) GLS, resting (r=–0.33, p=0.03) and exercise (r=–0.46, $p<0.01$) E'. Further, multivariate analysis demonstrated TL and PD were independent predictors of impaired resting GLS (B=0.09, CI: 0.01–0.18, p=0.04 and B=1.08, CI: 0.05–2.10, p=0.04 respectively). In addition PD were independent related with exercise E' (B=–0.01, CI: –0.020-(–0.001), p=0.03) and E/E' (B=1.28, CI: 0.14–2.42, p=0.03) after multivariate analysis.
Conclusion: The present study demonstrated an independent relationship between the severity of periodontitis and myocardial systolic and diastolic dysfunction both at rest and exercise status. The finding suggested patients with periodontitis thus required detailed clinical assessment to detect subclinical myocardial dysfunction in order to prevent adverse cardiac outcome.
Acknowledgement/Funding: This study was supported by the Research Grant Council of Hong Kong: General Research Fund (no. HKU 785611).

P6313 | BEDSIDE
Subclinical myocardial dysfunction detected by two-dimensional and three-dimensional speckle tracking echocardiography in asymptomatic type 1 diabetic patients

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Background: We sought to assess left ventricular (LV) function using two-dimensional (2D) and three-dimensional (3D) speckle tracking echocardiography

(STE) for the detection of preclinical diabetic cardiomyopathy, in asymptomatic type 1 diabetic patients, and to evaluate potential progression over a 6-year follow-up.
Methods and results: Sixty-six asymptomatic type 1 diabetic patients with no cardiovascular risk factors were compared to 26 matched healthy controls. Conventional, 2D and 3D STE were performed at baseline. A subgroup of 14 patients underwent a 6-year follow-up evaluation. At baseline, diabetic patients had similar LV ejection fraction (60 vs. 61%; p=NS), but impaired longitudinal function, as assessed by 2D global longitudinal strain (GLS) (–18.9±2 vs. –20.5±2; p=0.0002) and 3D GLS (–17.5±2 vs. –19±2; p=0.003). At follow-up, diabetic patients had worsened longitudinal function compared to baseline (2D GLS: –18.4±1 vs.-19.2±1; p=0.03). Global circumferential (GCS) and radial (GRS) strains were unchanged at baseline and during follow-up. Metabolic status did not correlate with GLS, whereas GCS and GRS showed a good correlation, suggestive of a compensatory increase of circumferential and radial function in advanced stages of the disease - long-term diabetes (GCS: –26±3 vs. –23.3±3; p=0.008) and in the presence of microvascular complications (GRS: 38.8±9 vs. 34.3±8; p=0.04).
Conclusion: Subclinical myocardial dysfunction can be detected by 2D and 3D STE in type 1 diabetic patients, independently of any other cardiovascular risk factors. Diabetic cardiomyopathy progression was demonstrated by a decrease in longitudinal function at follow-up, but did not extend to a clinical expression of the disease.
Acknowledgement/Funding: Federation Francaise de Cardiologie

P6314 | BEDSIDE
The superior value of quadripolar versus bipolar left ventricular leads for cardiac resynchronisation therapy: a cost effective analysis in a UK registry

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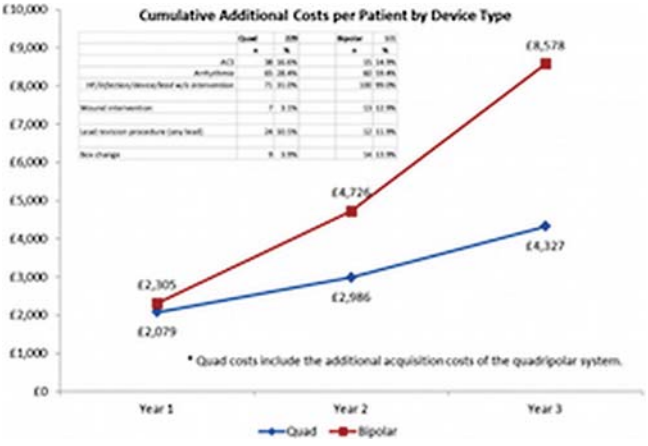
Background: Healthcare systems require evidence of value for money and clinical effectiveness of medical technology in real-world practice. We recently reported improved clinical outcomes in quadripolar (Q) left ventricular (LV) leads compared with bipolar (B) leads for CRTD delivery. We evaluated whether Q-based systems are cost effective given their £1200 higher purchase price.
Methods: Rehospitalisation episodes and reintervention rates were coded over a mean follow up 879 days amongst 330 patients. 2014/15 NHS tariffs were applied to estimate the cost of each lead to service commissioners. EQ-5D questionnaire values were applied to mortality and heart failure events to estimate quality-adjusted life year (QALY) differences. A 3-year time horizon was adopted; effects beyond 1 year were subject to a 3.5% annual discount.
Results: Groups were age and sex matched. A lower proportion of patients implanted with a quadripolar lead were hospitalised (Q:117 (51%) vs. B:72 (71%), p<0.001) and mean hospitalisations per patient were lower (Q:205/229=0.90 vs. B:200/101=1.98, p<0.001). Elective generator replacement was more frequent amongst those with a bipolar lead (Q:3.9% vs. B:13.9%, p=0.002). The higher purchase cost of quadripolar systems was offset by heart failure hospitalisations, system extraction and generator changes. As such, the use of a quadripolar CRTD system generated a cumulative cost saving (£227/patient) within 12 months of implantation with incremental savings over 3 years (Figure).



Conclusion: Implantation of quadripolar CRTD systems present a cost saving to the UK healthcare system compared with bipolar systems. With improved clinical outcomes and reduced overall costs, this data suggests quadripolar leads should become the gold standard for CRT delivery.
Acknowledgement/Funding: Rosetrees Trust. NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust

P6315 | BEDSIDE
Reduced-dose dual-source coronary computed tomography angiography (CCTA): is raw-data-based iterative reconstruction able to maintain diagnostic confidence?

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Introduction: The assessment of coronary artery disease with CCTA requires a good image quality and can be easily hampered by the noise generated in a reduced-dose acquisition. When faced with the challenge of providing diagnostic image quality at the lowest possible radiation dose, the medical community demonstrated the usefulness of iterative reconstruction (IR) algorithms, which reduce the level of noise. However IR algorithms are also known to change the texture of CT images and could lead to misdiagnosis by modifying the sharpness of the coronary borders.
Purpose: To evaluate image quality and diagnostic confidence of a raw-data-based iterative reconstruction technique (IR) in reduced-dose CCTA images in comparison with standard-dose filtered back projection (FBP) images.
Methods: 107 consecutive patients (72 males; 35 females), referred for a CCTA were prospectively included using a dual-source CT system in a high pitch (n=51) or a sequential mode (n=56) according to heart rate (mean DLP = 204.6 mGy.cm). From each acquisition, three series of images were reconstructed: standard-dose images reconstructed with FBP and considered as the reference standard (Group 1); and two series of reduced-dose images obtained with a prototype software which virtually increased the level of noise simulating a 30% dose reduction, and reconstructed with FBP (Group 2) or IR (Group 3). Two readers blindly evaluated each series for (a) objective noise and CNR; (b) coronary border sharpness, lesion detection; and (c) diagnostic confidence level using a 5-point scale.
Results: In Group 2, there was a significant increase in noise compared to Group 1 (36.8 HU ±6.73 vs 30.4 HU ±5.20; p<0.0001) and a CNR impairment (15.6±4.3 vs 18.7±4.5; p<0.0001). In Group 3, despite the 30% dose reduction, IR restored the objective image quality: mean noise= 31.1 HU ±5.4 (p=0.8) and CNR=18.5±5.0 (p=0.7). However the diagnostic confidence was altered when compared with Group 1 (p<0.0001), mainly rated as moderate with a blurred aspect of the coronary borders (81/107 [75.7%], p<0.0001) and a significant number of artefactual non-flow-limiting soft plaques described in vessels considered as normal in Group 1 (105/428 [24.5%], p<0.0001).
Conclusions: Raw-data-based iterative reconstruction allowed significant noise reduction but may be associated with blurring of the coronary luminal borders, which can decrease diagnostic confidence. When reporting reduced-dose CCTA with iterative reconstruction, false smooth plaque artifacts must be considered in diagnostic assessment and subsequent patient management.
Acknowledgement/Funding: SFR Research grant, ESTI Research grant, Lille University Hospital Research grant

P6316 | BEDSIDE
Submillisievert computed tomography with model-based iterative reconstruction before pulmonary veins radiofrequency catheter ablation of atrial fibrillation: impact on radiation exposure and outcome

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Background: The outcome of radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF) has improved thanks to left atrium (LA) anatomy reconstruction by computed tomography with adaptive statistical iterative reconstruction algorithm (CT-ASIR) before the procedure. However, CT-ASIR strategy is associated to an increase of cumulative effective radiation dose (ED) in these patients. Recently, a model-based iterative reconstruction algorithm (MBIR, GE Healthcare, Waukesha,Wisconsin) has been developed (CT-MBIR) for image noise reduction reducing the ED close to chest X-ray exposure. The aim of this study is to compare the CT and RFCA characteristics, AF recurrence after procedure and radiation exposure between RFCA guided by image integration with CT-ASIR versus CT-MBIR
Methods and materials: One-hundred twenty consecutive patients with drug-refractory paroxysmal or persistent AF were addressed to CT-ASIR (Group 1; N: 60; mean age 60.3±10.1 yo; male: 46) or CT-MBIR protocol (Group 2; N: 60; mean age 59.7±11.3 yo; male:45) for evaluation of LA before RFCA. All patients were subsequently treated by image integration-supported RFCA. Image noise, signal to noise ratio (SNR), contrast to noise ratio (CNR), RFCA procedural characteristics, rate of AF recurrence and CT radiation exposure were measured and compared between the two groups.
Results: The two groups were homogeneous in terms of demographic characteristics, cardiovascular risk factors, prevalence of persistent AF, medical therapy and echocardiographic characteristics. The mean follow-up was similar (578±284 vs. 591±278 days, respectively, p:ns). Group 2 showed a higher signal to noise ratio (25.9±7.1 vs. 13.8±5.1) and contrast to noise ratio (22.7±6.5 vs. and 14.08±4.1) of left atrium as compared to Group 1 (p<0.001). No differences were found in terms of RFCA parameter [procedural duration (130.9±130.6. vs. 143.8±80.4 min); fluoroscopy time (27.9±14.1.0 vs. 32.0±16.4 min); pulmonary

veins isolated (3.8±0.4 vs. 3.9±0.4)] and the rate of AF recurrence (31% vs. 29%) between Group 2 vs Group 1. Group 2 showed a 94% reduction of ED as compared to Group 1 (0.4±0.04 mSv vs 6.4±1.8 mSv, $p<0.01$).
Conclusions: CT-MBIR allows accurate non-invasive reconstruction of LA anatomy in AF patients undergoing to RFCA with a submillisievert effective radiation and comparable success rate of RFCA with CT-ASIR technique.

P6317 | BEDSIDE
Is CT verified vulnerable coronary plaque really prone to rupture in itself?

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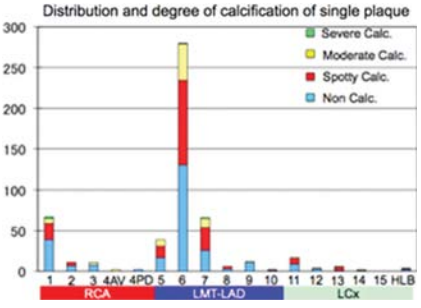
Background: As previously reported coronary CT angiography (CCTA) verified features of vulnerable plaque are low-density plaque (LDP) and positive vessel remodeling (PR). However, there is no available evidence whether only these 2 features positive plaque is really prone to rupture.
Methods: CCTA was carried out in 5267 consecutive patients (Nov/2006-July/2009) for suspected coronary artery disease. Of 5267 patients, 531 patients showed only an atherosclerotic lesion in their coronary tree, namely single plaque. The single plaques were observed mostly in proximal LAD (52.7%), followed by proximal RCA (12.1%) and mid LAD (12.4%). Of 531 single-plaques, 35 plaques (6.6%) showed vulnerable features of both of LDP and PR.
Results: Of 35 single plaques with features of both of LDP and PR, one case underwent coronary intervention immediately after CCTA. Of residual 34 cases, 31 cases (91%) were available for prognostic inquiry over 1 year after CCTA (1617±388 days). Interestingly, no cardiac event was observed in all the 31 cases during follow-up period (0%).



Conclusions: Although previous studies revealed that LDP with PR was vulnerable feature of a coronary plaque in patients with advanced coronary artery disease (CAD), in the present study, our data suggests that CCTA verified vulnerable features of coronary plaque, LDP and PR, do not provide predictive value of plaque rupture in patients with quite early CAD.

P6318 | BEDSIDE
Diagnostic performance of computed tomography perfusion in coronary artery disease

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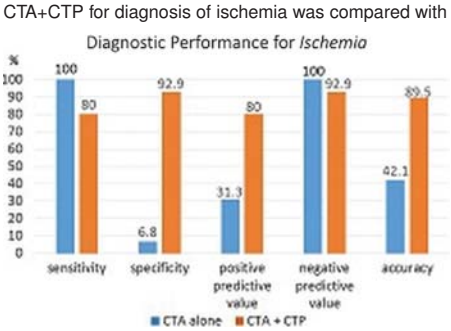
Background: Computed tomography perfusion (CTP) combined with computed tomography angiography (CTA) is an emerging methods that can provide anatomical and physiological information by one time examination. However, appropriate patient selection criteria of CTP is not well known.
Purpose: To assess the clinical implication of CTA+CTP over CTA.
Methods: We prospectively enrolled 19 coronary artery disease patients (67.0±9.8 years, male 73.7%) who were referred for clinically indicated CTA+CTP and single photon emission computed tomography (SPECT) or invasive fractional flow reserve (FFR) within 60 days of CT. The accuracy of CTA alone and CTA+CTP for diagnosis of ischemia was compared with SPECT or FFR as reference. We also compared the accuracy of SPECT and CTA+CTP for diagnosis of significant stenosis with quantitative coronary angiography as reference.
Results: For diagnosis of ischemia, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were 100%, 6.8%, 31.3%, 100%, and 42.1%, respectively in CTA, and were 80.0%, 92.9%, 80.0%, 92.9%, and 89.5%, respectively in CTA+CTP. For diagnosis of significant stenosis, sensitivity, specificity, PPV, NPV, and accuracy were 66.7%, 87.5%, 85.7%, 70.0%, and 68.4%, respectively in SPECT, and were 88.9%, 87.5%, 88.9%, 87.5%, and 88.2%, respectively in CTA+CTP.
Conclusion: CTA+CTP improved specificity and PPV for diagnosis of ischemia compared with CTA by decreasing false positive especially in calcified lesion. CTA+CTP also improved sensitivity and NPV for diagnosis of significant stenosis compared with SPECT by decreasing false negative especially in multi vessel or small vessel lesion due to the superior spacial resolution.



Diagnostic performance for ischemia

P6319 | BEDSIDE
Novel imaging method for real time cardiac computed tomography and coronary angiography image registration as a tool for chronic total occlusion intervention

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Background: Chronic total occlusions (CTO) guide software (prototype, SIEMENS) provides online navigational guidance in the CTO percutaneous coronary intervention (PCI) through the display of computed tomography angiography (CTA) image information as a 3D roadmap side-by-side with live angiography images. The CTA image orientation is synchronized with the C-arm, which also allows the selection of the ideal treatment projection angle without additional contrast medium or radiation exposure.
Objective: The aim of this study is to evaluate the benefit of the use of this novel system for CTO PCI.
Methods: A total of 258 patients, who underwent PCI for CTO lesions from September 2010 to December 2013, were included in this study. We divided two groups, Group A: 30 patients with and Group B: 228 patients without CT guidance. We compared procedural success rate, the amount of contrast media and the consumption of radiation exposure between two groups.
Results: There were not significant differences of baseline patient characteristics between group A and B: the prevalence of diabetes mellitus (43.3% vs. 41.2%, P=0.845), hypertension (80.0% vs. 74.0%, P=0.655) and chronic kidney disease (16.7% vs. 29.5%, P=0.194). Success rate of CTO coronary interventions (78% vs. 75%, P=0.55) and the amount of contrast media (183±63 vs. 189±84, P=0.705) did not differ between two groups, whereas radiation exposure was significantly reduced in CT-guided PCI group (1033.7±188.7 vs. 1904.3±126.1, P=0.006).
Conclusions: CT-guided PCI using CTO guide software significantly reduced the total consumption of radiation exposure while maintaining the success rate. Further studies are warranted.

P6320 | BEDSIDE
Distribution and predictors of direct costs of acute heart failure in Greece: a social security system perspective

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Introduction: Heart failure management constitutes a significant economic burden for the health care systems across Europe, accounting for 1% to 3% of total health care expenditures. Usually, this cost is covered mainly by the social security systems as it is true for Greece.
Purpose: The objective of this study was to estimate the total direct cost and the distribution of costs for the management of acute heart failure (AHF) from the Greek social security system perspective, as well as to identify which factors increase these costs.
Methods: Economic and outcomes data were extracted from the ESC Heart Failure Pilot Survey. Eight different secondary and tertiary cardiology departments across Greece have participated in this registry and recruited 177 patients hospitalised for AHF. The analysis was conducted from the Greek social security system perspective with 2014 as reference year. Only direct costs have been estimated including costs of hospitalisations, medications, other relevant cardiovascular interventions, clinical and laboratory follow-up, for up to one year after the index hospitalisation.
Results: The mean annual economic burden of the social security system per patient was estimated at €4,755±3,921, which accounts for more than a 25% of the national gross domestic product per capita. The mean costs of the index hospitalisation with a median 7-day length of stay was €2,292±3,092 and the mean annual costs after the index hospitalization was €3,006±2,571. About 67.5% of the latter was associated with in-patient care, 16.1% with drug treatment and 12.5% with laboratory monitoring. Physicians' costs accounted for only 3.9% of

the AHF outpatient management costs. Hospitalisation and total costs were significantly higher in male patients with reduced ejection fraction, renal dysfunction and atrial fibrillation ($p<0.05$). Other significant independent predictors of the total cost were anemia, uncontrolled hypertension and increasing levels of TSH.
Conclusion: AHF imposes a significant economic burden for the Greek social security system and national economy, mainly because of the often, long and costly hospitalisations. It is particularly important for the decision makers to have an estimate of the costs attributed to AHF, as they will have to plan and finance the care of the aging population.
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P6321 | BEDSIDE
Growth and geographical variation in the use of cardiac imaging in Australia may reflect ineffective utilisation

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Background: Growth rates and regional differences in the use of cardiac imaging are potential metrics of quality of care. The medical, social and service delivery correlates of high and low use may identify clues to an equitable provision of services. This study sought to define growth and regional variation in outpatient cardiac imaging in Australia.
Methods: Analyses are based on the rate of outpatient transthoracic (TTE), transesophageal (TEE) and stress echocardiography (SE) and single-photon emission computed tomography (SPECT) per 100,000 people in each Medicare Local (ML) in Australia. Numbers of tests from 2002–13 were obtained from Medicare Australia; number of doctors was obtained from the Health Workforce data and demographic data (total population, rural areas, and quintiles of disadvantage) were obtained from census data. Statistical analysis was performed using negative binomial regression.
Results: Over the last eleven years, TTE reimbursements/100,000 people rose from 1,780 to 3,497 (a 96% increase, 8.8% annualized growth per year), TEE from 33 to 61 and SPECT from 287 to 337. SE has the biggest increment (from 181 to 947), a total growth of 423% with an average growth rate of 38.5% per year. The relationships between the use of each cardiac imaging and demographics (mean age, gender, proximity to big cities, socio-economic level) and medical factors were analysed in outpatient tests reimbursed in 2012. The rate of TTE (age corrected) per 100,000 people varied from 382.8 to 7,184; TEE from 0 to 242; SE from 0 to 2,991 and SPECT from 0 to 955.8 tests per 100,000 people. The main correlate of TTE and TEE use per capita appears to be the number of doctors per 1,000 people (B=1.23 [97.5%CI 1.16–1.31] $p<0.01$; B=1.14 [97.5%CI 1.13–1.15] $p<0.01$; respectively), independent of regional burden of cardiovascular disease and social determinants. However, women were additionally associated with the use of TTE (B=1.13 [97.5%CI 1.01–1.26] p=0.03). The use of TEE seems to be less frequent when people with cardiovascular disease should be tested in outpatient environments (B=0.98 [97.5%CI 0.97–0.98] $p<0.01$). For SPECT, women, living in regional areas and doctors are the main drivers for testing (B=2.24 [97.5%CI 1.69–2.98] $p<0.01$; B=6.14 [97.5%CI 3.06–12.32] $p<0.01$; B=1.13 [97.5%CI 1.02–1.25] p=0.02 respectively). Interestingly, SPECT was negatively associated with increase in age (B=0.74 [97.5%CI 0.64–0.87] $p<0.01$).
Conclusion: Variation in the use of TTE in Australia is not illness-related and may be evidence of under- and over-utilization. An appropriate use process may contain this variation.

P6322 | BEDSIDE
Coronary artery calcification, left atrial, and left ventricular size measured from non-contrast cardiac CT predict incident heart failure hospitalization in the general population

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Background: Non-contrast cardiac computed tomography (CT) is increasingly performed especially in the absence of known cardiac disease.
Purpose: To determine the association of CT-derived left atrial (LA), left ventricle (LV) size, and coronary artery calcification (CAC) with future hospitalizations due to heart failure (HF).
Methods: Subjects without known cardiac diseases from the population based Heinz Nixdorf Recall Study were followed for incident hospitalization due to HF. From non-contrast cardiac CT, LA and LV area were measured from axial images and CAC was quantified by the Agatston score. We describe means of LA and LV size as well as median (Q25;Q75) of CAC-score for subjects with and without incident HF hospitalization. Cox-regression analysis determined the association of each CT-measure with incident HF hospitalization in unadjusted and HEART-score adjusted analysis. Hazard ratios (HR) and 95% confidence intervals are shown per standard deviation of LA/LV area and increase in log (CAC+1) by 1. Receiver operating characteristics was used to determine the improvement in prediction.
Results: From, 3944 subjects without known cardiac disease (59±8 years, 47% male, mean HEART-score 3.4±4.2%), 31 subjects (0.8%) were hospitalized due to HF during 10.3±2.0 years of follow-up. Hospitalized subject had higher baseline mean LA (20.6±5.5 vs. 17.6±4.2 cm^2, p=0.005) and LV sizes (48.1±9.2 vs. 41.2±7.2, p=0.0002) as well as higher median (Q1; Q3) CAC-score (11.3 [0;106.5] vs. 53.4 [7.2;439.9], p=0.0002). In unadjusted Cox analysis, all three CT-derived measures were significantly associated with incident HF hospitalization (for LA size: 3.24 [1.75–5.99] per 1SD, p=0.0002, for LV size: 5.65 [3.02–10.57] per 1SD, $p<0.0001$, for CAC-score: 1.82 [1.29–2.57] per 1 increase on the log scale, p=0.0007. HRs were slightly attenuated after adjustment for Heart-Score but remained significant for all three CT-measures (for LA: 2.72 [1.41–5.22], p=0.002; for LV: 4.32 [2.21–8.45], $p<0.0001$, for CAC: 1.57 [1.02–2.26], p=0.02). There was a tendency towards higher areas under the curve when adding CT measures to HEART-Score in receiver operating characteristics (0.694 to 0.741, p=0.38).
Conclusion: LA size, LV size, and CAC-score as measured from non-contrast cardiac CT are associated with incident HF hospitalization in the general population. Once cardiac CT is performed, quantification of LA and LV size in addition to CAC-score may identify subjects at early and subclinical stages of HF that qualify for further cardiac workup.

P6323 | BEDSIDE
Cost evaluation and comparison of three decision strategies for cardiac revascularization: results of the suspected CAD protocol of the European CMR registry

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Background: The public health burden of coronary artery disease (CAD) is important. Perfusion cardiac magnetic resonance (CMR) is generally accepted to detect and monitor CAD. Few studies have so far addressed its costs and cost-effectiveness.
Objectives: To compare in a large CMR registry the costs of a CMR-guided strategy vs two hypothetical invasive strategies for the diagnosis and the treatment of patients with suspected CAD.
Methods: In 3'647 patients with suspected CAD included prospectively in the EuroCMR Registry (59 centers; 18 countries) costs were calculated for diagnostic examinations, revascularizations as well as for complication management over a 1-year follow-up. Patients with ischemia-positive CMR underwent an invasive X-ray coronary angiography (CXA) and revascularization at the discretion of the treating physician (=CMR+CXA strategy). Ischemia was found in 20.9% of patients and 17.4% of them were revascularized. In ischemia-negative patients by CMR, cardiac death and non-fatal myocardial infarctions occurred in 0.38%/y. In a hypothetical invasive arm the costs were calculated for an initial CXA followed by FFR testing in vessels with ≥50% diameter stenoses (=CXA+FFR strategy). To model this hypothetical arm, the same proportion of ischemic patients and outcome was assumed as for the CMR+CXA strategy. The coronary stenosis - FFR relationship reported in the literature was used to derive the proportion of patients with ≥50% diameter stenoses (Psten) in the study cohort. The costs of a CXA-only strategy were also calculated. Calculations were performed from a third payer perspective for the German, UK, Swiss, and US healthcare systems.
Results: The CMR+CXA strategy reduced costs vs the CXA+FFR strategy by 14%, 34%, 27%, and 24% in the German, UK, Swiss, and US context, respectively. In comparison vs the CXA-only strategy, cost reductions were 59%, 52%, 61% and 71%, respectively. Sensitivity analyses varying costs of tests and Psten proved the robustness of results.
Conclusions: A CMR+CXA strategy to manage patients with suspected CAD is less costly than a hypothetical invasive CXA+FFR strategy when applied 1) in a real-world registry with a low to intermediate prevalence of disease, and 2) when costs for diagnostic work-up, treatment, and complication management are taken into account. These findings warrant further confirmation in prospective cost-effectiveness trials.

P6324 | BEDSIDE
Long-term clinical impact of coronary CT angiography in patients with recent acute-onset chest pain

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Background: The prognostic implications of a coronary computed tomographic angiography (CCTA)-guided treatment strategy has not been compared in a randomized fashion to standard care in patients with chest pain.
Purpose: To investigate the long-term clinical impact of a CCTA-guided treatment strategy in patients with recent acute-onset chest pain, as compared to standard care.
Methods: Patients referred with acute chest pain but normal electrocardiogram and troponins were randomized to treatment guided by either CCTA or standard care (bicycle exercise electrocardiogram or myocardial perfusion imaging). The primary endpoint was a composite of cardiac death, myocardial infarction (MI), hospitalization for unstable angina pectoris (UAP), elective revascularizations and readmission for chest pain.
Results: We randomized 299 patients to the CCTA-guided strategy and 301 to standard care. After inclusion 24 patients withdrew their consent. The median (interquartile range) follow-up duration was 18.7 (16.8–20.1) months. In the CCTA-guided group 30 patients (11%) suffered a primary endpoint versus 47 patients (16%) in the standard care group, p=0.04, hazard ratio (95% confidence interval) =0.62 (0.40–0.98). A major adverse cardiac event (cardiac death, MI, hospitalization for UAP and elective revascularization) was observed in 5 patients in the CCTA-guided group versus 14 patients in the standard care group, p=0.04, hazard ratio =0.36 (0.16–0.95). Events over time are illustreated in Figure 1.

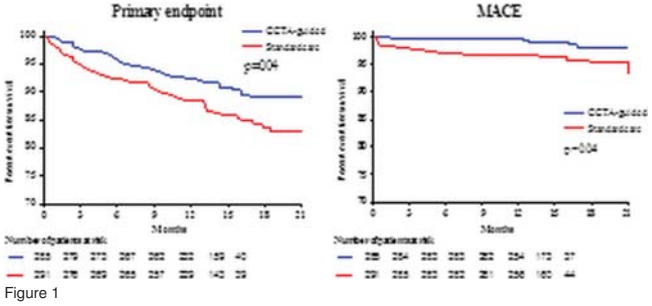

Figure 1

Conclusion: A CCTA-guided treatment strategy appears to improve clinical outcome in patients with recent acute-onset chest pain and normal electrocardiogram and troponins, as compared to standard care with a functional test.

P6325 | BEDSIDE
Is there a structural basis for vasovagal syncope? Cardiac functions in patients with vasovagal syncope

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Introduction: The pathophysiology of vasovagal syncope is not completely understood. In this study we aimed to evaluate the baseline echocardiographic parameters in patients with vasovagal syncope with special focus on RV and RA functions.
Materials and methods: We evaluated 42 patients with vasovagal syncope (VVS) and 41 age and sex matched healthy subjects. Patients with at least two syncopal attack and positive head-up-tilt test were enrolled in the study. All of the study participants undergone comprehensive echocardiographic examination early in the morning in fasting state.
Results: Among left ventricular function parameters, there were no significant difference between group.Right ventricular functional parameters also did not significantly differ between groups except for the maximal pulmonary systolic flow velocity (PVmax). PVmax was significantly lower in VVS group compared to control group. Right atrial area (RAA) was significantly higher and ratio of tricuspid filling velocities (Et/At) was significantly lower in VVS group. On multivariate analysis the independent predictors of vvs were found as PVmax (OR: 0.05, 95% CI: 0,004–0,751 p: 0.03) and Et/At (OR: 0,238, 95% CI: 0,065–0,874, p: 0.03).

Table 1. Comparison of echocardiographic

	VVS group (n=42)	Control group (n=41)	P value
Age (years)	34.3±10.0	31,4±5.7	0,115
LAA (cm^2)	15,5±2,8	15,0±2,5	0,406
Mitral E/A	1,2±0,34	1,6±1,1	0,205
E_t /A_t	1,1±0,44	1,4±0,35	0,011
RAA (cm^2)	13,9±3,3	12,6±2,5	0,041
PVmax (m/s)	0,9 (0,2)	1,0 (0,2)	0,004
TAPSE (mm)	22,4±2,8	23,3±2,5	0,126

Conclusion: The findings of this study indicate a subtle right atrial diastolic dysfunction in patients with VVS. Decreased right atrial contribution to RV filling may cause, a lower RV stroke volume which explains the lower PVmax values in our VVS group. All together, these findings may serve for a tendency to low output states and hypotension as in VVS.

P6326 | BEDSIDE
Improvement of ventricular contraction and dyssynchrony in patients with idiopathic ventricular arrhythmias undergoing catheter ablation

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Background: Idiopathic ventricular arrhythmias (VA) possess the risk of VA-related cardiomyopathy and catheter ablation offers beneficial effect. Three-dimensional echocardiography (3DE) has been used for evaluation of mechanical contraction and dyssynchrony in cardiac resynchronization therapy but rarely in patients with VA. We postulated that 3DE could demonstrate improved mechanical contraction and dyssynchrony in VA after ablation.
Methods: A total of 20 patients with VA and normal LVEF underwent ablation were enrolled after excluding structural heart disease, and received 3DE before ablation and 6 months after ablation. The speckle tracking analysis was performed offline with commercial software provided with the Artida Echocardiography.
Results: There was no difference of ejection fraction (EF) before and after ablation, while significantly increased circumferential strain (–22.2±8% vs. –28.2±4.5%, p=0.015) and longitudinal strain (–11.7±4.8% vs. –16.2±3.0%, p=0.001) were found after ablation. Dyssynchrony of ventricular contraction also improved after ablation, reflecting by lower standard deviation of time to peak radial and circumferential strain.

Table 1. Echocardiographic parameters before and after ablation

Variables	Before ablation	After ablation	P value
Ejection fraction, %	57.8±6.5	60.0±3.9	0.080
Radial strain (RS), %	21.6±11.8	27.8±7.6	0.208
RS_dyssynchrony index, sec	127.5±44.8	80.5±32.0	0.026
Circumferential strain (CS), %	–22.2±8.3	–28.2±4.5	0.015
CS_dyssynchrony index, sec	79.8±32.8	50.9±21.0	0.025
Longitudinal strain (LS), %	–11.7±4.8	–16.2±3.0	0.001
LS_dyssynchrony index, sec	111.7±65.8	84.7±33.0	0.147
Torsion, degrees	1.9±1.2	1.3±1.1	0.278
Torsion_dyssynchrony index, sec	131.3±84.7	138.1±81.6	0.877
Twist, degrees	5.3±3.1	4.4±3.2	0.425
Twist_dyssynchrony index, sec	120.8±74.5	163.7±101.4	0.262

Conclusion: Despite comparable ejection fraction before and after ablaiton, significant improvement of mechanical contraction and dyssynchrony was noted by 3DE analysis.

P6327 | BEDSIDE
The role of quality improvement approach on reducing systematic errors in echocardiographic hemodynamic parameters assessment

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Background: Accurate assessment of cardiac structures, ventricular function, and hemodynamics are the primary goal of any echocardiographic laboratory. Quality Improvement (QI) processes described by the American Society of Echocardiography (ASE) and the Intersocietal Commission (IAC) should be instrumental in reaching this goal. However no studies so far validated this approach to show the expected impact on echocardiology interpretation.
Purpose: To determine whether a QI process following the IAC and ASE guidelines will have an impact on the quality of echocardiology interpretation in a busy community hospital.
Methods: All patients undergoing transthoracic echocardiogram (TTE) followed by cardiac catheterization within 24 hours at Christiana Care Health System in 2011 and 2012 were identified, with 126 and 133 cases respectively. Hemodynamic parameters of left Ventricle End Diastolic Pressure (LVEDP), Pulmonary Artery Systolic Pressure (PASP), average E/E' and RA pressures on TTE correlated poorly with catheterization in 2011. An educational process developed on the basis of ASE and IAC recommendations was institutionalized to identify frequently encountered errors and to provide methods for improved performance at quarterly QI meetings. The process included bimonthly lectures for technologists, fellows and attendings concentrating on the common errors encountered as well as personalized feedback. The hemodynamic parameters were then re-examined in 2012 post-intervention.
Results: Following a teaching intervention in 2012, there was noted improvement amongst the following parameters on TTE and their catheterization correlates in 2012 vs. 2011. There was significant improvement in the correlation between invasive and echocardiographic hemodynamic measurements in both diastology [68% vs. 45% ($p<0.001$)], and RA pressures [33% vs. 21% (p=0.04)] respectively. Similarly there was a significant improvement in correlations between echo and cath LVEF (R2=0.77 vs. R2=0.71; $p<0.001$) as well as average E/E' and LVEDP (R2=0.39 vs. R2=0.00, p=0.006) in 2012 compared to 2011 and a trend to-

wards better correlation between echo and cath for PASP (R2=0.58 vs. R2=0.04, p=0.26).
Conclusion: The QI process, as recommended by ASE and IAC, can allow for identification as well as rectification of systemic issues in a large academic community hospital setting to a significant extent.

ISCHAEMIA AND CARDIOPROTECTION

P6328 | BENCH
Cardioprotection is impaired in cardiomyocyte specific TNF-deficient mice

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Purpose: Tumor necrosis factor alpha (TNF) is a pleiotropic cytokine that exerts a crucial role in the heart. Recent studies have implicated TNF in the cardioprotective effect of ischemic postconditioning (IPost) against ischemia reperfusion (I/R) injury by limiting infarct size and inhibiting mitochondrial permeability transition pore (MPTP) opening. A myriad of cell types, including cardiomyocytes and immune cells, synthesise TNF. We propose that TNF originating from the cardiomyocyte is required to mediate the beneficial effect of IPost.
Methods: Morphometric measurements, echocardiography and histological staining of heart sections with Picrosirius red were performed on cardiomyocyte-specific TNF-deficient mice (cmTNF–/–) for phenotype characterisation. Hearts of cmTNF–/– and wild-type mice (WT) were subjected to 35 min global ischemia/45 min reperfusion on the Langendorff system. IPost was elicited at the onset of reperfusion with 6x10sec alternating cycles of I/R. Infarct size was assessed by 2,3,5-triphenyltetrazolium chloride staining. Isolated mouse heart mitochondria were exposed to 25 min anoxia/3 min reoxygenation (A/R) and membrane potential was determined using JC-1 dye and flow cytometry to evaluate MPTP opening. Five or more mice were used per group.
Results: Body weight (32.8±0.8 versus 32.6±0.7 g) and heart weight-to-tibia length ratio (6.8±0.3 versus 6.8±0.8 mg/mm) were similar for cmTNF–/– relative to WT (p=ns). There was no significant difference in cardiac function between cmTNF–/– and WT. Picrosirius red staining revealed that collagen deposition in the hearts of cmTNF–/– (1.5±0.4%) was equivalent to WT (1.2±0.2%, p=ns). Following I/R, WT hearts presented with an infarct size of 50±3% that was markedly decreased to 19±1% by IPost ($p<0.001$). However, IPost failed to lower the infarct size of cmTNF–/– hearts (56±1%) compared to I/R (55±1%, p=ns). In isolated heart mitochondria exposed to A/R, cmTNF–/– exhibited a 60.9±4.2% reduction in membrane potential ($p<0.001$ versus WT).
Conclusion: These findings suggest that TNF produced by the cardiomyocyte contributes to the cardioprotective effect of IPost and most likely via regulation of the MPTP.
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P6329 | BENCH
Delta-opioid stimulation abolishes beneficial effect of ischemic preconditioning and postconditioning in human myocardium in vitro

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Purpose: Early restoration of myocardial perfusion remains the important way to reduce infarct size. Reperfusion has also been shown to induce myocardial necrosis in the mechanism known as ischemia-reperfusion (I/R) injury and it may decrease the potential benefits of reperfusion. Ischemic preconditioning (IPC) and postconditioning (POC) are well documented to trigger cardioprotection against I/R injury. Several investigators demonstrated in an animal model of I/R injury beneficial effect of IPC and POC is mediated via δ-opioid receptors but the class of opioid receptors responsible for this effect in humans remains unknown. The present study sought to assess the co-application of selective δ-opioid receptor agonist D-Ala D-Leu–enkephalin (DADLE) and IPC or POC on fragments of human myocardium in vitro.
Methods: Muscular trabeculae of the human right atria were electrically driven in the organ bath and subjected to simulated I/R injury in vitro. The single brief hypoxia period preceded the applied lethal hypoxia was used to achieve IPC of trabeculae whereas five brief hypoxia periods followed by lethal hypoxia were used to achieve POC. DADLE group trabeculae were subjected to IPC or POC with DADLE 10–6M used at the time of reoxygenation. Control group trabeculae were subjected only to the IPC or POC. The contraction force of the myocardium assessed as a maximal amplitude of systolic peak (%Amax) and diastolic function assessed as slope of trailing edge of the peak (Slope T) were obtained during the whole experiment's period. Local Bioethics Committee approval for the use of human tissue was obtained the experiments were performed according to the Declaration of Helsinki.
Results: Co-application of IPC and DADLE resulted in decrease of %Amax and Slope T during reoxygenation period as compared to IPC only (65.20±1.7 vs. 79.99±2.9; 34.96±3.4 vs. 49.34±6 respectively, $p<0.05$). Co-application of POC and DADLE resulted in decrease of Slope T as compared to POC only (24.80±2 vs. 35.15±1.9, $p<0.05$).
Conclusions: Previous studies utilized mainly the animal models to describe the influence of opioids on I/R injury. In our study the application of DADLE abolishes the cardioprotective effects of IPC or POC in simulated I/R injury in the fragments of human right heart atria. It remains in contrary to the previous reports with animal model of I/R injury.
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P6330 | BENCH
Suppression of Bim by microRNA-19a protected cardiomyocytes against hypoxia induced apoptosis via autophagy activation

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Purpose: In the era of percutaneous coronary artery intervention (PCI), microvascular obstruction (MO), deemed as one crucial complication, negates the potential benefits of reperfusion therapy. Distal thrombus debris embolization during primary PCI is most likely responsible for MO occurrence in ST-segment elevation myocardial infarction (STEMI) patients and leads to persistent hypoxia in coronary microcirculation with subsequent loss of cardiomyocytes. The microRNA-19a was recognized as the most important miRNA in the oncomiRs–miR-17–92 cluster and found a notable depression in MO myocardium using miRNAs microarray. However, the exactly role of miR-19a in MO related cardiomyocytes loss and the underlying mechanism remains to be elucidated.
Methods and results: Cardiomyocytes derived from neonatal SD rats were subjected to hypoxia or not and harvested for subsequent analysis. Expression of miR-19a was detected utilizing qRT-PCR. Apoptosis was assessed by TUNEL assay and immunoblotting for caspase-3 cleavage. The percentage of TUNEL positive cells increased in parallel to the elongation of hypoxic exposure, accompanied with significant accumulation of cleaved casepase-3, while expression of miR-19a gradually decreased, in a temporal dependent manner, to 74.27% 12 hours after disposal compared with normoxia group ($P<0.05$). Overexpression of miR-19a notably reduced apoptotic direct activator Bim expression and clearly ameliorated apoptosis induced by hypoxia accompanied with autophagy activation reflected by LC3II accumulation. In turn, cardiomyocytes transfected with EGFP-Bim constructs displayed marked resistance to the cytoprotective effect of miR-19a. Thereafter, dual luciferase reporter assay confirmed the direct binding of miR-19a to 3'UTR of Bim. Hence, it is reasonable to argue that miR-19a protected cardiomyocytes against hypoxia induced apoptosis via directly targeting Bim. Beyond the pro-apoptotic function, Bim likewise function in autophagy inhibition and thus prime cells to apoptosis. To further elucidate whether miR-19a protected cardiomyocytes against apoptosis by mean of autophagy induction, we then executed cells co-administrated with 3-methyladenine (3-MA), a potent autophagy inhibitor, and miR-19a to hypoxia. Notably, co-administration of 5nM 3-MA moderately increased TUNEL-positivity and caspase-3 cleavage compared to cells treated with miR-19a alone after prolonged exposure to hypoxia.
Conclusion: MiR-19a protected cardiomyocytes from hypoxia induced lethality at least partially via Bim suppression and the subsequent autophagy activation.
Acknowledgement/Funding: National Natural Science Foundation of China (Grant Number 81370322)

P6331 | BENCH
Hypoxia/reoxygenation could shift microRNA-150 from inhibition to activation of MEK4 expression in H9c2 cardiomyocytes

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Purpose: To investigate the different effects of MicroRNAs (miRNAs) participating in downstream gene expression and cellular conditions in association with diverse biological stimulations.
Methods: Our previous study revealed that microRNA-150 (miR-150) is significantly up-regulated in hearts under hypoxia/ reoxygenation injury. Persistent expression of miR-150 in H9c2 cells significantly increased in vitro cellular proliferation. We constructed miR-150 H9c2 stable clone and investigated the downstream gene expression under normoxia condition and hypoxia/ reoxygenation injury. Using luciferase reported assay, we verified miR-150 could manipulate MEK4 gene expression. The subsequent cellular responses of miR-150 of normoxia and hypoxia/ reoxygenation injury were checked with proliferation assay and apoptotic flowcytometry.
Results: We found that miR-150 could inhibit MEK4 expression under normoxia condition and stimulate H9c2 cardiomyocytes proliferation, which could be blocked with antagomir-150. However, under hypoxia/reperfusion injury, miR-150 could stimulate MEK4 activation, which in turn would prevent H9c2 apoptosis by way of p38MAPK/JNKs pathway, which could be reversed with antagomir-150 in a dose-dependent response. FLT3, a known target of miR-150 was used as an internal control, was suppressed in the miR-150 stable clone under normoxia and hypoxia/reperfusion injury. The suppression of FLT3 in the miR-150 stable clone could be reversed with antagomin-150. The luciferase reported assay fur-

ther proved that the different stimulus might change the binding affinity of miR to its target site.
Conclusion: Our study suggests that miR-150 could stimulate cell proliferation in normoxia condition and prevent hypoxia/ reoxygenation injury via differential regulation of its' downstream target. Persistent expression of miR-150 can rescue the cell from apoptosis uduring hypoxia/reoxygenation injury and increase the cardiomyocytic proliferation under normoxia.
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P6332 | BEDSIDE
Effect of remote ischemic preconditioning on extracellular vesicles in patients with acute ST-elevation myocardial infarction

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Background: Remote ischemic preconditioning (RIPC) before primary percutaneous coronary intervention (PCI) reduces myocardial injury and improves endothelial function in patients with acute myocardial infarction. Extracellular vesicles (EVs) are associated with inflammation, coagulation, and the development of vascular disease. We hypothesized that the mechanisms of RIPC are associated with changes in the levels of EVs.
Purpose: The aim of the current study was to assess the effect of RIPC on the numbers of EVs in the blood of patients with ST- elevation myocardial infarction (STEMI).
Methods: Forty-eight patients with STEMI were randomly divided into two groups: those who would receive RIPC and those who would not receive RIPC (intermittent arm ischemia-reperfusion through four 5-minutes- cycles of inflation/deflation with a blood-pressure cuff to 200 mm Hg) prior to primary PCI. Blood samples from some of the patients were collected at baseline at admission and on the 2nd day after primary PCI,.and centrifuged to obtain platelet-poor plasma. EVs from plasma were captured with 15-nm magnetic nanoparticles coupled with antibodies specific for different membrane antigens. We evaluated in patients' blood platelet–derived EVs (CD31-captured CD42+MHC class I+) and endothelium-derived EVs (CD31-captured CD42-MHC class I+) using an original nanotechnology-based assay for analysis of the antigenic composition of individual EVs.
Results: There was no significant difference in the number of EVs at admission between the two groups. In patients who had received RIPC there was a significant decrease, by 37.8% and 30.0%, respectively, in the numbers of platelet-derived EVs (CD31-captured CD42+MHC class I+) and endothelium-derived EVs (CD31-captured CD42-MHC class I+) in comparison with a significant increase in the number of EVs, by 44.6% and 10.5%, respectively, in patients without RIPC.
Conclusion: Remote ischemic preconditioning prior to primary PCI decreases the numbers of both platelet-derived and endothelium-derived EVs in STEMI patients. This decrease in the numbers of EVs can have an important bearing on the effects of RIPC.
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P6333 | BENCH
Mechanical stretch induces apoptosis regulator trb3 in cultured cardiomyocytes and volume-overloaded heart

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Aims: The expression of TRB3 (tribbles 3), an apoptosis regulated gene, increases during endoplasmic reticulum (ER) stress. How mechanical stretch affects the regulation of TRB3 in cardiomyocytes during apoptosis is not fully understood. We hypothesized that cardiomyocytes apoptosis induced by cyclic stretch is TRB3 dependent.
Methods and results: Neonatal rat cardiomyocytes grown on a flexible membrane base were stretched by vacuum to 20% of maximum elongation at 60 cycles/min. An in vivo model of aorta-caval shunt in adult rats was used to investigate TRB3 expression. Cyclic stretch significantly increased TRB3 protein and mRNA expression. Addition of c-jun N-terminal kinase (JNK) inhibitor SP600125 and tumor necrosis factor-α (TNF-α) antibody 30 min before stretch reversed the induction of TRB3 protein induced by stretch. Cyclic stretch induced the DNA-binding activity of growth arrest and DNA damaged inducible gene-153 (GADD153) by electrophoretic mobility shift assay. SP600125, JNK siRNA and TNF-αantibody abolished the binding activity induced by stretch. TRB3 promoter activity was enhanced by stretch and TRB3-mutant plasmid, SP600125, and TNF-αantibody attenuated TRB3 promoter activity induced by stretch. Cyclic stretch dramatically increased the TNF-α secretion from cardiomyocytes. Exogenous administration of TNF-α recombinant protein to the non-stretched cardiomyocytes increased TRB3 protein expression similar to that seen after stretch. Cyclic stretch not only increased the death rate but also decreased the viability of cardiomyocytes measured by a cell counter and MTT assay. The increases of TUNEL-positive nuclei in cardiomyocytes enhanced by stretch were significantly reversed by TNF-α antibody, TRB3 and JNK siRNA. TRB3 protein expression enhanced by stretch was inhibited by the addition of TRB3 siRNA. An in vivo model of aorta-caval shunt in adult rats also demonstrated the increased TRB3 protein expression in the myocardium.
Conclusion: Cyclic stretch induced TRB3 expression in cultured rat cardiomyocytes. The stretch-induced TRB3 is mediated by TNF-α, JNK and GADD153 pathway. These results indicate that TRB3 plays an important role in stretch-induced cardiomyocytes apoptosis. TRB3 is also enhanced by volume overload in rat myocardium.

P6334 | BENCH
Role of Two-pore channels in cardiac autophagy

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Introduction: Two-pore channels (TPCs) were initially identified as a novel family of nicotinic acid adenine dinucleotide phosphate (NAADP). It has been recently demonstrated that TPCs can couple the cell's metabolic state to endolysosomal function, and some authors have suggested that they can regulate autophagic processes in several tissues. Autophagy has been implicated in the pathogenesis of a wide range of cardiovascular pathologies, including heart failure. In previous studies in failing human left-ventricular myocardium, we have found correlated alterations in gene expression of TPC1 and TPC2 and markers of metabolism and cell viability.
Purpose: Since metabolic remodeling in heart failure is also associated with changes in autophagy, our aim was to clarify if TPCs play a role in cardiac autophagy regulation.
Methods: Neonatal rat cardiomyocytes were knockdown using a small interfering siRNA for TPC1, TPC2 and TPC1/2. 24 hours after transfection, cells were infected with adenovirus expressing GFP-LC3 and subsequently starved. Confocal microscopy was used to study LC3-puncta. Western blot was carried out to identify possible changes in LC3II/I and p62 accumulation by these conditions. Electron microscopy was used to determine the lysosome number and diameter in cardiac tissue of TPC1/2 knockout vs. wt mice.
Results: TPC2 and TPC1/2 but not TPC1 knockdowns induced an increase in LC3-puncta ($p<0.001$, n=4) and LC3II/I basal protein levels ($p<0.01$, n=5), while only TPC1 knockdown provoked statistically significant changes in starvation-induced LC3-puncta ($p<0.05$, n=4) and LC3II/I protein levels ($p<0.05$, n=5). Importantly, a significant increase in p62 levels was caused by the knockdown of TPC2 ($p<0.01$, n=5) and TPC1/2 ($p<0.05$, n=5) under basal conditions, and by TPC1 ($p<0.05$, n=5), TPC2 ($p<0.05$, n=5) and TPC1/2 ($p<0.05$, n=5) knockdown in starvation-induced conditions. Finally, an increase in the lysosome number and a decrease in the mean lysosomal diameter was observed in cardiac tissue of TPCN1/2 knockout (n=3) vs. wild type (n=3) mice.
Conclusion: TPCs seems to have a key role not only in autophagy initiation but also in autophagy progression as it was shown by the accumulation of p62. All these results point to a crucial role of TPCs in cardiomyocyte autophagy regulation, a mechanism that is involved in the pathophysiology of some cardiovascular diseases.

P6335 | BENCH
Biological pacemaker created by HCN4-overexpressing mouse embryonic stem Cell-derived cardiomyocytes

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Background: To establish a biological pacemaker, enhancement of the funny current (I_f) flowing through hyperpolarization-activated cyclic nucleotide-gated (HCN) channels and attenuation of the inward rectifier current (I_{K1}) flowing through inward rectifier potassium (Kir) channels are needed. Therefore, we generated HCN4-overexpressing mouse embryonic stem cells (mESCs) and induced cardiomyocytes that originally show poor I_{K1}. We investigated whether HCN4-overexpressing mESC-derived cardiomyocytes (mESC-CMs) function as a biological pacemaker.
Methods and results: The rabbit Hcn4 gene was transfected into mESCs, and stable clones were selected. The mESC-CMs were generated via embryoid bodies and purified under serum/glucose-free and lactate-supplemented conditions. Approximately 90% of the purified cells were troponin I-positive by immunostaining. In mESC-CMs, the expression level of Kcnj2, which encodes Kir2.1 essential to generation of I_{K1} currents responsible for stabilizing the resting membrane potential, was lower than that in an adult mouse ventricle. HCN4-overexpressing mESC-CMs expressed about 3-times higher level of Hcn4 than did non-overexpressing mESC-CMs. HCN4-overexpressing mESC-CMs showed significantly larger I_f and more rapid beating than did non-overexpressing mESC-CMs. The beating rate of HCN4-overexpressing mESC-CMs responded to ivabradine and isoproterenol.
Conclusions: We established HCN4-overexpresssing mESC-CMs that show rapid spontaneous beating and responses to drugs. The results show the pos-

sibility of application of HCN4-overexpresssing stem cell-derived cardiomyocytes as a biological pacemaker.

P6336 | BENCH
Relationship of cardiac IL33/ST2 system with natriuretic pepride system and inflammation in an experimental model of obesity

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Background: Obesity is a well-known risk factor of cardiovascular disease (CVD). Interleukin (IL)-33 acts via its receptor ST2 and is involved in the pathogenesis of inflammatory disorders including CVD. Recently there was also talk of its involvement in obesity.
Purpose: The aim of this study was to investigate cardiac alterations of IL33/ST2 system in obesity and its relationship with natriuretic pepdides (NPs) system as well as inflammatory mediators.
Methods: Cardiac mRNA expression of IL-33/ST2 system was evaluated by Real-Time PCR in cardiac biopsies from n=27 obese Zucker rats (O) and n=20 controls (CO). In the same sample groups, NPs and receptos were considered to assess cardiac function and IL-6 together with TNF-alpha to evaluate inflammatory process.
Results: Significantly lower mRNA levels of the soluble ST2 (sST2) were observed in O compared to CO [O: 0,990±0,685 (mean±standard deviation); CO: 3,29±3,23; p=0,034), while no significant difference for ST2L (transmebrane isoform), IL-33 and IL-1RAcP was detected. Correlations between IL-33/ST2 system and NP systems and inflammatory mediators is reported in table 1.

Table 1. Correlations of IL-33/ST2 system

	sST2	ST2L	IL33	IL1RAcP
A NP	ns	ns	ns	ns
B NP	r=0.514; p=0.009	r=0.600; p=0.001	ns	ns
C NP	r=0.704; p<0.0001	r=0.802; p<0.0001	r=0.493; p=0.002	r=0.375; p=0.029
NP Receptor-A	r=0.507; p=0.013	r=0.640; p=0.001	r=0.335; p=0.05	r=0.490; p=0.003
NP Receptor-B	r=0.535; p=0.007	r=0.681; p=0.0001	r=0.478; p=0.003	r=0.580; p=0.001
NP Receptor-C	ns	ns	r=0.539; p=0.001	r=0.556; p=0.001
TNF-alpha	r=0.591; p=0.002	r=0.775; p<0.0001	r=0.372; p=0.023	r=0.443; p=0.007
IL6	ns	ns	r=0.375; p=0.045	r=0.441; p=0.02

Conclusions: Expression of s ST2 in cardiac tissue decreased by obesity. The strong relationships with NP systems and inflammatory mediators could suggest a role for IL33/ST2 system in cardiac mechanisms associated to obesity.

P6337 | BENCH
IL-33/ST2 in angiogenesis and limb ischemia in mice

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Aim: Interleukin (IL)-33 is a cytokine that reportedly acts as danger signal released from cells after injury. Once released, IL-33 binds to the ST2 receptor present on the plasmalemma. The IL-33/ST2 signalling has been shown to induce angiogenesis in the setting of inflammatory diseases. However, the role of IL-33/ST2 in post-ischemic angiogenesis is still unexplored. IL33 availability can be compromised by a soluble form of ST2 (sST2) that act as a decoy receptor. We previously showed that high plasmatic levels of sST2 are correlated with severity of critical limb ischemia (LI) in diabetic patients. Here, we have studied the effect of secreted IL-33 on cultured endothelial cells (ECs) and the impact of ST2 gene deficiency and IL-33 gene therapy in post-LI blood flow recovery and angiogenesis in mice.
Methods: We have developed an adenovirus (Ad.) that allows production of a secretable form of mouse IL-33 (Ad.IL-33) and tested its effect on human umbilical vein ECs (HUVECs) seeded on Matrigel to study their angiogenesis responses. Unilateral LI was induced by left femoral artery occlusion in ST2 gene knockout (ST2–/–) and wild-type (WT) mice. The IL-33 gene therapy was performed by injecting either Ad.IL-33 or an Ad.Null (control) into the ipsilateral adductor muscle. Ischemic and non-ischemic limb muscles were harvested from terminally anaesthetized WT mice at 3 days post-surgery (n=3 per group). In different mice (n=10–13 per group), post-ischemic Blood Flow (BF) recovery was measured overtime by colour laser Doppler (Moore) for up to 3 (gene therapy protocol) or 5 weeks.
Results: HUVECs infected with Ad:IL-33 secrete high levels of IL-33 and showed improved angiogenesis capacities. Expression of IL-33, ST2 and sST2 were increased in ischemic muscles 3 days after LI. In ST2–/– mice, the BF recovery was impaired compared to WT mice (p=0.06, vs. WT controls at 5 weeks). IL-33 gene therapy significantly improved the BF recovery in WT mice (p<0.05, vs. the Ad.Null control at 3 weeks), but not in ST2–/– mice (p=NS vs Ad.Null in WT; P<0.05, vs. Ad.IL33 in WT).
Conclusions: The IL-33/ST2 system contributes to post-LI BF recovery. We successfully developed an Ad. for secreted IL-33 that produced angiogenic responses in cultured ECs. IL-33 gene therapy improved post-ischemic functional recovery in the model of LI, dependently of the presence of ST2 receptor in mice.

P6338 | BENCH
Statin therapy modulates epicardial adipose tissue inflammatory status

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Background: Epicardial adipose tissue (EAT) plays a role in coronary atherosclerosis by supporting local inflammation. Our previous data indicate that EAT might be also involved in the pathogenesis of aortic stenosis (AS). The benefits of statins has been in part attributed to their anti-inflammatory effect and it is known that statins induce EAT volume regression.
Purpose: To evaluate the effects of statin theraphy on EAT thickness and secretoty profile in patients with AS.
Methods: We measured EAT thickness by echocardiography in 95 pts with severe isolated AS, and in 30 healthy controls. In 20 AS pts, we collected EAT tissue and analyzed its secretome, together with plasma, by 27 cytokine multiplex immunoassay.
Results: AS patients had an increased EAT thickness compared to controls (p<0.001). After AS patients'stratification for EAT thickness median value, we observed no differences in demographic and clinical characteristics and cardiovascular therapy. Only statin use was higher in pts below EAT thickness median value (p<0.04). Levels of inflammatory mediators were significantly lower in patients taking vs non taking statins in EAT secretome but not in plasma (Table).

Table 1. Differences of inflammatory mediators levels in patients taking vs non taking statins in plasma and EAT secretome

Plasma	P value	EAT secretome	P value
IL-1β	0.366	IL-1β	0.000
IL-1ra	0.962	IL-1ra	0.000
IL-2	0.251	IL-2	0.000
IL-4	0.503	IL-4	0.000
IL-5	0.532	IL-5	0.010
IL-6	0.021	IL-6	0.004
IL-8	0.414	IL-8	0.000
IL-9	0.723	IL-9	0.000
IL-10	0.145	IL-10	0.002
IL-17	0.753	IL-17	0.000
IFN-γ	0.369	IFN-γ	0.000
TNF-α	0.091	TNF-α	0.000

Conclusion: These preliminary results suggest a potential beneficial effect of statins not only on the amount of EAT but also on its inflammatory status.

P6339 | BEDSIDE
Alprostadil treatment is associated with up-regulation of hypoxia-inducible factor 1s subunit HIF1alpha in monocytes from patients with sustained peripheral ischemia

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Background: The transcription factor HIF-1s activity is modulated by the oxygen level-depending expression of its subunit HIF1-alpha and accounts for the activation of target genes optimizing the utilization of O2 in oxidative stress. Patients suffering from secondary Rraynaud syndrome due to connective tissue diseases are often afflicted with ulceration and ischemic gangrene giving notice of said oxidative stress situations. Mononuclear cells contribute to the pathogenesis of peripheral ischemia. We hypothesize that HIF-1alpha expression in monocytes may serve as a marker and thus part of the pathway following reperfusion therapy.
Methods: Mononuclear cells from patients with connective tissue diseases and digital ulcerations due to secondary Raynaud syndrome as well as from healthy volunteers were isolated by ficoll gradient centrifugation. Monocytes were purified using magnetic bead-based separation technology depleting all CD14 negative cells. A plasmid-based quantitative Real-Time-PCR was established for HIF1 alpha and HIF2. The cDNAs HIF1alpha/HIF2 expression profile was measured in a Roche light cycler. The results were put in relation to the expression of a housekeeping gene (beta-actin/GAPDH).
Results: We recruited a total of 20 patients, 11 women and 9 men, with an average age of 55 years. HIF1alpha gene expression was significantly up-regulated in monocytes of tested patients following an i.v. alprostadil treatment period of 14 days (Wilcoxon matched-pairs signed rank test median 2,350 before vs 5,892 after alprostadil, p=0,0432). Interestingly, the HIF1alpha level before treatment was at a comparable level to the one of healthy controls (2,350±0,5047 patients vs 0,8593±0,2727, controls n=9, p=0,0616). HIF2 showed no significant changes, neither before nor after therapy (before 0,08752±0,0416 after 0,09273±0,06133 therapy and control group 0,06236±0,05147 p=0,7280). All patients showed clinical improvement following reperfusion therapy evaluated with wound scale and Negative Symptom Assessment (NAS)
Conclusion: HIF1alpha expression in monocytes from patients with Raynaud syndrome in consequence of a connective tissue disease does not differ from expression levels in healthy controls. However, following a 2-week treatment period with, alprostadil, HIF1alpha expression in monocytes was significantly increased

alongside with the clinical improvement. HIF1alpha expression in monocytes may therefore be a downstream effect of alprostadil treatment and could potentially evolve as a valuable target for the treatment of digital ulcera due to prolonged ischemia.

CARDIAC HYPERTROPHY AND GROWTH FACTORS

P6340 | BENCH
MicroRNA-223 displays a protective role against cardiomyocyte hypertrophy by targeting cardiac troponin I-interacting kinase

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Background: MicroRNAs play regulatory role in cardiovascular disease. MicroRNA-223 (miR-223) was found to be expressed abundantly in myocardium. TNNI3K, a novel cardiac troponin I (cTnI)-interacting and cardiac hypertrophy related kinase, is computationally predicted as a potential target of miR-223.
Purpose: This study was designed to investigate the cellular and molecular effects of miR-223 on cardiomyoctye hypertrophy, focusing on the role of TNNI3K.
Methods: Neonatal rat cardiomyocytes (CMs) were cultured, and CMs hypertrophy was induced by endothelin-1 (ET-1). In vivo cardiac hypertrophy was induced by transverse aorta constriction (TAC) in rats. Expression of miR-223 in CMs and myocardium was detected by real-time PCR (RT-PCR). MiR-223 and TNNI3K were overexpressed in CMs via chemically modified sense RNA (miR-223 mimic) transfection or recombinant adenovirus infection, respectively. Cell size was measured by surface area calculation using fluorescence microscopy after anti-α-actinin staining. Expression of hypertrophy-related genes was detected by RT-PCR. The protein expression of TNNI3K and cTnI was determined by Western blots. Luciferase assay was employed to confirm the direct binding of miR-223 to the 3'UTR of TNNI3K mRNA. Intracellular calcium was measured by sensitive fluorescent indicator (Furo-2). Video-based edge detection system was employed to measure cardiomyocyte contractility.
Results: MiR-223 was downregulated in ET-1 induced hypertrophic CMs and in hypertrophic myocardium compared with respective controls. MiR-223 overexpression in CMs alleviated ET-1 induced hypertrophy, evidenced by smaller cell surface area and downregulated ANP, α-actinin, Myh6 and Myh7 expression. Luciferase reporter gene assay showed that TNNI3K serves as a direct target gene of miR-223. In miR-223-overexpressed CMs, the protein expression of TNNI3K was significantly downregulated. MiR-223 overexpression also rescued the upregulated TNNI3K expression in hypertrophic CMs. Furthermore, cTnI phosphorylation was downregulated post miR-223 overexpression. Ad.rTNNI3K increased intracellular Ca2+ concentrations and cell shortening in CMs, while miR-223 overexpression significantly rescued these hypertrophic effects.
Conclusion: By direct targeting TNNI3K, miR-223 could suppress CMs hypertrophy via downregulating cTnI phosphorylation, reducing intracellular Ca2+ and contractility of CMs. miR-223/TNNI3K axis may thus be major players of CMs hypertrophy.

P6341 | BENCH
The heparan sulphate proteoglycan glypican-6 is increased in experimental and clinical heart failure and might play a role in cardiac fibrosis through PDGF-BB signalling

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Purpose: Cardiac remodelling due to chronic pressure overload is one of the leading causes of heart failure. Understanding the underlying molecular mechanisms is important for development of new therapies. Proteoglycans are glycosylated proteins that, despite playing important roles in connective tissues and wound healing, have received little attention in cardiac remodelling.We have investigated regulation of the six-membered glypican (GPC1–6) family, evolutionary ancient heparan sulphate proteoglycans anchored to the extracellular part of cell membrane, in murine pressure overload in vivo, in biopsies from patients and in cardiac fibroblasts.
Results: Mice subjected to aortic banding (AB; n=88) showed elevated left ventricular (LV) mRNA of GPC6 during concentric hypertrophic remodelling (1 and 3 weeks of AB; 2.8- and 1.9-fold) and during dilated, end-stage heart failure (16 and 18 weeks of AB; 2.0- and 2.4-fold). Immunoblotting confirmed GPC6 protein upregulation. There were minor alterations in GPC1–4 mRNA, while GPC5 was not expressed in the LV. LV GPC6 mRNA was 1.8-fold higher in LV tissue from explanted hearts of patients with end-stage, dilated heart failure (NYHAIII-IV, n=18) than in controls (n=7), correlating negatively with LV ejection fraction. Interestingly, in the AB mouse model, GPC6 mRNA correlated positively to mRNA of the fibrosis markers collagen I and III. In neonatal rat cardiac cells in vitro, GPC6 mRNA was 3.8-fold higher in fibroblasts than in myocytes, indicating fibroblasts to be the main source of cardiac GPC6. Adult mouse cardiac fibroblasts in vitro showed increased GPC6 mRNA during myofibroblast differentiation, correlating positively with the signature myofibroblast gene, α-smooth muscle actin (α-SMA). In HEK293 cells, GPC6 overexpression enhanced ERK1/2 and AKT phosphorylation, i.e. activation, induced by the platelet-derived growth factor B (PDGF-BB), suggesting that GPC6 acts as a co-receptor for PDGF-BB-mediated signalling. Supporting this, overexpression of GPC6 in NIH3T3 fibroblasts elevated α-SMA mRNA upon PDGF-BB stimulation.
Conclusion: Our data suggest that the cell membrane-localized proteoglycan GPC6 is involved in experimental and clinical heart failure progression, likely working as a co-receptor modulating pro-fibrotic PDGF-BB signalling in cardiac fibroblasts.

P6342 | BENCH
MicroRNA-378 suppresses myocardial fibrosis through a paracrine mechanism at the early stage of cardiac hypertrophy following mechanical stress

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Background: Excessive myocardial fibrosis is a main pathological process in the development of cardiac remodeling and heart failure, it is therefore important to prevent the excessive myocardial fibrosis. By using a microRNA array, we identified microRNA-378 (miR-378) which was cardiac enriched and deeply repressed when cardiac remodeling developed.
Purpose: To examine the effects of miR-378 on cardiac fibrosis following mechanical stress.
Methods and results: Mechanical stress, which imposed respectively to mice by transverse aortic constriction (TAC) procedure and to cardiac fibroblasts by stretch of the silicon dishes induced significant increases in fibrotic responses including myocardial fibrosis, fibroblasts hyperplasia and proteins and genes expression of collagens and matrix metallo preteinases (MMPs). All these fibrotic responses were attenuated by a chemically modified miR-378 mimic (Agomir) but exaggerated by the inhibitor (Antagomir) which was given to mice for three consecutive days after TAC by intravenous injections and to cells by direct addition to culture medium, respectively. Endogenous miR-378, which was specifically expressed in cardiomyocytes but not in cardiac fibroblasts, could be released from cardiomyocytes during early stage of mechanical stress in an exosome-dependent secretory machinery and inhibit fibrotic responses of cardiac fibroblasts. Mechanistically, miR-378-exerted anti-fibrotic effects were partially through suppression of p38 MAP kinase phosphorylation and activation of signal transducers and activators of transcription 3 in cardiac fibroblasts.
Conclusion: MiR-378 secreted from cardiomyocytes acts as an inhibitor of excessive cardiac fibrosis through paracrine mechanism.

P6343 | BENCH
TMEM43 mutation induces massive fibrosis and heart failure: a new mouse model to unravel therapeutic targets

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Arrhythmogenic right ventricular cardiomyopathy type 5 (ARVC5) is the most aggressive variant of ARVC. It is an inherited autosomal-dominant disease associated to sudden death in young males, so that 50% of males are dead at the age of fifty. ARVC5 is caused by a point mutation in the TMEM43 gene. The mechanisms by which the mutation in TMEM43 causes the disease and the cause for the arrhythmia in this condition are not known. To date, this disease has no cure. To extensively characterize the disease, we have generated a transgenic mouse model that carries the S358L human mutation in the TMEM43 gene. Our results indicate that the overexpression of the mutated TMEM43 protein indeed reproduces human ARVC5: all mice are dead by four months of age; they show biventricular systolic dysfunction and heart failure. Moreover, the hearts of these mice show fibrofatty replacement of the cardiomyocytes and impaired electrical function, also characteristic in human patients. Our preliminary results suggest that TMEM43 transmembrane protein is localized in the nuclear envelope. Bioinformatic analysis of the protein structure suggests interaction with emerin (EMD) and SUN2 proteins. The S358L mutation in one of the transmembrane domains of TMEM43 is predicted to reduce its mobility and, hence, augment nuclear stiffness. Thus, ARVC5 might result from disrupted mechanotransduction through interactions between S358L-TMEM43 and EMD and SUN2.
Identifying the underlying physiopathological mechanism in the mouse model is the first step to establish therapeutics and prevention or regression of this rare, lethal and poorly known human disease.
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P6344 | BEDSIDE
Pre-operative growth differentiation factor 15 (GDF-15) as a novel biomarker of acute kidney injury after cardiac bypass surgery

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Objective: Previously, we demonstrated that preoperative plasma GDF15 levels significantly improved the prognostic value of the EuroSCORE for mortality after cardiac surgery. Despite the strong correlation between GDF15 and renal function, no data are available regarding the potential interest of preoperative GDF15 levels to improve the prediction of acute kidney injury (AKI) after coronary artery bypass grafting (CABG).
Design: 134 patients operated on for CABG of whom 50 underwent off-pump surgery at our university hospital were included in this prospective, observational study. Exclusion criteria were age $<$18 years or $>$80 years, previous atrial fibrillation/flutter, previous severe renal failure (estimated glomerular filtration rate (eGFR) $<$30 ml/min), previous cardiac surgery, and emergency surgery. AKI was defined according to AKIN network criteria. GDF15 levels in plasma were measured at the time of anesthesia and 12 hours after surgery.
Results: 42 patients developed postoperative AKI which had significantly higher preoperative plasma GDF15 levels (OR=2.851; 95% CI: 1.32–6.13, p=0.008), higher preoperative serum creatinine levels (OR=1.025; 95% CI: 1.003–1.05; p=0.026), and most often underwent cardiopulmonary bypass (CPB) surgery (OR=2.67; 95% CI: 1.17–6.14, p=0.020). On ROC curves, GDF15 was found to be the best preoperative biomarker to predict AKI (AUC 0.83; CI 0.75–0.89), compared with eGFR (AUC 0.67; 95% CI 0.59–0.75 p=0.003) and NT-proBNP (AUC 0.62; CI 0.51–0.72 p$<$0.001). GDF15 level was also significantly better than the EuroSCORE in predicting AKI (AUC 0.62, 95% CI 0.54–0.70 p$<$0.001). The predictive model including high blood pressure, diabetes, preoperative eGFR and CPB surgery was significantly improved when preoperative GDF15 was added.
Conclusion: Preoperative GDF15 plasma levels are associated with postoperative AKI in patients undergoing CABG. Preoperative GDF15 may improve preoperative risk stratification and discrimination among candidates for surgery.

P6345 | BENCH
Cardiac Ampk alpha 1 promotes Ap-1 activity via Pkc-zeta

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Question: AMP-activated protein kinase (Ampk) regulates myocardial energy metabolism and is involved in the response to increased cellular stress. In failing hearts, an isoform shift of the predominant α2 isoform to the α1 isoform was observed.
Purpose: To identify possible isoform specific effects of Ampkα1 in cardiomyocytes.
Methods: Experiments were performed in Ampkα1-deficient and corresponding wild-type mice following pressure overload by transverse aortic constriction (TAC) or Angiotensin II infusion and in HL-1 cardiomyocytes.
Results: In HL-1 cardiomyocytes, overexpression of constitutively active Ampkα1 increased the phosphorylation of protein kinase Cζ (Pkcζ). Constitutively active Ampkα1 further increased Ap-1-dependent transcriptional activity and mRNA expression of Ap-1 target genes: c-Fos, Il6 and Ncx1, effects blunted by Pkcζ silencing. Angiotensin II treatment activated Ap-1 and increased c-Fos, Il6 and Ncx1 mRNA expression, effects blunted by Pkcζ or Ampkα1 silencing, but not by Ampkα2 silencing. In wild-type mice, angiotensin II infusion increased cardiac Ampkα1 protein abundance. In Ampkα1-deficient mice and wild-type mice, heart weight to body weight ratio and blood pressure showed a comparable increase following angiotensin II infusion. Nonetheless, the Ampkα1-deficient mice showed a blunted angiotensin II induced increase of cardiac Pkcζ protein abundance as well as c-Fos, Il6 and Ncx1 mRNA expression compared to wild-type mice. Following TAC, increased cardiac Ampkα1 protein expression was paralleled by increased Pkcζ abundance and c-Fos, Il6 and Ncx1 mRNA expression. The increase of Pkcζ abundance and c-Fos, Il6 and Ncx1 mRNA levels after TAC was blunted in the Ampkα1-deficient mice, paralleled by a better preserved ejection fraction.
Conclusion: Ampkα1 promotes myocardial activation of Ap-1, an effect requiring Pkcζ. The stimulatory effects of Ampkα1 on Ap-1 are isoform specific. Cardiac isoform shift of Ampkα subunits may therefore modulate cardiac stress signaling.

P6346 | BENCH
Pathological hypertrophy stimulation generates mitochondrial dysfunction and induces the expression of the mitochondrial motor protein Kif5B

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Purpose: Mitochondrial dysfunction is observed in many diseases, including cardiovascular syndromes. In late stage heart failure mitochondrial dysfunction has been reported, but it is unclear whether this arises already during cardiac hypertrophy development. We therefore investigated whether a single pathological or physiological hypertrophy stimulus would be able to affect mitochondrial function in vitro and investigate the involved factors.
Methods: Mitochondrial OXPHOS activities were investigated in primary neonatal rat cardiomyocytes (NRVCs) treated with pathological (phenylephrine; PE) and physiological (and insulin growth factor-1, IGF-1) stimuli. Mitochondrial oxidative consumption rate (OCR) was determined with a Seahorse flux analyzer Mitochondrial biogenesis and gene expression profiling was performed and Kif5b investigated.
Results: Cardiomyocytes were stimulated with PE and IGF-1, resulting in hypertrophy development as determined by cell size and protein synthesis measurements. In PE, but not IGF-1, stimulated cells this was accompanied by pathological gene expression (a.o. ANP). OXPHOS measurements revealed that complex II state 3 activity was diminished after PE stimulation only. In contrast, IGF-1 strongly stimulated complex I state 3 activity. The observed changes were not rapid, but developed during 24 hours stimulation. Within this time frame no mitochondrial biogenesis was observed and levels of OXPHOS complexes did not alter. Gene array analysis did show minor changes in mitochondrial metabolic gene expression in IGF-1 stimulated cells, whereas in PE treated cells, no obvious changes in metabolic routes were observed. Interestingly, Kif5B a gene reported to control mitochondrial localization was upregulated in PE treated cells only. Increased expression was confirmed in pathological hypertrophy animal models (TAC, MI), but not in physiological hypertrophy (exercise). Interestingly, in PE treated cells mitochondria were also more dispersed and this could be reverted by silencing of Kif5B. This silencing did not improve complex II activity in PE treated cells, but did further diminish it. This indicates that increased Kif5B expression is not responsible for decreased complex II activity, but is rather a compensatory mechanisms.
Conclusions: Pathological hypertrophy, induced by a single neurohormonal stimulus is accompanied by mitochondrial dysfunction, whereas physiological stimulation improves mitochondrial function. Increased expression of Kif5B under pathological conditions affects mitochondrial localization and may have a compensatory function.

P6347 | BENCH
Selective cathepsin K inhibition ameliorates left ventricular hypertrophy and diastolic dysfunction

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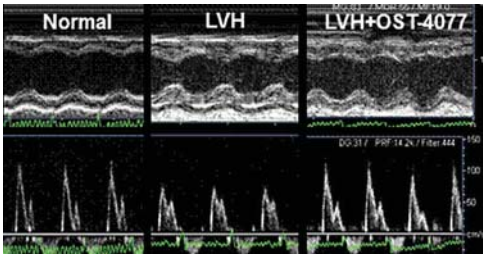
Background: The level of serum cathepsin K, a cysteine protease of the papain family, has been known to be elevated in pressure overload-induced cardiac hypertrophy. We hypothesized that pharmacological inhibition of cathepsin K, using a novel drug specific for cathepsin K, may protect against angiotensin II–induced cardiac dysfunction.
Methods: Male Sprague-Dawley (3-month-old) rats were given angiotensin II (600ug/kg/day) via mini osmotic pumps for up to 4 weeks to induce left ventricular hypertrophy (LVH). A subset of rats were given OST-4077 daily (100mg/kg QD) for selective cathepsin K inhibition. We assessed the LV geometry using 2D-echocardiography and the LV systolic/diastolic function using Doppler echocardiography and the pressure-volume (PV) conductance catheter. The pathways downstream of cathepsin K inhibition were analyzed using microarray analysis.
Results: The activity of cathepsin K was inhibited by selective oral cathepsin K inhibitor OST-4077. Cathepsin K inhibition significantly alleviated LVH and diastolic dysfunction in rats implanted angiotensin II-osmotic minipumps on echocardiography. Also, the dP/dtmax and dP/dtmin significantly improved by OST-4077 treatment on invasive cardiac catheterization, which lead to significant improvement of exercise capacity. OST-4077 showed potent inhibitory action against myocardial hypertrophy and fibrosis by histology. Of the 1,143 genes significantly upregulated or downregulated $>$1.5-fold in LVH rats, the expression of 673 genes were normalized by cathepsin K inhibition.



Conclusion: Our data suggests that OST-4077, an orally active selective cathepsin K inhibitor, may have the therapeutic potential for the treatment of left ventricular diastolic dysfunction and hypertrophy.

P6348 | BENCH
Adiponectin attenuates adverse cardiac remodeling following cardiac injury by up-regulating matrix metalloproteinase 9 expression

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Background: Adiponectin (APN) is a multifunctional immunomodulatory adipocytokine that inhibits left ventricular hypertrophy induced by pressure overload as well as hypertension and attenuates fibrosis after myocardial infarction. Coxsackievirus B3 (CVB3) causes severe myocarditis associated with intense extracellular matrix (ECM) remodeling, which might progress to dilated cardiomyopathy. Here, we investigated whether APN inhibits adverse ECM remodeling in vitro and in cardiac injury models by affecting matrix metalloproteinase (MMP) expression.
Methods: Cardiac cells were cultured in vitro. Cardiac injury was induced by experimental autoimmune myocarditis, CVB3 infection or myocardial infarction in APN-KO and WT mice. Gene expression and gelatinolytic activity/protein expression of MMPs was quantified by qRT-PCR and zymography, respectively. Activation status of protein kinases was determined by immunoblot. Collagen 1 turnover was assessed by CTXI ELISA.
Results: In cultured cardiac myocytes (CM) and fibroblasts (CF) APN upregulates MMP-9 gene and protein expression through activation of AMPK and ERK1/2 without affecting MMP-2, MMP-3 and MMP-13 expression levels. Both AMPK and MEK1 control the up-regulation of MMP-9 expression by proinflammatory stimuli in cardiac fibroblasts. Accordingly, APN further enhanced the up-regulation of MMP-9 expression triggered by TNFa, LPS and R-848 in CF. Conversely, cardiac fibroblasts from APN-KO mice displayed reduced expression of MMP-9 after stimulation with TNFa, LPS and R-848 ex vivo. In line with these observations, cardiac MMP-9 activity was attenuated in APN-KO mice in subacute CVB3 myocarditis at day 7 post infection and myocardial infarction. Moreover, splenic MMP-9 expression was also diminished in APN-KO mice at day 7 post-infection correlating with diminished immune cell infiltration in hearts of APN-KO mice. Accordingly, cardiac collagen split product (CTXI) accumulation was significantly reduced in hearts of APN deficient mice in CVB3 myocarditis and following myocardial infarction indicating attenuated collagen 1 turnover.
Conclusions: Our observations indicate that APN inhibits adverse cardiac remodeling following cardiac injury by inducing MMP-9 expression in resident cardiac and infiltrated immune cells. Persistently enhanced cardiac MMP-9 activity results in increased cleavage of accumulating collagens and augmented ECM turnover that might result in inhibition of fibrosis and cardiac dysfunction.

ION CHANNELS AND ELECTROPHYSIOLOGY

P6349 | BENCH
Nos1AP alters QTc intervals upon overexpression in mice

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Rationale: The QT interval duration (QTc) reflects cardiac depolarization. It may predispose individuals to ventricular tachycardia and sudden cardiac death if prolonged (long QTc), shortened (short QTc) or otherwise unregularly. Whole-genome association studies have linked genetic variations in the neuronal nitric oxide synthase adapter protein NOS1AP to variations in QTc intervals and sudden cardiac death.
Hypothesis: We hypothesize NOS1AP functions as an L-type-Ca2+ channel modulator via its interaction with the neuronal nitric oxide synthase NOS1. Therefore, alterations in myocardial NOS1AP expression should temper with QTc intervals and increase susceptibility to rhythm disorders.
Methods and results: We generated conditional double transgenic mice by crossbreeding pTRE-6xHN-Nos1AP animals with α-MHC-tTA mice; NOS1AP expression is therefore restricted to cardiomyocytes and under control of doxycycline (Tet-Off system). Double transgenic animals were investigated with the main focus upon electrical alterations. Heart rates were similar in NOS1AP overexpressing and non-induced animals. Atrial programmed stimulation repeatedly caused atrial tachycardia, while ventricular programmed stimulation caused VT in NOS1AP overexpressing mice. There was a clear decrease of QTc intervals in NOS1AP overexpressing mice paralleld by a significantly reduced survival (only 56% after 12 weeks vs 100% in non-induced mice. Induced QTc alterations and accompanied deaths subsided upon readministration of doxycycline.
We also investigated the functional effect of the human SNP rs16847548 (T/C). We found that this SNP decreased NOS1AP transcriptional activity in vitro and therefore suggest this leads to a decrease in NOS1AP expression in humans.
Conclusion: Myocardial overexpression of NOS1AP leads to short QTc syndrome with increased susceptibility to atrial and ventricular rhythm disorders and cardiac death. SNP rs16847548 in NOS1AP resulted in less NOS1AP promoter activity in vitro which could explain the alteration in QTc intervals.
In summary, not only mutations in ion channels themselves but also genetic alterations in the expression of ion channel modulators such as NOS1AP, have an impact on QTc intervals.

P6350 | BENCH
Cardiac sodium channel mutation associated with epinephrine-induced QT prolongation and sinus node dysfunction

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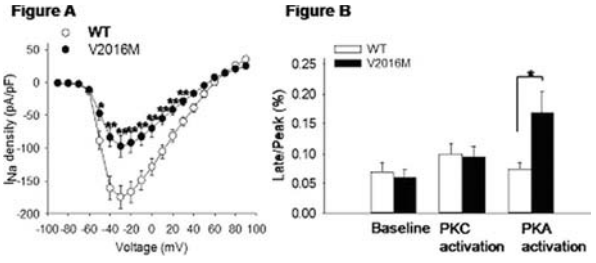
Background: Long-QT syndrome (LQT) is an inherited arrhythmia characterized by prolonged ventricular repolarization and malignant tachyarrhythmias. LQT1–3 caused by mutations in KCNQ1 (LQT1), KCNH2 (LQT2), and SCN5A (LQT3) accounted for approximately 90% of genotyped LQT patients. Most of the cardiac events in LQT1 occur during exercise, while patients with LQT3 tend to have arrhythmic events during rest or asleep.
Objectives: The purpose of this study is to identify a genetic mutation in a Japanese male who presented sinus node dysfunction and prolonged QT interval during an epinephrine stress test, and also clarify the electrophysiological properties of mutant channels.
Methods and results: As a result of comprehensive genetic analyses, we identified a heterozygous missense SCN5A mutation, V2016M, which changed the last amino acid of the cardiac sodium channel. Electrophysiological analyses revealed that the mutant channels exhibited a loss-of-function feature, decreased peak sodium current density (WT, 175.2±17.6 pA/pF; V2016M, 97.2±16.0 pA/pF; $p<0.01$, Figure A). In addition, the mutant channels showed gain-of-function features: increased late sodium currents by protein kinase A activation (WT, 0.07±0.01%; VM, 0.17±0.03%; $p<0.05$, Figure B), and impaired inactivation of sodium channels by protein kinase A or C activation.



Conclusions: We identified an SCN5A mutation in a patient with sinus node dysfunction and epinephrine-induced LQT which was an atypical phenotype for LQT3. Electrophysiological analyses indicated that this mutation presented both loss-of-function and gain-of-function features. The latter was observed by adrenergic stimulation. The electrophysiological properties of the mutant channels might be associated with the overlapping clinical features of the patient.

P6351 | BENCH
Abnormal expression of cardiac ion channels-associated genes in lamin A/C-related cardiomyopathy-specific induced pluripotent stem cell derived cardiomyocytes

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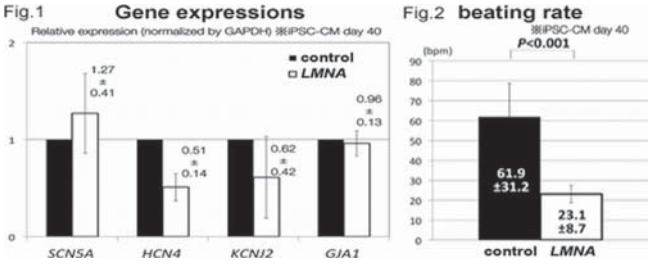
A lamin A/C gene, LMNA, encodes nuclear membrane proteins, lamin A and C, and lamins interact with numerous gene regulators and modulate gene-expression levels. The mutations in LMNA are associated with familial dilated cardiomyopathy (DCM) with cardiac conduction system disease (CCD) and malignant ventricular arrhythmias, but causal mechanisms is still unclear. Induced-pluripotent stem cells (iPSC) offer an opportunity to model human diseases in relevant cell types, and it is useful to reveal mechanisms of genetic disease development.
We generated iPSCs from fibroblasts obtained from a 52-year-old Japanese male with DCM and CCD carrying a deletion mutation (p.S303Cfs*27) in LMNA. iPSCs were differentiated into cardiomyocytes and analyzed at 40 days after cardiac differentiation. Gene expression analysis showed decreased LMNA mRNA levels in the patient-specific iPSCs-derived cardiomyocytes (LMNA-iPSC-CMs) by half compared to control-iPSC-CMs, suggesting that haploinsufficiency due to nonsense-mediated mRNA decay was the underlying cause. With regard to the cardiac ion channels-related genes, the expression of HCN4, that is required for the generation of pacemaker potentials (If current), was down-regulated in LMNA-iPSC-CMs compared to control-iPSC-CMs (0.51±0.14; p=0.0017, Fig. 1). The spontaneous beating rate in LMNA-iPSC-CMs was significantly slower rather than that of control-iPSC-CMs (23.1±8.7 vs 61.9±31.2; $p<0.001$, Fig. 2).
Human iPSC-based model of LMNA-related cardiomyopathy showed the low ex-



pression of HCN4 and slow beating rate in vitro. This disease-specific model might be helpful to clarify the causal mechanism of CCD phenotype in human LMNA-related cardiomyopathy.

P6352 | BENCH
PITX2c deficiency augments anti-arrhythmic effects of sodium channel blockers: results in a mouse model and validation in a simulation study of the human atrium

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Background and objectives: Polymorphisms close to the PITX2 gene on chromosome 4q25 are associated with incident and recurrent atrial fibrillation (AF). Carriers of variant rs10033464 respond relatively well to antiarrhythmic therapy with sodium channel blockers. To test whether reduced atrial PITX2 mRNA expression alters the electrophysiological effect of sodium channel blockers, we studied the effect of flecainide (Flec) in mice with heterozygous PITX2c gene deletion, a model for reduced Pitx2 mRNA expression and AF susceptibility.
Methods: We assessed the effect of 1μM Flec on left atrial (LA) monophasic, transmembrane and optical action potentials in Pitx2c+/– mice and their wild-type (WT) littermates. We measured conduction velocity (CV), action potential duration (APD), AP amplitude (APA), maximum upstroke velocity (dV/dtmax) and resting membrane potential (RMP) during atrial pacing at 80–120ms fixed-rate cycle lengths (CL); and effective refractory periods (ERP) with arrhythmia inducibility during programmed (S2) stimulation. Post-repolarisation refractoriness (PRR) was defined as the difference between ERP and APD90.
Using simulations of conduction with the Courtemanche human atrial model, we assessed whether the electrophysiological changes associated with reduced Pitx2 mRNA expression alters the response to sodium current (INa) block.
Results: Flec abolished arrhythmias in Pitx2c+/– (6/18 base vs 0/15 Flec, $p<0.05$) but less so in WT atria (3/15 base vs 3/12 Flec). Pitx2c+/– atria had a higher resting membrane potential (WT –70±0.7mV, n=30 cells vs Pitx2c+/– –68±0.7mV, n=32 cells, $p<0.05$) and lower APA (WT 78±1.2, n=30; PITX2c+/– 73±1.3, n=32). Flec had no effect on the RMP and reduced CV, APA and Vmax in both genotypes. Flec doubled the ERP increase in Pitx2c+/– atria compared with WT (Pitx2c+/– 14±2ms, n=13 vs WT 7±2ms, n=10; $p<0.05$), and tripled PRR (Pitx2c+/– 21±3ms, n=6 vs WT 6±4ms, n=6, $p<0.01$). Hearts with PRR were not susceptible to arrhythmias (0/17). As with isolated hearts, INa block prolonged PRR in the Pitx2c knockout simulation (500ms CL: reference model 30ms; Pitx2c knockout model 42ms) and had no differential effects of INa on RMP, CV, APD and dV/dtmax. The model, thus, qualitatively reproduced the experimental findings.
Conclusion: Flecainide effectively suppresses AF in mice with reduced Pitx2 mRNA expression. We propose that this genotype-specific antiarrhythmic effect can be explained by a higher resting membrane potential and higher PRR. These data support preferential use of flecainide for rhythm control therapy in carriers of genetic variants on chromosome 4q25.

P6353 | BENCH
Enhanced fast-inactivated state stability of cardiac sodium channels by a novel voltage sensor SCN5A mutation R1632C as a cause of multiple electrophysiological phenotypes

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Background: SCN5A, which encodes α-subunit of cardiac voltage-gated sodium channels, consists of four homologous but non-identical domains. The fourth segment (S4) in each domain is postulated to function as a voltage sensor, but each S4 is thought to have distinct functional roles. SCN5A mutations in each S4 and those in even the same S4 may cause diverse functional abnormalities and phenotypic manifestations. We identified a novel SCN5A R1632C mutation, located in the S4 of domain IV (DIV-S4) voltage sensor, in a 17-year-old male patient who experienced syncope due to atrial tachycardia during exercise, and presented with sinus node dysfunction and Brugada syndrome.
Purpose: We sought to elucidate the functional consequences of the SCN5A R1632C mutation.
Methods: Wild-type (WT) or R1632C SCN5A were coexpressed with hβ1 subunit in tsA201 cells, and whole cell sodium currents (INa) were recorded using patch-clamp methods.
Results: INa density, measured at –20mV, for R1632C was significantly smaller than that for WT (R1632C: –433±52pA/pF, n=14; WT: –672±90pA/pF, n=15, $P<0.05$), however, no significant changes were observed in steady-state activation and fast inactivation rate. Steady-state inactivation curve, assessed after 500ms depolarizing pulses, for R1632C was remarkably shifted to hyperpolarizing potentials compared to that for WT ($V_{½}$ for R1632C: –110.7±0.8mV, n=16; WT: –85.9±2.5mV, n=17, $P<0.01$). Steady-state fast inactivation curve, assessed after 20ms depolarizing pulses, for R1632C was also shifted to the same degree. Recovery from fast inactivation after 20ms depolarizing pulses for R1632C was remarkably delayed compared to that for WT (tau for R1632C: 246.7±14.3ms, n=8; WT: 3.7±0.3ms, n=8, $P<0.01$). To assess activity-dependent loss of INa availability, twenty times repetitive depolarizing potentials for 20ms at cycle lengths of 0.1, 0.5 or 2s were applied. WT INa remained constant during successive stimuli at all cycle lengths. However, at cycle lengths of 0.5 and 0.1s, R1632C INa at the second pulses decreased to 79% and 26% of initial current amplitudes, respectively, but remained almost constant throughout the following train of stimuli.
Conclusions: SCN5A R1632C showed a loss-of-function of INa by an enhanced fast-inactivated state stability with pronounced impairment of recovery from fast inactivation and severe activity-dependent loss of INa availability, which may explain the phenotypic manifestations observed in our patient. Our findings provided novel insights into the pathophysiological roles and structure-function relationships of DIV-S4 voltage sensor.

P6354 | BENCH
Do major ion channels of pacemaker clock also play a role in atrioventricular nodal conduction in young and aged rats?

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Purpose: Cellular mechanisms that influence atrioventricular (AV) nodal conduction are complex. Multiple studies have been performed to explain such mechanisms but none can fully explain the "riddle" of the AV node. The role of pacemaking channels on the AV nodal conduction has not been previously studied. Also with ageing there is an increase in the incidence of AV nodal dysfunction leading to AV block. We have studied the role of pacemaking ion channels and gap junctions on the AV nodal conduction with ageing.
Methods: Electrophysiological (EP) and immunohistochemistry experiments are performed on male rats aged 3 months (equivalent to 20 year old humans; n=24) and 2 years (equivalent to 70 year old humans; n=15). In the electrophysiology experiments, Atrio-hisian (AH) interval, Wenkebach cycle length (WCL) and AV node effective refractory period (AVNERP) was measured. We have used caesium (Cs+) (2 mM) to block HCN channels responsible for the funny current (If), and ryanodine (2 μM) to block RyR2 channels responsible for Ca2+ release from the sarcoplasmic reticulum in the two age groups. Protein expression was studied using immunofluorescence and confocal microscopy on sections from each group (from n=8 young and n=9 old rats) from different regions of the AV conduction axis: inferior nodal extension (INE), compact node (CN) and penetrating bundle (PB). We used the t-test for statistical analysis.
Results: Without drugs to block the HCN and RyR2 channels, there was a significant prolongation of the AH interval ($P<0.005$), WCL ($P<0.005$) and AVNERP ($P<0.001$) with ageing. In young rats (but not old rats), Cs+ prolonged the AH interval ($P<0.001$), WCL ($P<0.01$) and AVNERP ($P<0.01$). Ryanodine prolonged the AH interval ($P<0.01$) and WCL ($P<0.01$) in young and old rats. Immunofluorescence revealed that with ageing: Cx43 (a gap junctional protein) is downregulated in the PB ($P<0.05$); Cx40 (another gap junctional protein) is upregulated in the INE and CN ($P<0.05$); In terms of calcium handling proteins: RyR2 is downregulated in the CN and PB ($P<0.05$); SERCA2a is upregulated in the PB ($P<0.05$). A trend of down regulation was observed in HCN4 expression in the PB (P=0.051).
Conclusion: For the first time, we have shown that both HCN and RyR2 channels play a role in AV nodal conduction. With ageing the effect of If-current in the AV nodal conduction decreases. The change in RyR2 and SERCA2a reduces the cytosolic calcium concentration in the AV node with ageing. Both these effects are likely to decrease conduction across the AV node with ageing that can results in higher incidence of AV block.

P6355 | BENCH
Nitrated fatty acids suppress fibroblast differentiation and oxidative stress in a murine model of AngII-induced atrial fibrillation

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Background: Atrial fibrosis is one of the most striking features in the pathology of atrial fibrillation (AF), which is decisively driven by local and systemic inflammation. We have shown previously that nitrated fatty acids – potent endogenously-occurring anti-inflammatory lipid mediators – significantly attenuate the vulnerability for AF. Herein, we elucidated the underlying molecular mechanism.

Methods and results: In angiotensin II (AngII) treated wild-type mice nitro-oleic acid (OA-NO2) strikingly attenuated vulnerability for atrial fibrillation. Picrosirius red staining revealed that AF inducibility correlated with the degree of atrial fibrosis (amount of fibrotic areas/atrium, vehicle vs AngII + OA-NO2 vs AngII + vehicle: 1.0±0.2 vs. 2.7±1.0 vs. 0.7±0.4 sec, $p<0.05$). In this regard, OA-NO2 reduced transforming growth factor β (TGF-β) induced α smooth muscle actin (α-SMA) expression in 3T3 fibroblasts mediated by decreasing Smad2 activation suggestung that the protection from fibrotic remodeling was mediated by inhibition of myofibroblast transdifferentiation (Ctrl. vs TGF-β vs TGF-β/OA-NO2 vs OA-NO2 (i) α-SMA expression: 0.3±0.1 vs 0.8±0.03 vs 0.3±0.1 vs 0.1±0.03; (ii) Smad2 phosphorylation: 0.05±0.04 vs 0.49±0.07 vs 0.14±0.08 vs 0.05±0.04 $p<0.05$).
According to the significance of infiltrated macrophages in fibrosis, also activation of these cells by lipopolysaccharides or phorbolesters was reduced by OA-NO2 (vehicle vs. OA-NO2 treated macrophages (i) superoxide production (LPS): 1.46±0.13 vs. 0.67±0.09 mM/h, $p<0.05$; (ii) oxidative burst (PMA) 320±30 vs. 270±21 CL (RLU*1000), $p<0.05$). In this context, LPS-induced expression of NOX2 and activation of p38 MAPK in isolated macrophages was diminished by OA-NO2 (NOX expression, vehicle vs. LPS: 0,108±0.061 vs. 0.898±0.102, $p<0.05$; LPS vs. LPS/ OA-NO2: 0.898±0.102 vs. 0.068±0.024, $p<0.05$; p38 MAPK phosphorylation, vehicle vs. LPS: 0,089±0.008 vs. 0.953±0.075, $p<0.05$; LPS vs. LPS/OA-NO2: 0.953±0.075 vs. 0.628±0.071, $p<0.05$). Dihydroethidine staining of atrial sections strongly corroborates reduction of elevated ROS production in AngII treated mice by OA-NO2 in vivo (fluorescence intensity; vehicle vs. AngII: 5.84±2.45 vs. 12.65±1.19; AngII vs. AngII/OA-NO2: 12.65±1.19 vs. 3.54±1.10, $p<0.05$).
Conclusion: The current results reveal that OA-NO2 potently inhibits atrial fibrosis and subsequent atrial fibrillation by interfering with AngII-signaling on multiple levels. Nitrated fatty acids thus emerge as potential therapeutic agents for AF either by increasing endogenous levels by dietary intervention or as synthetic drugs.
Acknowledgement/Funding: Deutsche Forschungsgemeinschaft KL 2516/1-1 to A.K.; HE 6855/1-1 to J.K.H.; BA 1870/7-1, BA 1870/9-1 and BA 1870/10-1 to S.B.; RU 1876/1-1 and RU 1876

P6356 | BENCH
Cardiac electromechanical heterogeneity as a physiological state - an effort to tie up loose ends from electrophysiology, protein analysis, mechanical MRI and computational modelling

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Background: The heart has been suggested not to be a uniform entity but rather a heterogenic electromechanical organ.
Purpose: Electromechanical function and the expression of key proteins important for action potential and mechanical activity were systematically investigated in different regions of the heart. The acquired data were integrated using an in silico model.
Methods: Adult male wildtype rabbits (n=7) were examined by phase contrast magnetic resonance imaging (MRI) to assess cardiac wall movement velocities in regional segments (AHA-17 scheme). Segmental velocities were transformed into a deformation curve using a simplified deformation model. Briefly, intersegmental distances were calculated over time. By regarding intersegmental links as mechanical springs, a linear correlation between regional contraction and the calculated deformation curve was established. Vital cardiomyocytes were isolated from the left ventricular (LV) apex as well as LV, septum and right ventricular base by enzymatic digestion of the Langendorff perfused heart. Action potentials were recorded using patch clamping. Cav1.2, KCNQ1, Kv1.4, Kir2.1, Nav1.5, SERCA, RyR2, Phospholamban (PLB) and NCX expression were quantified by western blotting (WB).
Results: Action potential (APD90) was longer in LV apex than in all three base regions (median 291 vs. 202, 209, 196ms; n=26, 26, 23, 12; $p<0.01$, $p<0.05$, $p<0.05$). MRI revealed an earlier, longer and stronger contraction in LV apex than LV base (full width at half maximum of the contraction curve: 156 vs. 136ms; n=6 rabbits x 4 segments (apex), n=6x6 (base); $p<0.0001$; peak deformation 3.48 vs. 2.44mm; $p<0.0001$). WB showed downregulation of several proteins in LV apex vs. LV base: Cav1.2 (107 vs. 240 stand. densitrometric units; $p<0.05$), KCNQ1 (100 vs. 278; $p=0.07$), Kv1.4 (23 vs. 44; $p<0.05$), NCX (60 vs. 76; $p<0.01$), PLB (91 vs. 134; $p<0.05$). When quantitative differences were used in an in silico model, a contraction and action potential prolongation in LV apex vs. LV base could be reproduced (137 vs. 125ms; 208 vs. 193ms).
Conclusions: We demonstrate the presence of an electromechanical apicobasal gradient in healthy rabbit hearts, and identify regionally heterogeneous expression of five key proteins associated with this gradient. In silico simulation of the quantitative differences reproduced the experimentally observed gradient. Since effective mechanical activity is the sole purpose of the heart, one can reason that dominance of apical activity is important for efficient pumping, as otherwise the flow of apical volume through the constricted basal "pipe" would be hampered.

P6357 | BENCH
The role of pitx2c in generating regional action potential gradients in the murine left atrium

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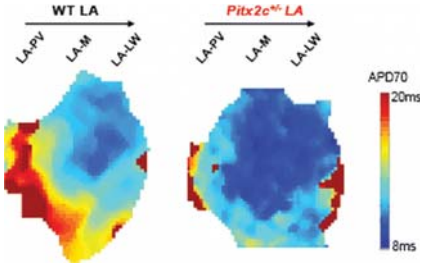
Background: Genetic variants adjacent to the Pitx2 locus associate with atrial fibrillation (AF) in populations and with recurrent AF in patients. Pitx2c mRNA is expressed in the adult left atrium (LA), and is enriched in the posterior LA wall, close to the pulmonary veins (LA-PV).
Purpose: We studied regional variations in the electrophysiological properties of the LA, including the LA-PV, and assessed whether reduced Pitx2c expression impacts on regional LA AP gradients.
Methods: Transmembrane action potentials (TAPs) were recorded from superfused WT and Pitx2c+/– murine LA paced at 100ms. TAPs were recorded from 3 LA regions: 1) the LA towards the junction with the pulmonary vein (LA-PV), 2) the medial dome (LA-M) and 3) the LA lateral wall (LA-LW). High spatial resolution AP duration distribution maps were recorded via a custom murine atrial optical mapping system.
Results: In WT, action potential amplitude (APA) was larger in the LA-PV (84±2mV) than LA-M (78±1mV) and LA-LW (77±2mV, n=11 atria). APs in the LA-PV were also longer than the other 2 regions; APD90 LA-PV 28±2ms, LA-M 21±0.7ms, LA-LW 19±1ms. In Pitx2c+/–, APA was reduced in all regions but this was most evident in the LA-PV, thereby decreasing the regional APA gradient (LA-PV 76±2mV, LA-M 75±3mV and LA-LW 71±2mV, n=12 LA). APD90 was shorter in all regions compared to WT but this was exaggerated in the LA-PV (LA-PV 22±2ms, LA-M 16±1ms and LA-LW 15±1ms). APD distribution maps confirmed regional APD gradients and showed that the LA-PV exhibits the greatest level of electrical heterogeneity.



WT and Pitx2c+/– APD70 distribution maps

Conclusion: We identify regional AP gradients in the murine LA. Pitx2c deficiency causes a reduction in these gradients and evokes electrical modification throughout the LA, with the most prominent remodelling occurring in the LA-PV area.

P6358 | BENCH
Transmural 2D living cardiac tissue slice model for investigating spatial heterogeneity of intracellular calcium handling in the heart

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Background: The spatial heterogeneity of intracellular calcium handling, in particular the transmural difference in the ventricle and its effect on the electrophysiological substrate, is largely unexplored despite the well established importance of the electrophysiological heterogeneity of the heart.
Purpose: To develop a novel living cardiac slice preparation for studying ventricular spatial heterogeneity of intracellular calcium handling.
Methods: Langendorff perfused heart was prepared from adult CD1 mouse (12–14 weeks old) and was then perfused with Ca2+ indicator Rhod2. Ventricular slices were prepared by sectioning the heart transversely from apex to base with a vibratome (Precisionary Inc, USA) in ice-cold oxygenated HEPES buffered solution (pH = 7.4 at 4℃) and slices were then returned to 35℃ gradually in 10 μM blebbistatin-containing bicarbonate buffered solution (pH 7.4). Slices were imaged by an optical mapping system equipped with an EMCCD camera (Evolve 128 Photometrics, USA) and paced at frequencies of 2–4 Hz by field stimulation.
Results: The optimal thickness of slice for CaT recording was found to be around 300 μm. A spatial heterogeneity of CaT (as shown in Fig.1) was observed in different regions of the heart characterised by CaT duration at 80% decay time (CaT80). CaT80 in endocardial regions was longer than in epiocardial regions (left

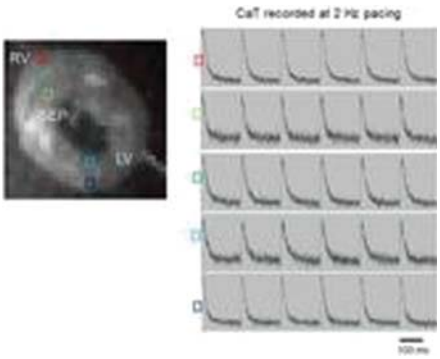

Figure 1

ventricle examined) (94.2±0.49 ms (endo, n=10) vs. 92.0±0.34 ms (epi, n=10), $p<0.01$). CaT80 in left ventricular apex was significant shorter (80.6±0.4 ms, n=10) than the mid (91.4±0.2 ms. n=10) and base (92±0.2 ms, n=10) regions ($p<0.01$, apex vs. mid or base).

Conclusion: The methodology described here thus provides a novel model system for the study of spatial heterogeneity of intracellular calcium handling in the heart.

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P6359 | BENCH
Deletion of PDK1 causes cardiac sodium current reduction in mice

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The AGC protein kinase family regulates multiple cellular functions. 3-phosphoinositide-dependent protein kinase-1 (PDK1) is involved in the pathogenesis of arrhythmia, and its downstream factor, Forkhead box O1 (Foxo1), negatively regulates the expression of the cardiac sodium channel, Nav1.5. Mice are known to die suddenly after PDK1 deletion within 11 weeks, but the underlying electrophysiological bases are unclear. Thus, the aim of this study was to investigate the potential mechanisms between PDK1 signaling pathway and cardiac sodium current. Using patch clamp and western blotting techniques, we investigated the role of the PDK1-Foxo1 pathway in PDK1 knockout mice and cultured cardiomyocytes. We found that PDK1 knockout mice undergo slower heart rate, prolonged QRS and QTc intervals and abnormal conduction within the first few weeks of birth. Furthermore, the peak sodium current is decreased by 33% in cells lacking PDK1. The phosphorylation of Akt (308T) and Foxo1 (24T) and the expression of Nav1.5 in the myocardium of PDK1-knockout mice are decreased, while the nuclear localization of Foxo1 is increased. The role of the PDK1-Foxo1 pathway in regulating Nav1.5 levels and sodium current density was verified using selective PDK1, Akt and Foxo1 inhibitors and isolated neonatal rat cardiomyocytes. In conclusion, through current study we have discovered that the peak Na+ is reduced in PDK1 KO mice and that this may be a cause of sudden death, through mechanisms that have been described for the Brugada Syndrome.

Acknowledgement/Funding: National Key Basic Research Program of China (973 Program), No. 2013CB531105 and National Natural Science Foundation of China, Project No. 81170159

P6360 | BENCH
Cardiac transcription factor MEF2C controls cardiac sodium channel gene SCN5A expression

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Introduction: It has been well documented that abnormal expression of cardiac sodium channel gene SCN5A is linked to arrhythmia, but phenotypic variability of mutations is a problem for genotype-phenotype correlations, suggesting that there are likely several mechanisms that control SCN5A expression. Elucidation of transcriptional regulators of SCN5A expression could provide insights into the fundamental mechanisms of cardiac arrhythmias as well as the identification of possible targets for developing novel antiarrhythmic therapeutics to correct the electrical remodeling associated with heart disease.

Methods: Lentiviral doxycycline Inducible MEF2C mammalian expression plasmid was constructed using standard cloning procedure and packaged in Lenti-X 293 cells. Human fetal cardiomyocyte cells were infected with lenti viral particles using TransDux virus transduction reagent. siRNA was transfected into cardiomyocyte using RNAiMAX reagent. Human SCN5A promoter fragments were cloned into pGL3-Basic vector and transfected into cardiomyocyte using Super-Fect reagent. Total RNA from cultured cells was isolated using RNAeasy mini plus kit. Real-time quantitative RT-PCR (RT-qPCR) was conducted to detect the target gene mRNAs.

Results: Ectopic expression of MEF2C was achieved by adding doxycycline in human fetal cardiomyocytes infected with inducible Mef2C lentiviral particles. SCN5A mRNA expression increased by addition of doxycycline in a dose-dependent manner. Knockdown of MEF2C by siRNA reduced SCN5A mRNA level by 22.3% (P=0.001). Luciferase mRNA driven by human SCN5A 2kb promoter increased 3.81 fold by overexpression of MEF2C compared to control (3.81±0.71 vs 1.00±0.12, P=0.002). The MEF2C binding site was been mapped between 750bp to 1000bp upstream of SCN5A transcription start site, which contains putative MEF2 binding sequences (ATATATATAAA).

Conclusions: Our results demonstrate that MEF2C is one of the major transcription factors regulating SCN5A transcription. The effect that MEF2C enhances SCN5A expression might be through its binding the cis-element (ATATATATAAA) located in the promoter region of SCN5A.

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P6361 | BENCH
Linagliptin, a dpp-4 inhibitor, suppresses the electrical remodeling and myocardial injury in rats

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Background: The dipeptidyl peptidase-4 (DPP-4) inhibitor is an incretin-based anti-diabetic medicine, whose cardioprotective and anti-fibrotic effects have been reported. However, the effect of DPP-4 inhibitor on the electrical and structural remodeling is unknown. We hypothesized that linagliptin, a DPP-4 inhibitor, suppresses cardiac remodeling in isoproterenol (ISP)-induced myocardial injury model.

Methods and results: Sprague-Dawley rats were assigned to 3 groups; 1) Sham, 2) ISP treated, and 3) ISP+linagliptin (5mg/kg/day) treated groups. Myocardial injury was induced by subcutaneous injection of ISP (70mg/kg). In the ISP+linagliptin group, linagliptin was orally administered for 14 days starting 1 week preceding ISP injection. Left ventricular ejection fraction was not significantly different among the groups in echocardiogram (p=0.141). In the electrophysiological study performed 1 week after ISP injection, ventricular effective refractory period (VERP) and monophasic action potential duration (MAPD) were markedly prolonged in the ISP group in comparison with the control (MAPD20: 14±6 vs. 12±4 ms, MAPD90: 58±8 vs. 44±8 ms, VERP: 74±22 vs. 38±10 ms, $p<0.05$, respectively). In contrast in the ISP+linagliptin group, such prolongation was suppressed and the parameters were significantly shorter than the ISP group (MAPD20: 6±1 ms, MAPD90: 34±6 ms, ERP: 52±14 ms, $p<0.05$, respectively). In the histology, ISP treatment induced myocardial injury, cardio-myocyte necrosis and reparative fibrosis especially in the endocardial area in the ISP group. However, the injured area was reduced by 43% in the ISP+linagliptin group (p=0.005).

Conclusion: Linagliptin suppressed electrical remodeling characterized by VERP and MAPD prolongations and reduced myocardial injury area.

MITRAL VALVE DISEASE

P6362 | BEDSIDE
Impact of new echocardiographic scoring system for predicting procedural outcome of percutaneous trasmitral valvuloplasty in patients with rheumatic mitral stenosis

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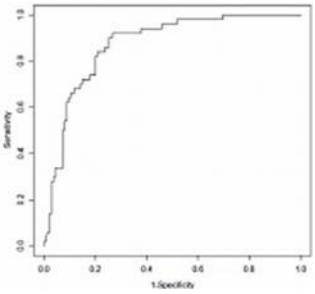
Background: Current echocardiographic scoring system for percutaneous mitral valvuloplasty (PMV) have limitations for predicting acute procedural outcome. The purpose of this study was to evaluate the impact of new echocardiographic scoring system in the prediction of procedural outcome of PMV in patients with rheumatic mitral stenosis.

Methods: 185 patients (mean age: 46±11 years, M:F= 37:143) who underwent PMV at our institution were enrolled. Procedural success was defined as increase of $\geq$50% of mitral valve area (MVA) or a final area of $\geq$1.5 cm^2, with no more than 1 grade-increase in mitral regurgitation (MR) severity assessed 24 hours after PMV. Logistic regression analysis was performed to predict the procedural success.

Results: PMV was successful in 135 patients (72.9%) and suboptimal in 50 patients (27%). Patients who had successful PMV were younger, lower the total echocardiographic score (Wilkins), lower pre-MR grade, lower values of subvalvular thickening and calcification among echocardiographic determinants. In logistic regression analysis, independent predictors of outcome for suboptimal results were pre-MR grade (OR 2.783, 95% confidence interval [CI], 1.042–7.434) and subvalvular thickening (OR: 7.998, 95% CI, 3.804–16.814). New scoring system for predicting the suboptimal results consisted of age, pre-MR grade and

	Multivariate analysis	
	OR(95%CI)	*P* value
Age	1.031(0.991-1.072)	0.1285
Echoscore	1.922(1.387-2.664)	0.0001
M	0.683(0.298-1.565)	0.3716
T	0.583(0.346-2.792)	0.9716
S	7.668(3.804-16.814)	<.001
C	1.256(0.629-2.508)	0.5144
Pre-MR (≥ 3+)	2.783(1.042-7.434)	0.0419

*Pre-MR grade was the number of grade 1 and 2 MR



4 echocardiographic determinants of Wilkins score with different impact factors according to logistic regression analysis and had an area under the receiver operating characteristic curve (AUC) of 0.784 (95% confidence interval [CI], 0.810–0.920) (Fig).

Conclusions: A new scoring system is an independent predictor of successful PMV and would help in identifying the best candidates for PMV.

P6363 | BEDSIDE
Noninvasive estimation of left ventricular filling pressure in patients with mitral regurgitation: a speckle tracking echocardiography study

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Background: It is exceedingly important to estimate pulmonary capillary wedge pressure (PCWP) in patients with mitral regurgitation (MR) to decipher the cause of dyspnea and determine the therapeutic strategy. However, there was a conflict in the use of E/e' to estimate left ventricular (LV) filling pressure in MR and echocardiographic parameters to predict PCWP in MR are not yet elucidated. We reported that PCWP was able to be accurately estimated by the novel KT index which is defined as log10 (left atrial (LA) active emptying function/LA minimum volume). Therefore, we examined the reliability of the KT index as a predictor of PCWP in both primary and secondary MR.

Methods: Echocardiographic parameters including LA dimensions, LA volume, LA phasic function, E/e', LA peak strain and estimated PCWP by KT index (ePCWP) were measured in moderate to severe MR (n=58, age: 67±8) just before catheterization and in normal subjects (n=26, age 67±11) during sinus rhythm. MR was divided into primary MR (n=27) and secondary MR (n=31). LA strain, phasic volume and emptying function (EF) were measured by speckle tracking echocardiography during sinus rhythm. The ePCWP was calculated as 10.8 –12.4 x KT index.

Results: LV mass was increased in MR compared to control (131±37 vs. 100±12g/cm^2, respectively) and LV ejection fraction reduced in MR (55±13 vs. 63±6%, respectively). LA phasic volume was increased in MR compared to control and LA phasic EF decreased in MR. E/e' and ePCWP were increased in MR compared to control (E/e': 18.2±8.2 vs. 10.5±3.3 and ePCWP: 16.6±4.9 vs. 7.7±2.7mmHg, respectively). There was correlation between PCWP and E/e', LA strain, LA minimum volume or active EF (r=0.31, r=–0.50, r=0.55 and r=–0.61, respectively, $p<0.05$). The best correlation was found between PCWP and ePCWP in MR including both primary and secondary MR (r=0.67, r=0.70 and r=0.67, respectively, $p<0.01$). Bland-Altman analysis confirmed the agreement between PCWP and ePCWP (mean bias 1.6±5.2mmHg). Multiple regression analysis revealed that ePCWP was an independent predictor of PCWP in MR. The ePCWP demonstrated good diagnostic accuracy (area under the curve of 0.86) and sensitivity (81%), specificity (71%), positive predictive value (83%) and negative predictive value (68%) to predict elevated PCWP>15mmHg using a cut off of 16mmHg in MR.

Conclusion: The ePCWP estimated by KT index was the most useful and reliable echocardiographic parameter to predict PCWP in patients with MR including both primary and secondary MR and may have an incremental value in a clinical setting to decide therapeutic strategy in MR.

P6364 | BEDSIDE
Long-term follow-up after percutaneous mitral valve repair using the mitraclip system

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Introduction and aims: Percutaneous mitral valve repair (PMVR) using the MitraClip system has become a valid alternative to surgery for patients with severe mitral regurgitation (MR), anatomical suitability, and high surgical risk. We report long-term outcomes after PMVR.

Methods: Between march 2009 and February 2014, 148 consecutive patients (mean age 75±10 years, 39.2% female) with moderate–severe (3+) or severe (4+) MR underwent PMVR at the University Heart Center Zurich. Clinical and echocardiographic data were prospectively collected. Clinical endpoints on follow-up included all-cause death, mitral valve surgery/reoperation, hospitalization for congestive heart failure, heart transplantation and New York Heart Association (NYHA) functional class.

Results: MR etiology was degenerative in 37% and functional in 57%, and 6% mixed. At baseline, 82% of patients were in NYHA class III/IV. Left ventricular ejection fraction was 45±18% and STS mortality risk score was 8.3±16%. Median follow-up was 1.9 days (interquartile range, 0.8 to 2.7). Acute procedural success (APS, defined as successful clip implantation with residual MR grade ≤2+) was achieved in 93% of patients. On echocardiographic follow-up, MR severity was 1+ and 2+ in 71% of patients. At 12 months, 63% of patients were in NYHA class I and II. Fifty-two (35%) patients died during follow-up (average annual mortality (19%/year). Overall, the composite endpoint (death; Reoperation; Heart failure hospitalization; heart transplantation) occurred in 84/148 (57%) patients. The following variables were independent predictors for higher event rates: age (p=0.026), LVEF (p=0.027), MR at discharge (p=0.005) and NYHA at baseline (p=0.001) and age (p=0.026). LVEDV (p=0.75) and functional etiology of MR (p=0.529) had no influence on outcome.

Conclusions: PMVR with the MitraClip system allows durable reduction of MR severity and improvement in patients' symptoms and functional status. Event rates, however, remain remarkably high despite successful treatment, reflecting advanced age and high comorbidity status of our population.

P6365 | BEDSIDE
Predictors of exercise capacity in asymptomatic patients with significant primary mitral regurgitation undergoing stress echocardiography

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Background: Primary mitral regurgitation (PMR) is progressive & results in reduction in exercise capacity.

Purpose: We sought to assess predictors of exercise capacity in asymptomatic significant PMR patients undergoing exercise stress echocardiography (ESE).

Methods: We studied 884 asymptomatic patients (58±14 years, 67% men) with ≥ III+ PMR that underwent treadmill ESE between 1/2000 and 12/2011. Clinical & ESE parameters were recorded.

Results: Mean body mass index (BMI), left ventricular (LV) ejection fraction, indexed left ventricular end-systolic dimension, mitral effective regurgitant orifice & rest right ventricular systolic pressure (RVSP) were 26±4 kg/m^2, 58±5%, 1.6±0.4 mm/m^2, 0.48±0.3 cm^2 & 31±12 mm Hg. There were 11% & 47% patients with coronary artery disease & hypertension; 31% were on betablockers. 5% ESE were positive for ischemia; while 89% patients had a decrease in LV cavity with stress & 3% had increase in LV cavity. Mean metabolic equivalents (METS) & peak-stress RVSP were 9.6±3 and 46±17 mm Hg. Regression analysis showing the association between METS & various predictors is shown in Table.

Predictors of exercise capacity (METS)

	Multivariable regression analysis	
	Beta	p- value
Age	–0.45	<0.001
Male gender	0.31	<0.001
Body Mass Index	–0.26	<0.001
Hypertension	0.02	0.7
Coronary artery disease	0.03	0.4
Beta blockers	–0.09	0.005
Resting LV ejection fraction	0.07	0.04
Indexed LV end systolic dimension	0.02	0.7
Mitral valve effective regurgitant orifice area	0.008	0.8
Resting RVSP	–0.162	<0.001
LV cavity response to stress	–0.09	0.02
Peak stress RVSP	0.03	0.4
Ischemic response on ESE	–0.09	0.006

Conclusion: In asymptomatic patients with ≥III+ PMR undergoing ESE, increased age, female gender, higher RVSP & ischemic response were inversely associated with METs.

P6366 | BEDSIDE
Left ventricular function analysis with 2D and 3D speckle tracking in secondary mitral regurgitation treated with transcatheter mitral valve repair with the MitraClip system

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Background: In current practice MitraClip (MC) treatment is predominantly used in patients suffering from secondary mitral regurgitation (sMR) due to relevant left ventricular (LV) pathologies. The effect of the procedure on LV volumes and function has been reported controversial. 3D speckle tracking (ST) analysis of LV geometry and function, theoretically, overcomes the limitations of a 2D geometric approach.

We, therefore, sought to determine the impact of transcatheter mitral valve repair (TMVR) with the MC system on global and regional LV function using two- and three-dimensional (2/3D) ST and conventional echocardiographic parameters.
Methods and results: 109 consecutive patients with sMR (age 77.3±7.3 years) at high surgical risk (EuroScore 16.9±15.2%) underwent successful MC implantations and completed 6 months follow-up (FU) including standardized 2 and 3D transthoracic echocardiography (TTE) prior to MC and after FU. Conventional echocardiographic parameters as well as 2D strain values were reduced at baseline but did not improve significantly 6 months after MitraClip implantation (2D global longitudinal strain (GLS): –8.5±4.1%, –9.0±4.5%, p=0.47; LV ejection fraction (LVEF): 33.1±15.8%, 43.1±14.9%, p=0.97). Furthermore, 2D volumes were unchanged during FU (2D endsystolic volume (ESV): 65.9±8.9ml, 67.4±9.2ml, p=0.12; enddiastolic volumes (EDV): 181.1±73.8ml, 159.8±52.5, p=0.07).
In contrast to 2D echocardiography, 3D ST analysis showed significant amelioration of LV volumes and ejection fraction (EF): 3D ESV (181.8±70.6ml, 131.4±54.9ml, p=0.008), 3D enddiastolic volume (EDV) (231.6±76.6ml, 177.4±58.0ml, p=0.013) and 3D EF (33.1±9.2%, 37.6±11.3%, p=0.015) improved significantly. Interestingly, 3D GLS showed the most significant amelioration 6 months after MC (–7.8±3.3%, –11.2±5.9%, p=0.006).
Conclusion: In contrast to 2D echocardiography, 3D ST analysis showed beneficial effects of interventional mitral valve repair with the MC system on LV volumes und function in patients with sMR. These data suggest, that 3D imaging might be superior to 2D echocardiography in patients with complex cardiac pathologies.

P6367 | BEDSIDE
Predictors of long term outcome post surgical treatment of ischemic mitral regurgitation - results from Polish multicenter registry - PIMAR

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Objective: The long term outcome data on surgical treatment (CABG, SVR, MVR, MVplasty, ablation) of ischemic secondary mitral regurgitation (SMR) are limited. The aim of this study was to determine the long term survival and the factors associated with this survival in patients with SMR and ischemic heart failure (CAD-HF) treated surgically.
Methods: 430 consecutive patients with CAD-HF (mean LVEF 38±8, EDV 135±56 ml, ESV 77±46 ml, previous MI in 72% of pts) and mild, moderate or severe SMR entered prospectively a multicenter (14 centers) registry. Surgical interventions comprised of: CABG in 103 pts, CABG+MVplasty in 227 pts, CABG+MVR in 20 pts, CABG+MVplasty+SVR in 18 pts, combined procedures in 62pts). Eight-years survival data were obtained in all subjects. Clinical outcome data with an overall mortality as a primary endpoint, was collected in 319 patients.
Results: 30-days mortality was 6,1% in the analyzed group. Long term survival (5-years, 8-years overall mortality was 74% and 66% respectively (figure1). There was significant difference in survival regarding baseline LV systolic function (EF<35% vs >35%, p=0.02), however no difference has been shown according to the baseline LV dimensions (EDD>65 mm vs EDD<65mm, p=0.2). Multivariable analysis showed preoperative IABP (HR 2,62; 1,44–4,78; p=0,001), NYHA III, IV (HR 2,06; 1,20–3,54; p=0,008), diabetes (HR 1,84; 1,04–3,24; p=0,03), age (HR-1,03; 1,00–1,07; p=0,02), diabetes (HR-1,66; 0,96–2,88) as significant survival predictors.

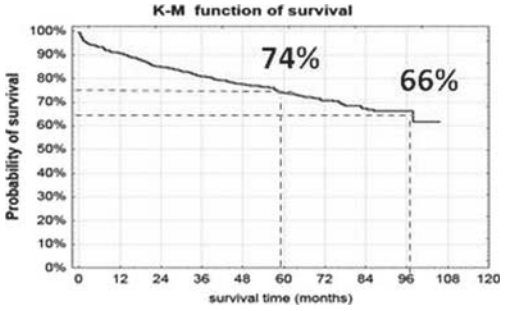

figure 1

Conclusions: 1. When treated surgically, CAD-HF patients with LV systolic dysfunction and concomittant SMR reached satisfactory outcome (5 years survival 74%, 8-years survival 66%).
2. Independent predictors of long term survival are: preoperative use of IABP, advanced heart failure class, diabetes, and the patient's age
Acknowledgement/Funding: POLKARD 2006-2009

P6368 | BENCH
Mitral valve prolapse: crosstalk between human valve endothelial and interstitial cells

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Introduction: Mitral valve prolapse (MVP) is a common disorder, afflicting >176 million people worldwide, characterized by extracellular matrix remodeling and changes in matrix metalloproteinases (MMP) expression. On the surface, it is present the endothelial monolayer (VECs) that continuously interact with the interstitial cells (VICs) embedded within the valve layers. Osteoprotegerin (OPG) is involved in a myriad of physiological and pathological processes. In the vascular environment, OPG is constitutively secreted by endothelial cells and their progenitors, as well as smooth muscle cells. OPG can be a decoy receptor for RANK and TRAIL or interact with syndecan (SDC), an heparan sulfate proteoglycan.
Purpose: Since OPG pathological effects are not well understood, we investigated the OPG role in the crosstalk between human endothelial and interstitial cells isolated from patients undergoing mitral valve repair due to mitral valve prolapse.
Methods: Human VECs and VICs were isolated from freshly resected posterior leaflets obtained from patients who underwent mitral valve repair. β-glycerolphosphate and ascorbic acid (βGAA) treatments were used to promote VECs activation. Immunofluorescence, Western blot and quantitative PCR were performed to evaluate VEC and VIC phenotype. Moreover, enzyme-linked immunosorbent quantitative assay (ELISA) was employed to assess cell OPG secretion. Human Phospho-Mitogen-Activated Protein Kinase (MAPK) array kit was used to investigate the signaling pathways. Finally, MTT analyses were utilized to evaluate βGAA and OPG cytotoxicity.
Results: In vitro βGAA treatment induced overespression of vimentin, SMA, MMP9, BMP4, collagen-1 and collagen-3 through ERK activation. Interestingly, this activation caused the upregulation of OPG mRNA levels and its cellular secretion. Thereafter we investigated SDC1 expression on both cell populations and we found that the expression of SDC1 was increased by 14.4±2.1 fold in VICs compared to VECs ($p<0.01$). Moreover, we identify a reactive oxygen species (ROS) overproduction in VECs and an increased proliferation in VICs directly induced by OPG.
Conclusion: VECs treated with βGAA mimic the cellular changes seen in myxomatous mitral valve. Additionally, activated VECs increase the secretion of OPG that in turns enhance VEC oxidative stress status and VIC proliferation. Further analyses are required to understand better the initial stage of mitral valve prolapse; nevertheless our data show, for the first time, the OPG involvement in mitral valve endothelial and interstitial cell crosstalk.

P6369 | BEDSIDE
Is left ventricular systolic dysfunction a prognostic determinant of patients undergoing mitraclip?

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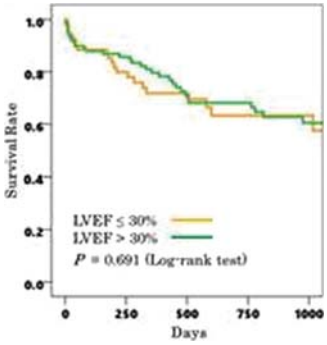
Background: Left ventricular systolic dysfunction (LVSD) is associated with poor outcomes after mitral regurgitation (MR) surgery. Therefore, LVSD is the most striking characteristic of the patients who were denied surgery. Percutaneous mitral valve repair using mitraclip is a novel treatment option for MR patients with a high surgical risk. However, the impact of LVSD patients undergoing mitraclip remains unclear.
Purpose: In the present study, we aimed to clarify the impact of LVSD on the long-term outcomes of MR patients who underwent mitraclip procedure.
Methods: The present study enrolled 194 consecutive patients treated with mitraclip. The median follow-up period was 484±432 days. Severe LVSD was defined as LVEF ≤30%.
Results: In a total of 194 patients after mitraclip implantation, 75 patients (39%) had severe LVSD. Patients with severe LVSD were primarily male and younger. Logistic euroSCOREs were comparable between the two groups. Functional MR was more common in patients with severe LVSD, while New York Heart Associ-



Survival rate after MitraClip

ation (NYHA) classification was similar between the two groups. N-terminal pro-B-type natriuretic peptide (NT-proBNP) was significantly higher in patients with severe LVSD. In addition to similar improvements in MR severity, NYHA classification, and NT-proBNP levels, the survival rate was not different between the two groups. Among patients with severe LVSD, the long-term survival rate was significantly lower in patients aged ≥75 years, those with NT-proBNP >5,000 pg/mL, and those with atrial fibrillation (AF).
Conclusion: Severe LVSD was not associated with a worse outcome after mitraclip implantation. However, we need to carefully observe LVSD patients who are elderly, have a high NT-proBNP level, and AF, as these may be considered high-risk subjects.
Acknowledgement/Funding: Japan Society for the Promotion of Science

P6370 | BEDSIDE
Long-term outcome and change of right ventricular function in patients with LVEF <25% after MitraClip-implantation: comparison between left ventricular dysfunction alone and biventricular dysfunction

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Background: MitraClip (MC) is a new technology for treatment of mitral regurgitation (MR) in patients with high surgical risk. Little is known about long-term outcome and change of right ventricular (RV) function in patients with left ventricular ejection fraction (LVEF) <25% with or without RV dysfunction.
Methods: This study included consecutive 64 patients with moderate to severe or severe mitral regurgitation and left ventricular ejection fraction (LVEF) <25%, who successfully underwent MC-implantation between March 2009 and April 2014 in our heart center. Patients were separated into two groups; tricuspid annulus plane systolic excursion (TAPSE) ≥15mm AND right ventricular end-diastolic diameter measured at base in 4-chamber view (RVEDD) ≤42mm (only LV dysfunction group, 14 patients) and TAPSE <15mm OR RVEDD >42mm (biventricular dysfunction group, 50 patients).
Results: At baseline biventricular dysfunction group had higher NT-proBNP level (8063 pg/ml, IQR 3258 - 13805 pg/ml vs 4725 pg/ml, IQR 2106 - 7547 pg/ml, p=0.003) and higher ratio of implantable device therapy (82% vs 43%, p=0.007). Kaplan-Meier analysis revealed the biventricular dysfunction group to have significantly worse 2-year-outcome (83% vs 41%, P=0.020, combined endpoint; all-cause mortality, surgery, procedure failure, LVAD, re-do procedure). On the other hand, in biventricular dysfunction group RVEDD (48±8 mm vs. 42±6 mm, P<0.001) and TAPSE (14±4 mm vs. 18±4 mm, P<0.001) significantly improved one year after MC implantation, whereas stayed unchanged within normal range in only LV dysfunction group. Systolic pulmonary artery pressure (PAPs) significantly improved in both biventricular dysfunction group (55±10 mmHg vs. 48±9 mmHg, P=0.006) and only LV dysfunction group (55±16 mmHg vs. 48±10 mmHg, P=0.036). Even in patients who died between 6 months and 1 year, RVEDD, TAPSE and PAPs improved at 6 months follow-up compared to baseline (statistically not significant).
Conclusions: Patients with biventricular dysfunction had significantly worse outcome compared to patients with LV dysfunction alone. Nevertheless, the RV function improved significantly in biventricular dysfunction group and stayed unchanged in only LV dysfunction group. We should not hesitate to perform MC-implantation even for the patients with not only LV dysfunction alone but also biventricular dysfunction, if we have no other therapeutic option. MC-implantation does no harm to right ventricle.

P6371 | BEDSIDE
Infective endocarditis: absence of microbiological diagnosis is an independent risk factor for inhospital mortality

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Background: Infective endocarditis (IE) is associated with high inhospital mortality. New microbiological diagnostic techniques have significantly reduced the proportion of patients without etiological diagnosis, mainly in operated patients in whom valve tissue is available. Our hypothesis was that absence of microbiological diagnosis could be associated with a poorer prognosis.
Methods: Prospective cohort of 2000 consecutive patients with IE. Data were collected in 26 Spanish hospitals. Duke criteria were used.
Results: From the 2000 patients, 296 (14.8%) had negative blood cultures but etiological diagnosis was achieved with other methods (polymerase chain reaction (PCR), serology and other cultures) in 121 (6.1%). Accordingly there were 175 patients (8.8%) with no microbiological diagnosis (group A) and 1825 with diagnosis (group B). Group A patients had a higher inhospital mortality: 57 (32.6%) vs. 490 (26.9%), p=0.13. The univariate difference did not reach statistical significance, but patients in Group A had a lower risk profile than those in Group B, with less comorbidity (Charlson index 1.9±2.0 vs. 2.3±2.0, p=0.03) and lower surgical risk (EuroSCORE 23.1±21.1 vs. 29.6±25.2). However they presented heart failure more frequently (51% vs. 39%, p=0.004). Multivariate analysis showed that the absence of microbiological diagnosis was an independent predictor of inhospital mortality (table).

Independent predictors of mortality

	OR (95% CI)	P
Charlson Index	1.1 (1.1–1.2)	<0.001
Sex	0.7 (0.5–0.9)	0.021
Abscess	0.6 (0.5–0.8)	0.001
New Heart Failure	2.4 (1.8–3.2)	<0.001
EuroSCORE	1.03 (1.02–1.03)	<0.001
Surgery	0.6 (0.5–0.8)	0.002
Absence of microbiological diagnosis	1.8 (1.1–2.9)	0.016
Phrosthetic IE	1.4 (1.02–1.9)	0.035

Conclusion: Approximately 9% of patients with IE had no microbiological diagnosis. Absence of microbiological diagnosis was an independent predictor of in-hospital mortality.

AORTIC VALVE DISEASE

P6372 | BEDSIDE
Incidence, predictors and impact on prognosis of estimated systolic pulmonary artery pressure and its improvement after transcatheter aortic valve implantation; a multicenter registry

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Background: Elevated estimated systolic Pulmonary Artery Pressure (esPAP) represents a common finding in patients (pts) with aortic stenosis. Prognostic impact of esPAP after trancatheter aortic valve implantation (TAVI) remains to be determined.
Purpose: All-cause mortality of one year follow-up (FU).
Methods: All consecutive pts undergoing TAVI between January 2007 and December 2012 in 5 European Centre were retrospectively included and divided into two groups according to esPAP: <40 mmHg and >40 mmHg.
Results: From a total of 674 pts, 319 (47%) had esPAP>40 mmHg (median 50 [IQ, 41–60] mmHg vs 35 [IQ 30–38] in the other group). Pts with esPAP>40 mmHg had a lower ejection fraction (51.4±13.8 vs 55.6±5.9%; p<0.001), larger left ventricle volumes, and higher rate of diastolic disfunction, significant mitral regurgitation and right ventricle disfunction (p<0.05, Figure). esPAP>40 mmHg was associated with higher mortality both at 30-days (4.5% vs 8.5% p=0.03) and at a median FU of 477 days (17% vs 26% p=0.03). In this group, there was a reduction of esPAP from median values of 50 (41–60) to 40 (32–50) mmHg after TAVI. Improvement of esPAP from above to below 40 mmHg was reported in 113 (27%) pts. esPAP reduction was more frequent in the absence of moderate or severe mitral regurgitation and of right ventricle dysfunction (OR 2:1.3–4 and OR 4.20:2–16, respectively). At multivariate analysis, esPAP independently predicted all cause of death at mean FU (HR 2.3, 1.2–4.9, for esPAP>40 mmHg; HR 1.2, 1.05–1.5 for esPAP as a continuous variable).

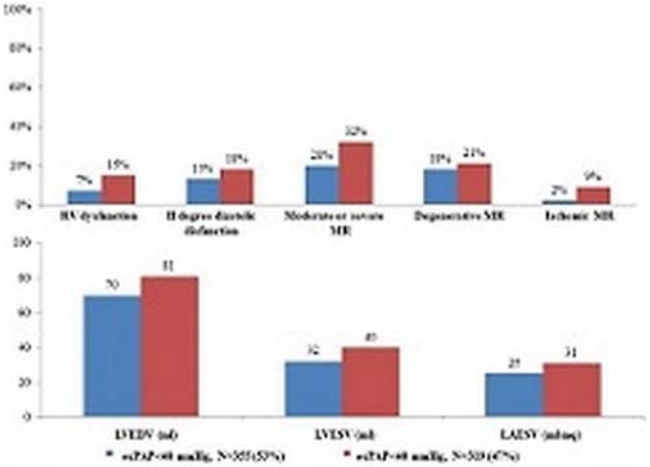

Figure. Pre-procedural echocardiographic data. esPAP: estimated systolic pulmonary artery pressure; LAESV: left atrium end systolic volume; LVEDV: left ventricular end diastolic volume; LVESV: left ventricular end systolic volume; MR: mitral regurgitation; RV: right ventricle.

Conclusion: Elevated esPAP represents a common finding in pts undergoing TAVI, leading to increased all-cause mortality at one-year FU. Therefore esPAP could be a useful tool to stratify the risk of TAVI pts.

P6373 | BENCH

Pulmonary hypertension and transcatheter aortic valve implantation in patients with severe aortic stenosis: prevalence, prognosis, and evolution

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Background: Pulmonary hypertension (PH) is considered a poor prognosis factor in patients with severe aortic stenosis (AS) undergoing surgical aortic valve replacement or transcathteter aortic valve implantation (TAVI). However, few studies have characterized PH by invasive right heart catheterization and the impact of pulmonary vascular resistance (PVR) has never been investigated.
Methods: One hundred and seventy one consecutive patients with symptomatic severe AS prospectively underwent invasive right heart catheterization before TAVI. PH was defined as a mean pulmonary arterial pressure (PAP) >25 mm Hg. The primary end-point combined the incidence of death and re-hospitalization for heart failure at one year.
Results: PH was present in 99 (57.9%) patients. The primary end-point occurred in 40 (23.4%) patients including 24 (14.0%) deaths and 16 (9.4%) readmissions for heart failure. Systolic PAP, transpulmonary pressure gradient, and PVR were significantly higher in patients experiencing an event (46.9±12.1 vs. 40.8±12.0 mm Hg, p=0.03; 12.6±4.5 vs. 10.1±3.7 mm Hg, p=0.01; 2.7±1.0 vs. 2.0±0.8 WU, p=0.002, respectively). Systolic PAP>40 mm Hg and PVR>2.05 WU were selected by receiver operating curve for predicting cardiac events. By multivariate Cox regression analysis, independent predictors of cardiac events were: body mass index (OR 1.08, 95% CI 1.02–1.14, p=0.005), mitral regurgitation (OR 1.64, 95% CI 1.16–2.33, p=0.02), and a spectrum of systolic PAP>40 mm Hg with PVR>2.05 WU (OR 2.6, 95% CI 1.39–4.89, p=0.003).
Conclusions: PH is frequent in patients presenting with severe aortic stenosis before TAVI, and is an independent predictive factor of death and re-hospitalization after TAVI when associated with elevated PVR. Further studies are warranted to confirm our results in a larger population.

P6374 | BEDSIDE

Modified surgical cutdown as access route for transfemoral transcatheter valve implantation (TAVI): Early and long-term results in 100 consecutive patients

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Background: Femoral access for transcatheter aortic valve implantation (TAVI) is usually achieved percutaneously using dedicated closure devices. However, complications such as femoral artery stenosis, occlusion or bleeding are possible. We report the success and complication rates of a modified, minimally invasive surgical cutdown technique to access the femoral artery for TAVI.
Methods: In 100 consecutive patients (n=45 male, mean age 81±7 years, mean log. EuroScore 20±14) TAVI (Edwards Sapien XT, n=69; Edwards Sapien 3, n=29; St. Jude Portico, n=2) was performed using a modified surgical cutdown technique of the femoral artery. The fascia over the anterior vessel wall was exposed via a miniaturized skin incision of 2 cm. Two opposing U-stitches (Prolene 4.0) were placed in the vessel wall. The femoral artery was punctured within the loop of the U-stitches. Major vascular complications (vessel occlusion, access site bleeding requiring surgical revision or transfusion) and minor vascular complications were determined at hospital discharge, 30 days post procedure, and 6 months. At 6 month follow-up an additional Doppler ultrasound evaluation of the femoral artery was performed.
Results: The mean diameter of the target vessel was 7.5±1.2 mm. Femoral sheath size was 14 F in 23 cases, 16 F in 20 cases, 18F in 29 cases and 20F in 28 cases. The primary success rate via the intended access route (successful implantation of the prosthesis without need for cross-over) was 100%. Mean duration of the procedure was 63±37 minutes. One patient died during the procedure (annular rupture), 5 patients during the initial 30 postoperative days (2 due to sepsis, 1 due to heart failure, 1 as a consequence of distant bleeding [abdominal wall], 1 due to tension pneumothorax). No further deaths occurred thereafter. Major complications of the arterial access occurred in 2 patients (2%), with access site bleeding treated surgically in one patient and by implantation of a stent graft in another. A total of 18 patients needed transfusions, mainly due to already preoperatively documented anemia. Minor access site complications were detected in 6% of the patients (seroma n=2; lymphatic fistula n=1, delayed wound healing n=3) but did not require specific intervention. After 6 months, none of the access site arteries showed occlusion or stenosis in Doppler ultrasound.
Conclusion: A minimally invasive, modified surgical cutdown technique provides rapid and safe arterial access for TAVI and has an early and long-term safety profile that compares favorably to percutaneous closure devices.
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P6375 | BEDSIDE

Impact of chronic lung disease on outcome in patients undergoing transcatheter aortic valve replacement

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Background: Chronic lung disease (CLD) is deemed to negatively affect the outcome of patients undergoing Transcatheter Aortic Valve Replacement (TAVR) although data from the literature are inconclusive and little is known concerning the different impact of the diverse grades of CLD in a real world setting.
Methods and results: Among 980 consecutive patients included in CoreValve Italian Registry, 284 (29%) presented with a diagnosis of CLD in 8 high volume centers.
One-year overall mortality was similar between patients without CLD and those with mild CLD (HR 1.4 (0.94–2.4), p=0.06). Patients presenting with moderate CLD (defined as FEV1 50% to 59% of predicted, and/or on chronic steroid therapy aimed at lung disease) or severe CLD (defined as FEV1 <50% predicted, and/or room air partial pressure of O2 <60 mm Hg or room air partial pressure of CO2 >50 mm Hg) had a significantly higher mortality compared to patients without CLD [HR 1.7 (1.2–3.41),p=0.01, and HR 2.1 (1.9–2.9),p=0.002, respectively]. After adjustment, severe CLD, with or without severe pulmonary hypertension was an independent predictor of mortality.
At 1-year, an improvement in the NYHA class as well as the rate of hospitalization for heart failure were consistent across all the subgroups according to CLD severity.
Conclusions: Moderate to severe CLD is associated with higher 1 year all cause mortality after TAVR. However, the observed benefit in terms of NYHA class and the effect on re-hospitalization should always be considered when judging the clinical equipoise of the TAVR with respect to the standard medical therapy.

P6376 | BEDSIDE

Abnormal gas diffusion in aortic stenosis: the link between left and right heart

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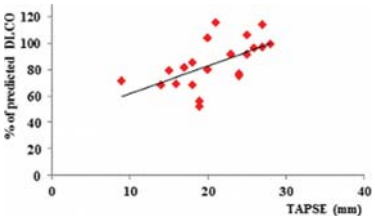
Background: An altered diffusion capacity for carbon monoxide (DLCO) has relevant clinical and prognostic implication in several cardiac and pulmonary diseases. The correlation between DLCO and exercise response in aortic stenosis (AS) has never been investigated. The aim of our study was to analyze the correlation between the DLCO and cardiac and functional parameters in moderate-to-severe aortic stenosis (AS).
Methods: 21 moderate-to-severe AS (age 73±9 y, male 81%, LVEF 61±16%, mean aortic gradient 29±16 mmHg) underwent a symptom-limited cardiopulmonary exercise testing (incremental ramp protocol) combined with exercise-echo. The DLCO was measured using single breath technique.
Results: A good correlation was found between % of predicted DLCO (age, sex and height), degree of rest and peak mitral regurgitation (MR) (Sperman's rho –0.60 and –0.57, p=0.004 and 0.009) and left atrial function (LA peak atrial longitudinal strain, rho –0.54 p=0.02). Irrespective of AS severity, % of predicted DLCO correlated with echo parameters of peak and rest right ventricular (RV) function, such as TASPE (rho rest 0.66 p=0.001, peak 0.50 p=0.035), RV fractional area change (rho rest 0.63 p=0.002, peak 0.63 p=0.002) and RV free wall global longitudinal strain (rho –0.61 p=0.016). A lower % of predicted DLCO was associated with reduced exercise capacity (lower peak oxygen consumption and workload; rho 0.56 and 0.55, p=0.001 and 0.009).



Conclusions: Our results suggest a link between increased LV pressure, consequent MR, lung capillary injury and RV dysfunction and in AS, expressed by an impaired DLCO. An altered gas diffusion capacity may explain the pathophysiological basis of exercise intolerance.

P6377 | BEDSIDE
Comparison of stroke rate between the balloon expandable Edwards Sapien valve and the self-expandable Corevalve for transcatheter aortic valve replacement

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Background: Transcatheter aortic valve implantation (TAVI) has been used increasingly to treat inoperable or high surgical risk patients with severe symptomatic aortic stenosis. Although mortality rates are declining, stroke continues to be an issue.
Aim of the study: The aim of our study was to compare thirty day rate between the balloon expandable Edward Sapien Valve (ESV) and the self-expandable Medtronic CorValve system (MCV).
Methods: 573 patients with severe aortic stenosis and high surgical risk underwent consecutively TAVI in local anesthesia between april 2010 and October 2014. Major and minor stroke was defined according to the VARC II criteria. 30 day stroke rate and 30 day mortality were evaluated.
Results: 361 pts (age 80.6±0.34 years) with severe aortic stenosis (pmean 43.1±0.77 mmHg, AVA 0.68±0.01 cm^2) and high surgical risk (log Euroscore 22.0±0.67%) underwent successfully TAVI with the MCV and 212 pts (age 81.7±0.41 years, log Euroscore 18.6±0.82%, pmean 44.2±1.12 mmHg, AVA 0.68±0.02 cm^2) underwent TAVI with the ESV. In the total cohort occurred 12 strokes (2.1%) during the first 30 days. There was no significant difference between the 30 day stroke rate between the two valve types (MCV vs ESV= 1.7% vs 2.8%; p=0.264), but there were more major strokes in the ESV group compared to the MCV group (MCV vs ESV: 0.8% vs 2.4%;p=0.273). There was a trend to more pre-dilation in the 30 day stroke group, but this did not reach statisticially significance. 83.3% in the stroke group vs 69.1% in the group without stroke, p=0.235.
30-day mortality was significantly higher in patients with stroke compared to those without stroke (25% versus 3.9%; p=0.013)
30 day mortality in the MCV group (5.5%) compared to the ESV group (2.4%) was higher, but this did not reach statistical significance (p=0.052).
Conclusion: TAVI was associated with a 30-day stroke rate of 2.1%. There was no significant difference in 30-day stroke rate between the two valve types, although there was a trend of more major strokes in the ESV group. 30 day mortality was significantly higher in patients with stroke.

P6378 | BEDSIDE
In-hospital results of transfemoral TAVI: Analysis of the French national database

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Aims: France is the birthplace of TAVI with the first in man procedures carried out in Rouen in 2002 and since the commercial availability in 2007 TAVI has received continuously positive appraisals by the HAS (Haute Autorité de santé). As a leading country in the adoption of the technology we sought to evaluate the available French data on TAVI to determine how the outcomes have evolved and improved over time.
Methods and results: Data on procedures and outcomes was derived from the French national hospital database (PMSI - Programme de Médicalisation des Systèmes d'Information). Overall the number of TAVI procedures annually has grown from 2449 in 2011 to 3748 in 2013 and during that time the proportion of transfemoral TAVI has increased from 81% to 88%. For both TF and TA TAVI the reported in-hospital mortality has decreased significantly; from 7.01% to 5.53% for TF and 12.47% to 10.73% TA. Since August 2012 balloon and self-expandable devices have been reported separately and in 2013 there were 1213 balloon expandable and 944 self-expandable TF TAVI performed with respective in-hospital mortality of 4.7% and 7.0% (p=0.023). Self-expandable TF TAVI was also associated with and increased total length of stay (12.06 vs. 9.95 days; $p<0.001$) and incidence of permanent pacemaker (22.2% vs. 8.5%; $p<0.001$) compared to balloon expandable. Average patient age was not statistically different between the groups (82.43 vs. 83.04) but Charlson scores were higher for self-expandable TAVI patients (3.38 vs. 2.92; $p<0.001$). When accounting all reimbursement for procedures and devices balloon expandable TAVI was €839 less expensive than self expandable TAVI (€28,861 vs. €29,520; $p<0.001$).
Conclusions: The number of TAVI procedures carried out in France has increased by more than 50% between 2011 and 2013 and is increasingly performed via a transfemoral approach. There has been an observed improvement in mortality for all TAVI since 2011 but in 2013 (the latest data available) there was a significant improvement associated with balloon versus self-expandable TAVI which was accompanied by a reduced average length of stay and total cost to the healthcare system.

P6379 | BEDSIDE
Comparison of Transcatheter Aortic Valve Replacement Approach on Early and Late Mortality Among Severe Aortic Stenosis Patients

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Background: Studies have shown conflicting results regarding impact of approach on outcome of severe aortic stenosis (AS) patients undergoing transcatheter aortic valve replacement (TAVR).
Purpose: Our aim was to compare early and late mortality of transfemoral (TF) and transapical (TA) TAVR patients, and assess predictors for mortality.
Methods: Severe AS patients undergoing TAVR at our institution between May 2007 and December 2014 were included. Baseline demographic, clinical and imaging parameters were compared, and landmark analysis models were generated to assess outcomes.
Results: Among 645 severe AS patients undergoing TAVR, TF approach was used in 514 and TA in 131. Baseline characteristics were similar with the exception of lower body mass index (BMI) and higher STS score and rate of peripheral vascular disease among TA patients.
Procedural complications were more common in the TA group; major bleeding (15% vs. 6%, $p<0.001$) and acute kidney injury >1 (8% vs. 1.4%, $p<0.001$). Landmark analysis demonstrated higher adjusted cumulative mortality rates at 30 days among TA patients, compared with TF (log-rank<0.001, HR=4.54, p=0.003), with similar mortality rates at 1-year (log-rank=0.64). STS score was an independent predictor of early mortality (HR=1.15, $p<0.001$) together with pulmonary artery pressure above 60mmHg (HR=5.1, p=0.001) only in the TA group, while BMI<20kg/m^2 was a significant predictor of early mortality in the TF group (HR=2.75, p=0.03).

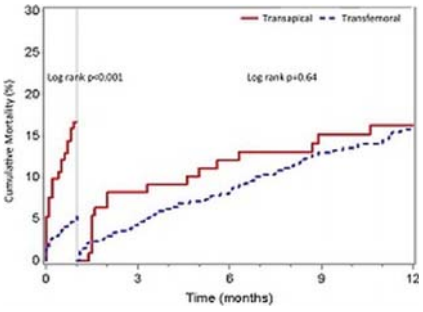

Figure 1. Landmark at 1 month

Conclusions: These data suggest that the TA approach, although it demonstrates similar mortality beyond one month, should be sparingly used given its high mortality rate within 30 days. The introduction of the new lower profile TF delivery systems for TAVR may mitigate the need for this more invasive TA approach.

P6380 | BENCH
Unsupervised network analysis of genome wide association study data identifies the epidermal growth factor receptor as the most connected hub in aortic valve calcification

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Background: Aortic valve calcification (AVC) can lead to aortic stenosis and is independently associated with adverse cardiovascular events. Relatively little is known of the pathogenesis of this condition. A recent genome wide association study (GWAS) with 6492 subjects identified a single nucleotide polymorphism (SNP) in the LPA locus as being associated with AVC at genome-wide significance. However the stringent requirements for genome-wide significance means that analysing the data on a per-SNP basis misses many important findings. Network analysis allows additional information to be extracted from the data.
Purpose: To identify biologically relevant associations with AVC through network analysis.
Methods: We used the AVC GWAS data publicly available from the Framingham Heart Study. We mapped the SNPs to associated genes using the Versatile Gene-based Association Study (VEGAS) implementation in Fast Association Tests (FAST). We then used the Protein-interaction-network-based pathway analysis (PINBPA) app in Cytoscape to map this data to the IntAct protein interaction network (PIN). An unweighted greedy search algorithm through gene-based p-values was used to identify non-overlapping subnetworks of interacting genes.
Results: After correcting for multiple testing, no single gene retained statistical significance. Greedy search of the PIN identified two subnetworks, one with 515 gene products and a smaller one with 25 gene products. As in many biological networks, the larger subnetwork had a power law distribution of in- and out-degree of the nodes, indicating the existence of high-degree hubs. Using a standard measure of centrality (Betweenness Centrality), Epidermal growth factor receptor (EGFR) was the most connected hub in the network.
Conclusions: This study highlights the power of network analysis of GWAS data. Previous studies in mice have shown that inhibition of EGFR leads to AVC. Our unsupervised network analysis identified EGFR as the most connected genomic hub associated with AVC in humans. The current use of EGFR inhibitors as can-

cer therapies should be monitored for signals of harm related to aortic valve disease.

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P6381 | BEDSIDE
Prognostic impact of electrocardiographic abnormalities in patients with severe aortic stenosis

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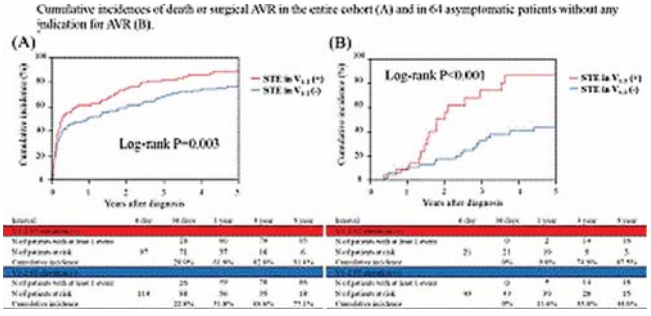
Background: ST-segment elevation (STE) in leads V1–2 is often observed in patients with severe aortic stenosis (AS), but its prognostic significance remains unknown.
Purpose: This study aimed to investigate the clinical significance of STE in leads V1–2 in patients with severe AS.
Methods: We retrospectively evaluated baseline electrocardiograms (ECG) and 5-year clinical outcomes in 211 consecutive patients with severe AS. Severe AS was defined as peak aortic jet velocity (Aortic Vmax) >4.0 m/s, or mean aortic pressure gradient >40 mmHg, or aortic valve area (AVA) <1.0 cm^2. The primary outcome measure was the composite of death or surgical aortic valve replacement (AVR).
Results: STE in leads V1–2 (J-point deviation ≥0.15 mV) was present in 97 patients (46%). Patients with STE in leads V1–2 had greater Aortic Vmax and smaller AVA than patients without. With median follow-up period of 4.9 years, the cumulative 5-year incidence of death or AVR was significantly higher in patients with STE in leads V1–2 than in patients without (91.4% versus 77.1%; P=0.003) (Figure A). After adjusting for echocardiographic index of AS severity and other confounders, STE in leads V1–2 was independently associated with higher risk for death or AVR (hazard ratio, 1.58; 95% confidence interval, 1.11–2.27; P=0.01), but other ECG findings such as left ventricular hypertrophy and strain pattern were not. In 64 asymptomatic patients without any indication for AVR at initial diagnosis of severe AS, the cumulative incidence of death or AVR was significantly higher in patients with STE in leads V1–2 than in patients without (87.5% versus 44.6%; P<0.001) (Figure B).



Conclusions: STE in leads V1–2 independently predicted poorer prognosis and more frequent need for AVR in patients with severe AS.

AORTIC VALVE INTERVENTIONS

P6382 | BEDSIDE
Differences in the diagnostic ability and analysis of 18F-FDG-PET/CT-Angiography in infective endocarditis between prosthetic valves and intracardiac devices

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Background: Diagnosis of infective endocarditis (IE) in prosthetic valves and intracardiac devices represents a clinical challenge because modified Duke criteria (DC) and echocardiography (ECHO) have limitations. 18F-FDG-PET/CT-Angiography (PET/CTA) has shown in recent studies an added value in this clinical scenario. However, the diagnostic ability and the analysis of the PET/CTA may vary between valves and devices.
Purpose: To analyze the differences in the diagnostic yield and image analysis between valves and devices, in a cohort of patients included between Nov-2012 and Jan-2015 in a mayor prospective study conducted in our hospital, which counts with a multidisciplinary IE unit.
Methods: We analyzed 92 patients with suspected IE. The initial diagnosis with the DC, the PET-CTA results, and the DC adding PET-CTA information were compared with a final "expert team" diagnostic consensus. We made a visual interpretation of the images and we also evaluated the differences between the semi-quantification analysis.
Results: There were 64 prosthetic valves and tubes and 28 cardiac devices. PET/CTA was performed and compared with ECHO findings with an intermediate correlation (kappa: 0.26 for valves and 0.36 for devices). In our series, the sensitivity, specificity and positive and negative predictive values were similar between prosthetic valves (51%/92%/91%/55% for the DC, 87%/92%/95%/82% for the PET/CTA and 90%/88%/92%/85% for DC + PET/CTA) and devices (50%/100%/100%/60% for the DC, 87%/100%/100%/86% for the PET/CTA and 94%/100%/100%/92% for DC + PET/CTA).
The semi-quantitative analysis showed that in prosthetic valves, a cut-off value of SUVmax ≥3.7 and a SUVmax-background ratio ≥2.8 discriminated positive cases with a sensitivity of 92% and a specificity of 72% and 71% respectively. Cut-off values of 6.89 and 3.45, respectively, achieved a specificity of 100% to confirm infection. This semi-quantification was not useful for devices, with cut-off values under the background of the patients (SUVmax 1.21 and ratio of 1.06) and a very low specificity (50%).
Conclusions: Although the image interpretation of devices is more complex, based only on the visual analyses because the semi-quantification was not useful for discrimination, the added diagnostic value of PET-CTA to the DC was significant in both valves and devices.

P6383 | BEDSIDE
A positive 18F-FDG PET/CT on admission predicts new embolic events but not mortality in patients with infective endocarditis

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Introduction: IE is associated with high mortality and severe complications. Among them, embolic events (EE) are the most severe and their prediction remains difficult.18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) has recently proved useful for the diagnosis of IE and has been proposed as a new major diagnostic criterion for prosthetic valve IE. However, the prognostic significance of a positive 18F-FDG PET/CT and its value in predicting embolic events are unknown.
Purpose: To assess the value of a positive 18F-FDG PET/CT in predicting EE and death in patients with IE.
Methods: From January 2011 to April 2014, 222 patients with definite IE by modified Duke criteria (168 (76%) men, mean age = 64 years) underwent 18F-FDG PET/CT. Among them, 98 (44%) presented with a positive 18F-FDG PET/CT (valvular or prosthetic valve uptake).
18F-FDG PET/CT valvular or prosthetic valve uptake was classified as absent, minimal, moderate, or severe, by semi-quantitative analysis.
All patients underwent repeat clinical, biological and echocardiographic follow-up at 1, 3, 6 months and 1 year. Primary end points were the occurrence of a new embolic event under therapy and the 1-month and 1-year mortality.
Results: Among the 98 patients with positive 18F-FDG PET/CT, valvular uptake was classified as severe in 52 (53%).
New embolic events were more frequent in patients with severely positive than negative 18F-FDG PET/CT (33% vs 8%, respectively, p<0.05), while mortality was similar in both groups.
Conclusion: An intense 18F-FDG PET/CT valvular or prosthetic valve uptake predicts embolic events but not mortality in IE. The additional predictive value of a positive 18F-FDG PET/CT uptake as compared with traditional markers of embolic risk and death needs further investigations.

P6384 | BEDSIDE
The role of aortic valve velocity and stroke volume index in predicting the outcomes of severe aortic stenosis with preserved ejection fraction in elderly

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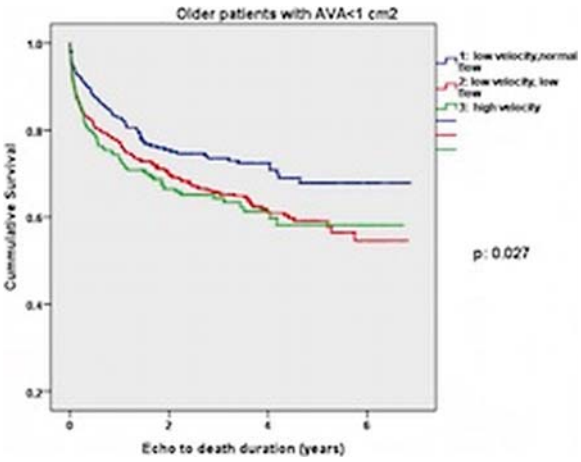
Background: The role of aortic valve velocity and transaortic flow on predicting the outcomes of severe Aortic stenosis with preserved ejection fraction is not well defined.
Purpose: To examined the incidence of aortic valve replacement and mortality in those ≥75 years of age with different transaortic velocities and flow.
Methods: We identified consecutive patients ≥75 years old presenting to our echo lab with an aortic valve area (AVA) <1.0cm^2 and EF≥50% regardless of symptoms. We stratify patients depending on maximal transaortic velocity (Vmax ≥4m/s vs. <4m/s) and stroke volume index (SVI <35 ml/m^2 vs ≥35ml/m^2). All patients were retrospectively followed for the occurrence of aortic valve replacement (AVR) or death.
Results: A total of 917 patients were included in analysis, of which 318 died and 90 had AVR. Mean follow up was 2.45±1.9 years. The mean age of this population was 85.4±5.6 years. In patients with a low peak velocity, those with a SVI <35 ml/m^2 were found to have significantly higher mortality [169/454 (37%)]

compared to those with a SVI ≥35 ml/m^2 [75/264 (28%); p=0.016]. Furthermore, the low velocity, low flow patients had similar mortality to patients with high velocities [74/199 (37.1%)]. AVR occurred much less frequently in the low velocity, low flow patients [21/454 (4.6%)], compared to the high velocity patients [49/199 (24.6%); p<0.001]. This discrepancy between mortality and surgical intervention is depicted in the graphs below.



Conclusion: In older patients with normal EF and severe aortic stenosis, those with low velocity, low flow as reflected by a SVI <35 ml/m^2, represent a high risk group. They are much less likely to have an AVR than elderly patients with high velocity aortic stenosis despite having the same prognosis.

P6385 | BENCH
Atorvastatin diminishes gene expression of tumor necrosis factor-alpha in left atrial appendage but not interferon-gamma and interleukin-4 in rheumatic heart disease

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Background: Up to now Rheumatic Heart Disease (RHD) still remains a significant cause of morbidity and mortality in developing countries. Inflammatory response, represented by Tumor Necrosis Factor-alpha (TNF-α), Interferon-gamma (IFN-γ) and Interleukin-4 (IL-4) have been having a role in RHD. Atorvastatin is possibly considered to have an anti inflammatory effect.
Purpose: To affirm that atorvastatin diminishes gene expression of TNF-α and IFN-γ and increases gene expression of IL-4 as the inflammatory response in RHD.
Methods: This was an experimental study, recruited 53 RHD patients. They were planned to undergo cardiac valves surgery and given atorvastatin vs placebo 6 weeks prior to surgery. Gene expression method was applied to probe Messenger Ribo Nucleic Acid (mRNA) TNF-α, mRNA IFN-γ and mRNA IL-4 expression from excised valves and Left Atrial Appendage (LAA) as the study outcomes.
Results: There were no significant differences between the study groups, in term of gender proportion, ages, echocardiographic and clinical indicators and treatments administered. Atorvastatin group presented lower gene expression of TNF-α in LAA with p=0.005 (95% CI 0.05–0.58) after being adjusted with gender and ejection fraction. But it was not proved in cardiac valves. There were no differences of IL-4 and IFN-γ gene expression in cardiac valves and LAA.
Conclusions: Atorvastatin diminishes inflammation in LAA patients of RHD by suppressing TNF-α gene expression. There were correlations between suppressed gene expression of TNF-α and IFN-γ with increased gene expression of IL-4 level.
Acknowledgement/Funding: Grants from National Cardiovascular Centre, Harapan Kita Hospital, Jakarta Indonesia

P6386 | BEDSIDE
Thrombolysis in elderly patients with prosthetic heart valve thrombosis

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Background: There is no previous study that has evaluated thrombolytic therapy (TT) in elderly patients with prosthetic valve thrombosis (PVT).
Purpose: To investigate the safety and efficacy of low dose and/or slow infusion TT strategies in PVT patients aged ≥65 years.
Methods: Between 1993 and 2014, 25 (17 female) patients aged ≥65 years (median 70, range 65–82 years) underwent TT for PVT as a first-line treatment strategy. The TT regimens used were slow (24-hour) infusion of 1.5 million Units of Streptokinase in 2 patients, slow (6-hour) infusion of 25 mg recombinant tissue plasminojen activator (t-PA) in 11 patients, and ultra-slow (25-hour) infusion of 25 mg t-PA in 12 patients. The primary outcomes were treatment success and in-hospital adverse cardiovascular event (mortality, hemorrhage, embolism, rethrombosis, reoperation due to TT failure) rates.
Results: The overall success rate was 88%. Adverse events occured in 5 (20%) patients. These included 3 (12%) patients with major (one death, one need for reoperation due to rethrombosis after initially successful TT, and one need for reoperation due to failed TT) and 2 (8%) patients with minor (one transient ischemic attack and one venous puncture site hematoma) events. Higher thrombus burden (thrombus area ≥1.1 cm^2 by reciever operating characteristic curve analysis, sensitivity 100%, specificity 84%, area under curve 0.92, 95% confidence interval 0.81–0.99, p=0.004) and high New York Heart Association Class (III/IV vs I/II status, 44.4% vs 6.3%, respectively, p=0.04) were the predictors of adverse events. Age (p=0.1), elapsed time since valve surgery (p=0.44), coronary artery disease (p=0.27), hypertension (p=1), diabetes (p=0.6), stroke or transient ischemic attack (p=1), aspirin use (p=0.62), heart rhythm (p=1), leading symptom (p=0.06), thrombosed valve position (p=0.66), valve brand (p=0.75), presence of valve obstruction (p=0.13), baseline valve area (p=0.28), mean gradient (p=0.23), left ventricular ejection fraction (p=0.54), TT protocol (p=1), increasing number of TT sessions (p=0.08) and higher TT dose (p=0.19), did not seem to predict adverse events.
Conclusion: Prolonged infusions of low doses of TT (mostly t-PA) agents provide successful and safe thrombolysis in elderly patients with PVT. However, patients with excessive thrombus burden and poor functional capacity are still under higher risk of adverse events.

P6387 | BEDSIDE
Preprocedural hemodynamics improve the discriminatory value of the aortic regurgitation index in patients undergoing transcatheter aortic valve implantation

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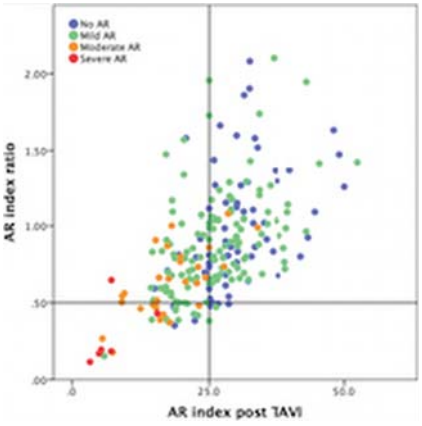
Background: Hemodynamic parameters such as the aortic regurgitation (AR) index are helpful for the assessment of paravalvular leakage (PVL) in patients undergoing transcatheter aortic valve implantation (TAVI). However, the AR index is confounded by several periprocedural characteristics such as heart rate or preprocedural hemodynamics.
Purpose: The aim of this study was to increase the prognostic value of the AR index.
Methods: The AR index was calculated before and after TAVI in 635 patients. In a next step, the AR index ratio was calculated as quotient of the post- and preprocedural ARI. The severity of PVL was assessed in all patients by angiography and echocardiography.
Results: In a development cohort of 268 patients from two independent TAVI centers, we found that an AR index ratio cut-off value of 0.50 further increased the discriminatory value of the post-rpocedural AR index and is the optimum predictor of 1-year mortality. Patients with a post-procedural AR index <25 had a significantly lower 1-year mortality after TAVI if the AR index ratio was >0.50 (35.4% vs. 63.2%, P=0.002)
In a second step, the AR index ratio was validated prospectively in 367 patients (age 81.4±6.3 years, logistic EuroSCORE 22.7±15.7). The AR index ratio helped to reduce the rate of more than mild PVL (15.0% vs. 7.4%, P=0.001) and further improved outcomes. Patients with a post-procedural AR index <25 still had a significantly lower 1-year mortality after TAVI if the AR index ratio was >0.50 (24.2% vs. 43.7%, P=0.04).



Association between ARI ratio and PVL

Conclusions: The negative prognostic value of an AR Index below 25 is significantly attenuated in patients with an AR index ratio >0.50. A low pre-procedural AR index before the procedure indicates resilience against the clinical impact of a low post-procedural AR index.

P6388 | BEDSIDE
Influence of nutrinional status on survival after transfemoral transcatheter aortic valve implantation

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Background: Suboptimal nutritional status is a known predictor for worse outcome after cardiac surgery. The nutritional status of fragile elderly patients is frequently suboptimal, and might be of paramount importance for outcome/survival after transcatheter aortic valve implantation (TAVI)
Purpose: We sought to provide insight in the influence of periprocedural nutritional status on survival after TAVI in the fragile elderly TAVI population.
Methods: All patients (n=117) who underwent a transfemoral TAVI and a documented pre-procedural serum albumin between 19–11–2010 and 20–1-2014 were included. Preprocedural albumin levels were assessed in all patients to reflect current nutritional status. Patients were subdivided in high and low albumin level based on a even distribution of the groups; the cutoff between low (group 1) and high (group 2) was defined as 41 g/L. We performed albumine-based comparison and Kaplan Meijer analysis to evaluate differences in short and longer term survival after TAVI.
Results: Mean age was 79,6±8,8 years. Survival in the group of patients with high albumin levels was significantly higher as compared to the low-albumine group (p=0.029) with Log-Rank (Chi-Square: 4.779). (Fig. 1: Kaplan-Meier)

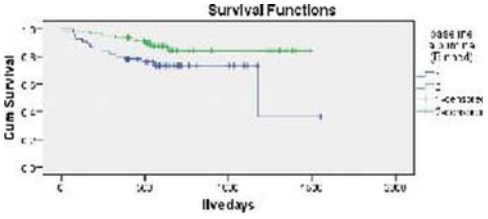

Figure 1. Kaplan-Meier survival

Conclusion: Short- and longterm survival after transfemoral TAVI is significantly lower in patients with suboptimal nutritional status, indicated by lower prepocedural albumin levels.

P6389 | BEDSIDE
Impact of paravalvular leak on mitral regurgitation change after transcatheter aortic valve replacement for aortic stenosis and its prognostic implications

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Background: The prevalence of at least moderate mitral regurgitation (MR) in patients with severe aortic stenosis reaches 20%. MR severity can improve after Transcatheter Aortic Valve Replacement (TAVR).
Purpose: To assess the echocardiographic determinants of MR change after TAVR and its impact on prognosis.
Methods: We evaluated 244 patients (48% Males, age 79.88±7.33) with severe aortic stenosis referred to our institution for TAVR from 2008.
Echocardiography was performed before implantation and within 6 months after. MR was graded according to the MR index, on a scale of 1 to 4+.
MR change was defined as an improvement of at least 1 grade. Patients with organic mitral valve disease (rheumatic, congenital and prolapse) were excluded. The presence of Paravalvular Aortic Regurgitation (PAR) was evaluated and graded according to the Valve Academic Research Consortium-2 criteria.
The combined endpoint was defined as death, myocardial infarction, stroke, heart failure hospitalization.
Results: 130 (53.3%) patients have a baseline MR degree >2 +.
Baseline MR degree, Ejection Fraction (EF), transaortic mean gradient (MG) were: 1.61±0.965, 52.15%±14.26, 54.86 mmHg±17.40, respectively.
At 6 month echocardiographic follow-up, in the overall population MR degree was 1.41±0.88, EF 54,14±10.33%. Significant (>2+) PAR was detected in 72 patients (32%). The prevalence of MR change was significant lower in patients with PAR >2+ than in patients without (22% vs 37.8%, p 0.01). Subgroups analysis showed that both patients with MR improvement and patients with no MR improvement have significant changes in pre and post EF (51.57±13.70 vs 54.80±10.30, p 0.0002; 53.84±14.17 vs 55.41±10.34, p 0.034).
At multivariate analysis, PAR >2+ was the only significant predictor of lack of MR improvement after TAVR (OR 3.2 (CI 1.2–8.4); p 0.001), whereas pre and post TAVR End Diastolic Volume, pre and post TAVR EF, pre and post TVAR MG did not enter in the model.
The prevalence of combined end-point was similar in patients with no MR improvement compared with MR improvement group (56.8% vs 43.2%, respectively; χ^2=2.18, p 0.14).
Conclusions: These data demonstrated that a significant percentage of patients present a MR reduction after TVAR; PAR >2+ is a predictor of lack of MR improvement after TVAR. Moreover, there is a trend in the excess of events in patients without improvement of MR after TAVR even though does not reach the statistical significance.

P6390 | BEDSIDE
Three-year outcomes of transcatheter aortic valve implantation in patients with STS score less than or equal to 7%: a comparative analysis between different risk strata from the ADVANCE study

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Introduction: Transcatheter aortic valve implantation (TAVI) has been increasingly offered to intermediate surgical risk patients with severe aortic stenosis (AS), although the effectiveness of TAVI in this particular population remains poorly investigated.
Purpose: The purpose of this sub-analysis was to assess 3-year clinical outcomes among patients with Society of Thoracic Surgeons (STS) score less than or equal to 7% compared to the outcomes of patients with STS score greater than 7% who underwent TAVI.
Methods: Data were drawn from the ADVANCE study, which enrolled patients with severe AS treated with implantation of a self-expanding transcatheter valve. Events were independently adjudicated based on VARC-1 definitions. A total of 996 patients were implanted, and for the purpose of this analysis those with an available STS score were dichotomized into two groups: STS≤7% (n=797, mean STS score 4.3±1.5%) and STS>7% (n=298, mean STS score 11.3±5.0%).
Results: At 3-years, the STS≤7% group reported lower rates of all-cause mortality (28.6% vs. 45.9%, p<0.01) and cardiovascular mortality (19.0% vs. 30.2%, p<0.01) as compared with the STS>7% group. No differences were observed with regards to cerebrovascular accidents, vascular complications, bleeding and myocardial infarction during 3-year follow-up. Mortality at 3-years was higher in STS≤7% patients with moderate/severe paravalvular regurgitation (PVR) measured at discharge than in those with mild or less PVR (39.9% vs. 22.9%; HR, 1.98; 95% CI, 1.37–2.86; p=<0.001). In contrast, the severity of PVR at discharge did not affect mortality in STS>7% patients (42.9% versus 44.6%, moderate/severe vs. none/mild; HR, 1.04; 95% CI, 0.62–1.75; p=0.861; p for interaction=0.047).
Conclusions: In the ADVANCE study, TAVI was commonly offered to patients with STS score ≤7%. Compared with patients having STS >7%, they showed reduced all-cause and cardiovascular mortality rates at 3-year follow-up. Complication rates were low and stable in both groups, demonstrating the safety of this procedure across patients at varying levels of surgical risk.
Acknowledgement/Funding: Medtronic, Inc., funded the ADVANCE study

P6391 | BEDSIDE
Temporal trends in procedural death after transcatheter aortic valve implantation

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Background: Although transcatheter aortic valve implantation (TAVI) has been used in thousands of high-risk patients with severe aortic stenosis (AS) during the last decade, the causes and trends of procedural death have not been carefully analyzed.
Objectives: To assess the causes of procedural death after TAVI and their temporal trends since the beginning of the TAVI era.
Methods: From October 2006 to April 2014, 601 high-risk AS consecutive patients underwent TAVI in our center, using either the Edwards SAPIEN/SAPIEN XT (ES/XT) or Medtronic CoreValve (MCV) prostheses. The transfemoral approach was used as the first choice and the transapical or subclavian approaches as alternatives. Causes of procedural death (VARC-2: <30 days or during index hospitalization) were classified as: heart failure, cardiac rupture, vascular complications and intensive care complications. Patients were divided in 3 tertiles according to the date of the procedure: 1 to 200, 201 to 200 and 401 to 601.
Results: ES/XT and MCV devices were used in 390 (65%) and 211 (35%) patients, respectively, and transfemoral, transapical and subclavian approaches in 74%, 19% and 6%, respectively. Overall, procedural mortality occurred in 45 patients (7.5%): age, 83±7 years; men, 51%; logistic EuroSCORE, 26±16%. The main cause of procedural death was heart failure (42%), followed by cardiac rup-

ture (27%), intensive care complications (20%) and vascular complications (11%). There was no difference in mortality according to the type of device used (8.5% vs 5.7%, p=0.28), but death occurred more frequently after transapical than transfemoral TAVI (16.8%, vs 4.7%, p<0.001). Mortality decreased over time: 11.9% in the first, 6% in the second and 4.5% in the third tertile (p<0.001). This decrease was mainly due to a reduction in cardiac failure-related death (6.5% in the first tertile, vs 1.5% in the third, p=0.021). There were no vascular complications-related death in the third tertile (0 vs 1% in the first tertile, p=0.47). However, no decrease was observed in the rate of death related to cardiac rupture (2.5% in the first tertile vs 1.5% in the third, p=0.72), as well as those due to intensive care complications (2% in the first tertile vs 1.5% in the third, p=0.99).
Conclusions: Procedural mortality after TAVI substantially decreased over time. The improvement was driven by a decrease in deaths due to post-TAVI heart failure and disappearance of those due to vascular complications. However, efforts should continue to prevent the occurrence of cardiac rupture and to improve the management of patients requiring post-TAVI intensive care.

CARDIOMYOPATHIES

P6392 | BEDSIDE
Cardiac extracellular volume quantified by cardiac magnetic resonance reflects degree of cardiac and neurological involvement in familial transthyretin amyloidosis

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Introduction: Amyloidotic cardiomyopathy (AC) in familial amyloid polyneuropathy (TTR-FAP) determines prognosis and treatment options. CMR T1 mapping techniques are useful to assess myocardial extracellular volume (ECV) and might be useful to evaluate cardiac disease and neurological involvement in TTR-FAP.
Purpose: We hypothesized that ECV could detect AC in TTR-FAP patients and that cardiac ECV could reflect the degree of neurological impairment caused by TTR amyloid extracardiac deposits.
Methods: 31 genetically proven TTR-FAP patients (19 males; mean age 49±12 years; 26 V30M) underwent a T1 mapping CMR study and a neurological evaluation with NIS-LL score (exploration of the sensitivity, motor and reflexes in the lower limbs), Norfolk-QOL questionnaire (symptoms and quality of life) and Karnofosky index (general health status). Confirmed AC was defined by a positive 99mTc-DPD scintigraphy (uptake grade≥2) or by left ventricular hypertrophy with typical amyloid gadolinium kinetics/enhancement at CMR for those subjects without DPD-scan (10 patients).
Results: 5 patients had AC (4 determined by scintigraphy and 1 by CMR). Mean ECV was increased in patients with AC (0.490±0.131 vs. 0.289±0.035; p=0.026). ECV correlated with age (R=0.467; p=0.008), NTproBNP (R=0.846; P=0.000), maximum wall thickness (R=0.621; p=0.000), left ventricular mass index (R=0.685; p=0.000), left ventricular ejection fraction (R=–0.378; p=0.036), NIS-LL (RS=0.604; p=0.001), Norfolk-QOL (RS=0.529; p=0.003) and Karnofsky (RS=–0.517; P=0.004). A cut-off value of ECV=0.357 calculated by ROC curve, was diagnostic of AC with 100% sensibility and specificity (P<0.001). ECV and NTproBNP values were the only cardiac parameters that significantly correlated with neurologic scores.
Conclusions: ECV quantification by CMR allows identification of AC in TTR-FAP and correlates with the degree of neurological impairment. This non-invasive technique could be a useful tool for early diagnosis and to track cardiac and extracardiac amyloid disease.
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P6393 | BEDSIDE
Late gadolinium enhancement on cardiac magnetic resonance for the prediction of non-sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy

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Introduction: Myocardial fibrosis has been implicated in the pathogenesis of ventricular arrhythmias in hypertrophic cardiomyopathy (HCM) patients. Late gadolinium enhancement on cardiac magnetic resonance (LGE-CMR) imaging represents a non-invasive way to assess myocardial fibrosis.
Purpose: Evaluate the capacity of the extension of LGE for the prediction of non-sustained ventricular tachycardia (NSVT).
Methods: We conducted a multicentric retrospective study involving all patients with HCM referred to LGE-CMR in 10 centers. The left ventricle extension of LGE was evaluated according to the American Heart Association 17-segment model. The timeliest proximate 24-hour ambulatory ECG monitoring (holter) to the CMR was used for the investigation of NSVT (≥3 consecutive ventricular beats, ≥120 bpm).
Results: A total of 216 patients were enrolled, with a mean age of 59.3±14.4 years and 60% males. The New York Heart Association class was 1.9±0.5, 34.4% patients had resting left ventricle outflow tract obstruction (48±38mmHg) and the left ventricle ejection fraction (LVEF) by transtoracic echocardiography was 65.5±8.9%. LGE was detected in 66.7%, with a median LGE extent of 12%.
Of all patients, 80.6% (n=174) had at least one holter on the follow-up and NSVT was detected in 42 patients (24.1%). Patients with NSTV had greater septal diameter (19.5 vs 17.3mm, p=0.007) and LGE extension (27.3 vs 12.5%, p<0.001).
The multivariate analysis (logistic regression), which included age, gender, LVEF, septal diameter and LGE extension, revealed LGE extension as an independent predictor of NSVT (adjusted odds ratio 1.03, 95% confidence interval: 1.01–1.06, p=0.004). The area under the receiver-operating characteristics curve was 0.72 and a cut-off of 18% had a sensitivity and specificity of 62% and 69%, respectively, for the prediction of NSVT.
Conclusion: The extension of LGE was an independent predictor of NSVT in this population. LGE-CMR may represent an additional marker to enhance sudden cardiac death risk stratification in HCM patients, particularly in those with intermediate risk.

P6394 | BEDSIDE
Myocarditis: cardiac magnetic resonance findings in follow-up

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Background: Myocarditis is characterized by acute or chronic inflammation of myocardial tissue. Cardiac magnetic resonance (CMR) has become an established non-invasive diagnosis tool for acute myocarditis. However, it is less established as a prognostic tool. Our aim was to assess the CMR findings after the first episode of acute myocarditis.
Methods: We studied 33 patients with acute myocarditis whose CMR was performed during clinically acute myocarditis and 9±3 months later. A CMR protocol was applied and the prognostic value was assessed using a combination of death, heart transplant, hospitalization for cardiac cause and recurrent myocarditis as main outcome.
Results: The mean of age was 32±9 years and 24 (72%) patients were men. Troponin I elevation was found in all patients (mean peak level of 22±23 ng/ml). Mean BNP, C-reactive protein values at admission were 241±443 pg/ml and 96±93 mg/dl, respectively. An abnormal ECG was present in 21 (64%) patients. CMR was displayed at 4±2 days after admission and mean left ventricular (LV) ejection fraction was 55±10% (12 (36%) patients presented ejection fraction <55%). Late gadolinium enhancement (LGE) was presented in all patients, mostly subepicardial and involving 4 or more myocardial segments (mean 5±3). Myocardial oedema was found in 25 (76%). After 9±3 months all cases had persistence of LGE, although but less expressive, involving less myocardial segments (mean 3±2). No one had myocardial edema. All patients, except one, presented LV ejection fraction recovery but systolic dysfunction persisted in 8% cases. The LV end-systolic and end-diastolic volumes and LV mass decreased. At 38-month clinical follow-up, only two suffered a second episode of acute myocarditis. No deaths, heart transplant or re-hospitalizations for other cardiac cause occurred.
Conclusion: In our population we found a high persistence of LGE in CMR follow-up studies after an acute myocarditis episode. Although the low rate of cardiovascular events, persistence of LGE had no impact on prognosis. Many doubts still exist and clinical implications of imaging findings must be clarified, to help us better identify patients with a poor prognosis due to a complicated course myocarditis.

P6395 | BEDSIDE
Differential cytokine profiling in chagasic patients treated with amiodarone and stratified with Lown and NYHA classifications

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Background: Chagas is a tropical disease caused by the protozoan Trypanosoma cruzi. It occurs mainly in Latin America but has now spread worldwide by immigration. The disease is characterized by heart failure, arrhythmias and sudden death. How to determine which of the factors involved in evolution towards the heart disease might indicate response to treatment is one of the biggest challenges. The inflammation balance for control of the infection to avoid tissue damage is a key point in the pathology progression that needs clarification.
Purpose: Thus, the aim of this work was to determine the Th1/Th17/pro-inflammatory (IL-6, IL-2, TNF, IL-17 and IFNg) and Th2/anti-inflammatory (IL-4

and IL-10) serum profile in Venezuelan Chagasic patients stratified with Lown and NYHA classifications and treated with amiodarone, an antiarrhythmic drug with reported trypanocidal activity, to evaluate progression and response to the treatment.
Methods: Sera samples from 38 chagasic patients, clinically classified by NYHA and Lown criteria, were analyzed for cytokines using a human Th1/Th2/Th17 cytometric bead array kit in a FACSCanto cytometer. Treated and untreated patients were paired in function to their clinical status. The Wilcoxon rank-sum statistic was used for testing the hypothesis of significant difference between two groups (treated and untreated) and Principal Component Analysis (PCA) was used for reducing the data dimensionality, while keeping more than 98% of the original variance.
Results: Non-Treated (n=7) vs Treated (n=15) paired groups were quite different considering IL6, IL-2 and IL4 ($p<0.039$), while IL-10 remains almost similar ($p=0.2251$). IL-10 high producers frequency was significant lower in patients with high risk for sudden death (Lown 3 and 4 stage, n=14) regarding to Lown stages 0–2 (n=24). IL-17 and IL-2 high producers was higher in advanced NYHA stage (3–4, n=6) while IL-10 remains similar. PCA analysis seems to suggest the possibility of finding a good discriminant function between the represented groups in such a transformed space.
Conclusions: To our knowledge, it is the first report about the anti-inflammatory role of the amiodarone, suggesting an inmunomodulatory and/or parasiticidal effect in Chagas disease. Moreover, low IL-10 and high IL-17 level producers seem to identify patients with high risk of heart failure and sudden death.

P6396 | BEDSIDE
Effects of paediatric human immunodeficiency virus infection on electrical conduction of the heart

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Background: Heart conduction disorders, such as prolongation of QT interval, have been reported in HIV-infected adults. However, little is known about such disorders in paediatric HIV, particularly in relation to delineation of the effects of HIV infection from treatment.
Methods: This cross-sectional study was performed in 165 perinatally-acquired HIV-infected (56 newly diagnosed antiretroviral treatment (ART) -naive, 58 ART-exposed) and 51 healthy age-matched children in Indonesia. We performed 12-lead ECG examinations to measure cardiac conduction parameters; QTc and QoTc (corrected using the Bazett's formula), and PR intervals. The associations between HIV infection/treatment status and ECG intervals were evaluated using general linear modelling with further adjustment for potential confounders or explanatory variables. Findings are presented as (adjusted) mean differences between each of the two HIV groups (ART-naïve and ART-exposed) and healthy children.
Results: Compared to healthy children, QTc intervals were longer in ART-naïve (difference 18.3 milliseconds, 95% confidence interval (CI) 7.3 to 29.3) and, to greater extent, in ART-exposed HIV infected children (difference 27.9 milliseconds, 18.3 to 37.4). Following adjustment for RR interval, age, and height, prolongation of PR interval was seen only in ART-naïve HIV infected children, (difference 12.8 milliseconds, 2.3 to 23.3). Neither cardiac mass or function, high sensitivity C-reactive protein, lipid profile, gycoslyated haemoglobin levels, systolic and diastolic blood pressure, nor postnatal parental smoking exposure affected these associations. No difference in QoTc interval was observed between the groups.
Conclusions: Prolongation of QTc interval occurs in ART-naive HIV infected and, to a greater extent, in the ART-exposed children. In addition, ART-naive HIV infected children have a longer PR interval than healthy children.

P6397 | BEDSIDE
Abnormal Q-wave in anterior wall but not in inferior wall on surface ECG is marker for cardiac death in long-term follow-up of subjects with chronic Chagas disease

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Introduction: Abnormal Q-waves on surface ECG are markers of myocardial scar, cardiac dysfunction and life threatening arrhythmia. In chronic Chagas' disease, ventricular tachycardia (VT) relates to the presence of myocardial scar. Prognostic value of the location of myocardial scar based on surface ECG is undefined.
Methods: In a prospective longitudinal long-term follow-up study (Search-Rio Study), 100 outpatients (34 to 74 years old, 62 females) with chronic Chagas' disease and complaint of palpitation were admitted. Surface ECG assessed abnormal Q-wave, defined as $>100\mu V$ deep and >40ms width, as marker of myocardial scar according to the location: anterior (AW):V1-V4, and inferior (IW) wall: L2,L3,aVF. Echocardiogram assessed left ventricular ejection fraction (LVEF). Ambulatory ECG and medical records assessed VT episodes and survival during follow-up. Contingency tables, one-way ANOVA and Cox proportional hazard model assessed abnormal Q-wave location. Data are presented as mean±SEM, median or rate. ($\alpha<0.05$).
Results: In a follow-up of 8.2±2.4 years, 22 subjects had VT (median 2.4 years; incidence: 17±2‰/year) and 20 died (median 3.3 years; mortality rate: 22±2‰/year). In multivariate Cox proportional hazard model (No Q-wave: HR=1), AWQ-wave (HR: 3.6; 95% CI [1.4–9.3]; p=0.009) but not IWQ-wave (HR: 1.5; 95% CI [0.3–6.2]; p=0.62) was predictor of cardiac death. No association between abnormal Q-wave and LVEF was found (No Q-wave: 68.6%±1.8%; AWQ-wave: 60.7%±5.3%; IWQ-wave: 65.5%±7.7%; p=0.27; Levine's test p=0.18). No differences on LVEF<50% distribution according to Q-wave location was found (p=0.26; Table). A significant association between Q-wave location and VT during follow-up was observed (p=0.001; Table).

Abnormal Q-wave, LVEF and VT

	No Q-wave	Anterior wall Q-wave	Inferior wall Q-wave	p-value
LVEF <50%	12.8%	28.5%	12.5%	0.26
VT	17.9%	57.1%	0%	0.001

Conclusions: In chronic Chagas' disease, abnormal Q-wave in anterior and not in inferior wall is a long-term marker for cardiac death. Additionally, abnormal Q-wave in anterior wall is associated with spontaneous VT episodes in longterm. However, location of electrical markers of myocardial scar is weakly related to left ventricular systolic function in this population.
Acknowledgement/Funding: State University of Rio de Janeiro

P6398 | BEDSIDE
Electrocardiographic criteria and outcome in patients with arrhythmogenic right ventricular cardiomyopathy

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Current literature in arrhythmogenic right ventricular cardiomyopathy shows that electrocardiographic markers such as epsilon waves and the amount of T wave inversions of electroanatomic scar size predicts arrhythmic risk. The amount of T wave inversions with increasing electroanatomic scar size were normal T waves, negative T waves in V1 to V3, negative T waves in V1 – V3 extending to lateral leads and negative T waves in both precordial and inferior leads. This study was conducted in a large number of patients to correlate ECG findings to the outcome of each patient.
Methods: In 321 patients (207 males, mean age 46.7±11.3 years) the amount of T-wave inversions and outcomes of the patients were correlated. T-wave inversions in 4 leads or more (high risk group) were found in 61 patients and T-wave inversions in a maximum of 3 leads (so-called low risk group) could be revealed in 260 patients.
Results: In 38 out of 61 patients with T-wave inversions in 4 or more leads recurrent ventricular tachycardia or ventricular fibrillation occurred. In the low risk group at least 35 out of 260 patients were characterized by ventricular tachycardia or ventricular fibrillation. In the high risk group VT/VF were present in 62%; in the low risk group VT/VF occurred in 15%. These results were highly statistically significant with a p value <0.000001. Specificity was high with 86%; negative predictive value was higher with 90%.
Conclusions: It is known that the amount of T-wave inversions characterizes scar size thus predicting arrhythmic risk. In this analysis it was shown that the amount of T-wave inversions had a strong correlation to outcomes of the patients. T-wave inversion is an excellent parameter to predict ventricular tachycardia or ventricular fibrillation in the course of the patients with arrhythmogenic right ventricular cardiomyopathy.

P6399 | BEDSIDE
Exercise capacity in hypertrophic cardiomyopathy; predictors and effect of treatment with losartan

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Background: Reduced exercise capacity is common in hypertrophic cardiomyopathy (HCM) and a predictor of adverse outcome. Studies of animal models of HCM and pilot studies in patients have suggested beneficial effects of angiotensin II receptor blockers on structural and functional parameters including an increase in exercise time.
Purpose: Our aims were to assess the effects of losartan on exercise capacity compared to placebo and to identify predictors of exercise capacity in patients with overt HCM.
Methods: We studied 130 adult patients (52±13 years, 35% female) who were randomly allocated to treatment with losartan (100 mg/d) or placebo for 12 months. Patients were assessed with a symptom-limited exercise test, echocardiography and CMR or CT (patients with ICD) before and after treatment.

Results: Mean exercise capacity remained unchanged from baseline to 12 months follow-up in both groups (placebo 7.6±2.9 to 7.7±2.8 METS, p=0.49 and losartan 7.7±2.4 to 7.5±2.5 METS, p=0.33) and did not differ between groups (mean difference –0.3 METS [95% CL –1.0 to 0.3], p=0.28). Exercise capacity correlated strongly with NYHA class (r=–0.44, p<0.0001) and patients in NYHA class 1 had a significantly higher exercise capacity than patients in NYHA class ≥2 (8.4±2.7 METS vs. 5.8±1.9 METS, p<0.0001). In multivariate analysis of baseline data, a small left ventricular end-diastolic volume (LVEDV) (–0.61METS [95% CL –0.96 to –0.27] per 10 ml/m^2 decrease, p=0.0010) elevated E/ e' (–0.15 METS [95% CL –0.27 to –0.03] per 10% increase, p<0.0001) and female sex (–1.28 METS [95% CL –2.52 to –0.04], p=0.048) emerged as independent predictors of low exercise capacity. Patients with LVEDV index in the lowest quartile achieved a significant lower exercise capacity than patients in the upper quartile (6.4±2.5 METS vs. 9.3±2.9 METS, p<0.0001). Losartan had no effect on the predictors of exercise capacity. There was a significant increase in left atrial volume in both groups from baseline to follow-up (placebo 7.2±14.0 ml/m^2, p=0.0013 and losartan 5.9±13.7.0 ml/m^2 p=0.0086). There was no correlation between the change in left atrial volume and the change in exercise capacity in the individual patient (r=–0.04, p=0.73).

Conclusion: Losartan could not improve the reduced exercise capacity seen in adults with overt HCM. Low exercise capacity was predicted by female sex, low left ventricular end-diastolic volume and elevated E/ e'. Future studies may reveal if angiotensin II receptor blockers can affect left ventricular structure and function and have an accompanying beneficial effect on physical capacity in earlier stages of HCM.

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P6400 | BEDSIDE

Obstruction in asymmetric hypertrophic cardiomyopathy: a multicentre study

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Introduction: Obstruction at rest is described in about 25% of patients with asymmetric hypertrophic cardiomyopathy (HCM) and determines the natural history of the disease.

Aim: Characterize a Portuguese population of patients with asymmetric HCM and compare patients with and without obstruction at rest.

Methods: Portuguese multicentre study including all patients diagnosed with asymmetric HCM in 11 hospitals. We evaluated the clinical, genetic, electrocardiographic, echocardiographic and cardiac MRI data. We compared these parameters between patients with and without obstructive HCM.

Results: We included 346 patients with asymmetric HCM (61% male, mean age 61±14 years). About 60% of patients were symptomatic, and dyspnea (56%), angina (16%) and syncope (11%) were the most common symptoms. The average thickness of IVS was 19±5 mm and the posterior wall 11±3 mm. Obstruction at rest was present in 32% of cases and latent obstruction in 13% of cases. Mitral regurgitation was detected in 23% of cases. Delayed enhancement was found in 61% of patients undergoing cardiac MRI. Most patients were in sinus rhythm (80%). About 20% of patients had a history of atrial fibrillation and 18% had a history of non-sustained ventricular tachycardia (NSVT). About 6% of patients had pacemaker and 11% ICD. Cardiac death was found in 1.4% of cases (mean follow up of 5 years). Family history of HCM was identified in 26% and family history of sudden death in 17% of cases. Genetic testing was performed in 167 patients (48%) and revealed genetic mutations in 67 cases (40%) in the following genes: MYH7 – 10 patients (14.9%); MYBPC3 – 41 patients (61.2%); TNNT2 – 5 patients (7.5%); TNNI3 – 3 patients (4.5%); MYL2 – 1 patient (1.5%); TPM1 – 4 patients (6.0%); TCAP – 1 patient (1.5%); CSRP3 – 2 patients (3.0%). One patient was a compound heterozygote for mutation of genes MYBPC3 and TPM1.

Patients with obstructive HCM reported more often dyspnea (p=0.012). The posterior wall thickness was greater (p=0.001) and mitral regurgitation was more frequent (p=0.001) and severe (p<0.001). Bifascicular block was more frequent (p=0.016) and the presence of negative T waves in ECG was less frequent (p=0.015). NSVT were less frequent (p=0.005).

Conclusions: In this study, patients with HCM were frequently symptomatic. Genetic testing was positive in 40% of cases and MYBPC3 was the most commonly mutated gene. Obstruction at rest was present in 32% of the patients with HCM. Patients with obstructive asymmetric HCM were more symptomatic and presented higher frequency and severity of mitral valve regurgitation.

P6401 | SPOTLIGHT

Inheritance of left ventricular deformation: the BUDAPEST Twins study

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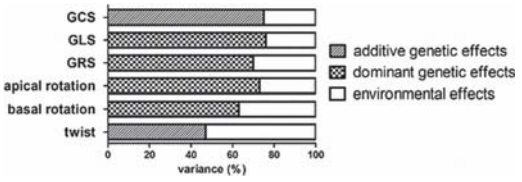
Although diagnostic and prognostic value of left ventricular (LV) deformation is widely recognized, data on its determinant factors are still scarce. The BUDAPEST Twins study was established to assess the genetic and environmental effects on different cardiovascular phenotypes. The aim of our present study was to estimate the heritability of LV mechanical function by quantifying myocardial strains in twin pairs.

Two hundred and twelve twin siblings were recruited (65 monozygotic and 41 same-sex dizygotic twin pairs, mean age 57±9 years). Siblings with coronary artery disease, any cardiomyopathy or severe valvular disease were excluded. Beyond the standard echocardiographic protocol, parasternal short axis- and apical views were obtained, optimized for speckle tracking analysis. Using dedicated software, global circumferential (GCS), longitudinal (GLS) and radial (GRS) strains were calculated by averaging the corresponding values of the 16 LV segments. Apical counter-clockwise, basal clockwise rotation and their net difference, the LV twist were also measured.

After adjusting for age and sex, the univariate additive genetic (A), dominant genetic (D) and unique environmental (E) effects model showed 75% additive genetic component in the variance of GCS, while 46% for twist. Similarly high, but dominant genetic effects (D) were found regarding GLS, GRS, apical rotation and basal rotation (D: 77%, 70%, 74% and 62%, respectively). Unique environmental effects were responsible for the rest of the variance (E: 23% to 54%).



Our study demonstrated high heritability of LV deformation. Role of unique environmental factors is less prominent. These results urge to search for the responsible genes determining LV deformation, whilst also highlight the importance of advanced echocardiographic screening.

ACUTE PULMONARY EMBOLISM

P6402 | BEDSIDE

Right-sided heart thrombus in the patients with atrial fibrillation and acute pulmonary embolism: impact on in-hospital prognosis

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Aim of the study: The aim of the study was to determine the prevalence of thrombus in the right side of the heart (RHT), and its potential impact on prognosis in patients with acute pulmonary embolism (APE). The secondary aim of the study was to assess the association between the presence of RHT and the presence of AF.

Methods: The study group consisted of 1006 consecutive patients with APE (598 females, 408 males), with a mean age 65.9±14.6 years. We excluded 31 patients due to a lack of information on the presence or absence of RHT.

Results: As compared to patients without RHT, patients with RHT had lower systolic blood pressure (108±48 vs 125±31 mmHg, p=0.004), higher heart rate (109±22 vs 101±27 bpm, p=0.037) and a higher prevalence of right ventricular (RV) overload (94% vs 74.6%, p=0.001). RHT was detected in 50 (5.1%) pts. The overall mortality rate was 3 times higher in patients with RHT as compared to those without RHT (32.0% vs 13.5%, OR 3.02, p=0.001). The rate of complications was 2 times higher in patients with RHT as compared to those without RHT (40% vs 21.5%, OR 2.44, p=0.004). There were no differences in the prevalence of RHT in patients with AF as compared to patients without AF (6.9% vs 4.5% OR 1.60, p=0.147. The mortality rate in patients with AF and RHT was significantly

higher as compared to those with AF but without RHT (50% vs 20.5% OR 3.86, p=0.014). In turn, in patients without AF but with RHT the mortality rate was twice as high as in those with neither AF nor RHT (24.2% vs 11.2%, OR 2.57, p=0.041). Univariate analysis revealed an association of death with age (p=0.03, OR 1.23), fibrynolysis (p<0.001, OR 4.30), history of heart failure (p=0.007,Or 1.99), active infection (p=0.007, OR 1.96), immobilization (p=0.001, OR 2.02), lower systolic blood pressure (p<0.001, OR 0.77), higher heart rate (p<0.001 OR 1.21), AF detected during admission (p<0.001, OR 2.18), elevated cTnT (p<0.001, OR 2.75), catecholamines use (p=0.000, OR 9.34), RHT (p=0.001, OR 3.02) and RV overload (p<0.001, OR 4.09). In multivariate analysis the independent predictors of death were: RHT (p=0.026, OR 2.35), age (p=0.005, OR 1.29), heart rate on admission (p=0.019, OR 1.11), shock (p=0.000, OR 9.96) and RV overload (p=0.012, OR 2.53).
Conclusion: RHT was an independent predictor of death in patients with APE. The mortality rate was three times higher in patients with RHT as compared to those without RHT. The presence of RHT was comparable in patients with and without AF. The mortality rate in patients with AF and RHT was 3 times higher than the rate in patients with AF but without RHT.

P6403 | BEDSIDE
Predictive value of TDI assessment of right ventricular function in patients with acute pulmonary embolism

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The aim was to determine whether the assessment of right ventricular function using tissue Doppler imaging (TDI) of the tricuspid annulus (TA) could be used as a prognostic marker in patients with pulmonary embolism (PE).
Materials and methods: Echocardiography (EchoCG) and pulsed TDI were performed in 167 patients with acute PE and normal left ventricular ejection fraction, and in 35 matched healthy volunteers (CG). The tricuspid annulus systolic (S tr_v) and diastolic velocities were acquired in apical four-chamber view using TDI.
Results: TDI EchoCG established: In patients with PE systolic and early diastolic TA velocities were significant lower that in CG (p<0.001). In 62 (37%) of PE patients we estimated signs of RV dysfunction: high right atrial (RA) pressure (IVC diameter >2.1 cm and inspiratory collapse <50%) and RA dilatation (>18cm^2). In PE patients with RV dysfunction S tr_v was significant lower 10.8 ± SD 1.5 cm/s that in patients with normal RV function 11.8 ± SD 1.8 cm/s (p<0.05). During the 30-day follow-up period 8 (13%) patients with RV dysfunction and S tr_v≤10.5 cm/s had recurrent PE and 4 (6.5%) patients died. In patients with S tr_v>10.5 cm/s we observed 1 patient with recurrent PE and no deaths occurred. The major complications (recurrent PTE and death) had a significant higher rate in patients with RV dysfunction (p<0.01).
Conclusion: In clinical settings TDI EchoCG in PE patients was a valuable, non-invasive method for evaluation of RV function. The establishment of RV dysfunction was related with significant increase in major complications, which should enhance clinical attention and care to those patients at risk. According to our results, normotensive patients without signs of right heart failure or serious comorbidity belong to a low-risk group which could be early discharged within 24 h and treated out of hospital.

P6404 | BEDSIDE
Computed-tomography-findings of inferior vena cava perforation after inferior vena cava filter deployment and its prognosis

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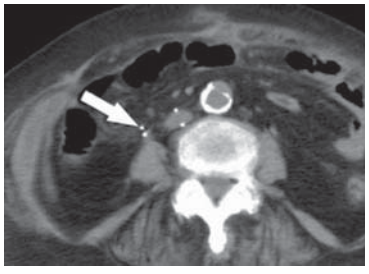
Objective: The indication of inferior vena cava filter (IVC-filter) is inconclusive because of possible IVC-filter-related adverse events. Although several reports introduced the computed tomography (CT) findings of IVC-filter with IVC-perforation and its clinical significance, no enough evidence is available.
Methods: From Jan/1st/2011 to Aug/31st/2014, 57 consecutive patients who underwent metallic IVC-filter insertion were retrospectively reviewed. Of 57 cases, 54 cases for Gunther-tulip and 3 cases for Greenfield and clear images of abdominal CT were obtained in 41/57 (72%) cases. The definition of IVC-perforation is a part of the IVC-filter protruded over the IVC wall existing other tissue between the part of the filter and the IVC wall on CT findings (see figure).



Results: Obvious IVC-perforation was observed in 11/41 cases (27%) and no adverse events have occurred (0%) during follow-up period (287±279 days). Of these, 4/11 cases were planed to remove the IVC-filter and the IVC-filters were safely retrieved in all cases without any complications.
Conclusions: IVC-perforation is a kind of shocking finding, however, our data suggests it rarely causes clinically devastating events and can be retrieved safely.

P6405 | BEDSIDE
Patient selection in outpatient and short-stay treatment in pulmonary embolism - comparison of different criteria (PESI, sPESI, Hestia and RVD on CT) in relation to ESC 2014 guidelines

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Background: Over the latest decade wide spectrum of studies have presented possible solutions of how to select low-risk pulmonary embolism (PE) patients to home treatment. Several risk scores have been introduced as prediction tools for the recognition of low death risk individuals. Universal consensus for how to use these criteria is lacking and there is a need for clarification for which one to implement.
Purpose: To compare three scores – Pulmonary Embolism Severity Index (PESI), simplified Pulmonary Embolism Severity Index (sPESI) and Hestia – and documented right ventricular dysfunction (RVD) on computer tomography (CT) to find out if these criteria recognised the same or different patients to be treated at home and also evaluate the current practice of patient selection in outpatient and short-stay treatment of PE in Finland based on ESC 2014 guidelines recommendation.
Methods: From January 2010 to July 2012, 276 patients with acute, symptomatic PE were screened retrospective from electronic patient records. 233 patients, aged 16–93 years, were included in the final analysis. All patients were treated accordingly to local Finnish guidelines. Statistical computations were performed by R statistical software version 3.0.2. and IBM SPSS version 21. The concordance of the scores was analysed by Cohens' and Fleiss' kappa.
Results: The most significant difference was found when documented RVD on CT was compared to PESI, sPESI and Hestia - almost half of the patients were classified differently. The best concordance was found between PESI and sPESI, but still only 0.71 that means substantial agreement. All of the patients (n=19) who would have been sent to home using only PESI (n=9), only sPESI (n=1) or both of them simultaneously (n=9) had RVD on CT. There were 5 patients with PESI class I or II with clinical signs of RVD, one of these patients had PESI class I (young and tachycardic) and four patients had PESI class II (3 were tachycardic and 2 had oxygen demand). When all four criteria scores were revised in our study population, 40–60% of patients could have been treated early at home, but only 9 patients (3.9%) were discharged straight from the emergency ward to home. At or below 48 hours of hospital stay were discharged 43 patients (18.5%).
Conclusions: Although PE patient is classified as low risk group, there might still be RVD, and the patient should be treated in the hospital. The effort should be projected to accomplishing universal consensus of how to manage rapid and accurate risk stratification recognizing especially low mortality risk patients, patient safety being major concern.

P6406 | BEDSIDE
Usefullness of right ventricular rate pressure product to assess right ventricular dysfunction and mortality in acute hemodynamically stable pulmonary embolism

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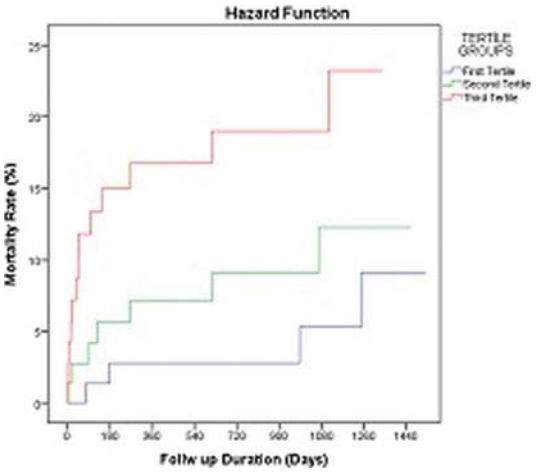
Introduction: Acute pulmonary embolism (APE) manifests with an acute increase in right ventricular afterload leading hemodynamic compromise. With neurohormonal activation, right ventricular (RV) compensatory response plays a crucial role in clinical progress. As a simple indicator of RV energy consumption, right ventricular rate-pressure product (rRPP) may utilize determination of RV dysfunction (RVD). We aimed to investigate the relationship between rRPP and RVD in acute hemodynamically stable pulmonary embolism.
Methods: 218 consecutive patients admitted with APE (54% male, mean age 61.2±8.9) between 2010–2014 were included in the study and divided into tertiles with respect to rRPP. Patients were followed-up median 28.9 months. RVD was defined as right-to-left ventricular dimension ratio >1.0 in the relevant transverse plane. rRPP was calculated as the product of admission heart rate documented by ECG and echocardiography derived systolic pulmonary artery pressure.
Results: The prevalence of RVD was highest in the highest rRPP tertile (34%, p=0.011), and rRPP had a close relationship with troponin levels (β=0.480, p<0.001). In multivariate analysis, rRPP was delineated as an independent predictor of RVD (OR: 1.119, 95% CI: 1.008–1.678, p=0.003). In ROC analysis, a cut of value 4983.7 for rRPP has a 69% sensitivity and 63.4% specificity for predicting RVD in APE (AUC 0.732 p=0.001). Kaplan-Meier analysis for long-term mortality, demonstrated higher mortality rate in third rRPP tertile compared with other tertiles (p=0.10, Chi-square=6.551).



Conclusion: As an indicator of RV compensatory response, rRRP seems to be an independent marker of RVD and mortality. A bedside examination, the assessment of this calculation may be beneficial in clinical assessment of these patients.

P6407 | BEDSIDE
Course of vascular obstruction after pulmonary embolism as assessed by ventilation-perfusion lung scan follow-up

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Background: We investigated the course ofresidual pulmonary vascular obstruction (RPVO) from discharge up to 3 - 6 months after pulmonary embolism (PE).
Methods: Prospective registry including 202 consecutive patients with PE who survived the acute phase (high risk PE: 12.4%, intermediate-risk: 65.8%, and low- risk: 21.8%). Patients with a prior history of chronic pulmonary disease were excluded. Ventilation-perfusion (V/Q) lung scan was performed in all patients before discharge, and again at follow-up (between 3 and 6 months after discharge). Treatment was in accordance with current guidelines. Evolution of RPVO was determined as the relative changein lung perfusion (in %) between discharge and follow-up V/Q scans.
Results: Between both lung scans, RPVO decreasedfrom 29.1±15% to 10.9±11.4%, with an average relative change of 61.7±33.4%. Overall, 49 patients (24.2%) presented a full resolution of lung perfusion.Relative changein RPVO was <50% in57 (28%), including 18 (8.9%) patients who showed no modification on lung scan. The relative changein RPVO was constant,regardless of the level of RPVO at discharge (p=0.07). Patients who presented full resolution on the second lung scan (n=49) had significantly lower RPVO at discharge as compared to those without full resolution (21.7±10.1% vs. 31.4±16.0% respectively, p<0.001), and almost 75% of those with full resolution had RPVO<30% at discharge. Multivariate logistic regression showed that high-risk PE and right ventricle (RV) to left ventricle (LV) ratio (by quartiles) at discharge were independently related to unfavorable course of RPVO during follow-up (high-risk PE: OR 3.6, 95% CI 1.54–8.43,p<0.001; RV/LV ratio: OR 3.42, 95% CI 1.12–9.45, p=0.03).
Conclusion: Our findings suggest that systematic lung scan follow-up should not be considered after PE, except in patients with high-risk PE or those with echocardiographic signs of RV pressure overload at discharge.

P6408 | BEDSIDE
Effect of atrial fibrillation on the in-hospital prognosis of patients with acute pulmonary embolism

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Aim of study: Atrial fibrillation (AF) has been extensively studied in the context of heart failure, hypertension, and acute myocardial infarction, however data on the prognostic implications of AF in acute pulmonary embolism (APE) are both scare and conflicting. The aim of this study was to assess the prognostic value of AF detected on hospital admission, in predicting short-term all-cause mortality, in patients with APE.
Methods: This was a retrospective, observational analysis of consecutive patients who were diagnosed with APE. The study group consisted of 1006 consecutive patients (598 females, 408 males), with a mean age 65.9±14.6 years.
Results: Overall in hospital mortality rate was 15.3%. AF was detected in 239 (23.8%) patients. Paroxysmal AF was detected in 60 patients (25.1%) and non-paroxysmal AF in 179 (74.9%) patients. The mortality rate was significantly higher in patients with AF 23.4% (56 deaths) as compared to patients on sinus rhythm 12.7% (97 deaths) (OR 2.09, CI 95% [1.44;3.02], p<0.001). There were no differences in the mortality rate between patients with paroxysmal AF and non-paroxysmal AF (15% (9 deaths) vs 26.6% (47 deaths), OR 2.02, CI 95% [0.96;4.71], p=0.067). Univariate analysis revealed an association of death with age (p=0.00, OR 1.25), fibrynolysis (p<0.001, OR 4.34), syncope (p=0.027, OR 1.55), history of heart failure (p=0.019, OR 1.79), active infection (p=0.014, OR 1.82), immobilization (p<0.001, OR 2.22), lower systolic blood pressure (p<0.001, OR 0.76), higher heart rate (p<0.001, OR 1.21), AF during admission (p<0.001, OR 2.09), persistent/permanent AF (p<0.001, OR 2.47), elevated cTnT (p=0.001, OR 2.56), use of catecholamines (p=0.000, OR 9.69), right heart thrombus (p=0.003, OR 2.75) and right ventricular (RV) overload (p<0.001, OR 4.09). However in multivariate analysis, AF was not an independent predictor of death (OR 2.4, CI 95% [0.85;1.43], (p=0.174)). Independent predictors of death were: age (p=0.008, OR 1.27), heart rate (p=0.018, OR 1.11), shock (p=0.000, OR 4.35), cTnT (p=0.043, OR 1.76), RV overload (p=0.007, OR 2.67).
Conclusion: Patients with APE who experience AF during hospital admission have a 2-fold higher risk of death and complications as compared to patients without AF.

P6409 | BEDSIDE
Comparisson of rivaroxaban and vitamin K antagonists anticoagulant therapy after thrombolysis in patients with intermediate and high risk pulmonary embolism

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Background: The novel guidelines recommend several novel anticoagulant drugs and vitamin K antagonists for the treatment of pulmonary embolism. However, in all studies which studied novel anticoagulants, patients who received thrombolytic therapy were excluded and the exact protocol for the introduction of NOACS are not established.
Methods: Seventy-five consecutive patients with either high or intermediate risk PTE who admitted in the single coronary care unit of university hospital during received thrombolytic therapy at admission. After thrombolytic therapy all patients were on continuous infusion of unfractionated heparin until hemodynamic stabilization when they started either bridging with enoxaparin and vitamin K antagonists for or rivaroxaban at dose 15 mg twice daily. Composite end point of death, major bleeding and need for mechanical ventilation at 30 days were compared between 34 and 41 patients who received vitamin K antagonists or rivaroxaban, respectively. Only patients who were on oral anticoagulant therapy (OAC) for at least 1 day are included in the study, and major bleeding was related to OAC if patient were on rivaroxaban for at least 2 doses and on vitamin K antagonists when INR was reached the 2.0 value. International Society of Thrombosis and Haemostasis criteria for major bleeding were used in this study.
Results: The two groups were similar in relation to age (62±15 vs 59±17 y, p=0.401), gender distribution (p=817), simplified PESI score at admission (2.0 [1.0–2.5] vs 1.0 [1.0–2.0]) and the distribution of high risk patients (8 [23.5%] vs 6 [14.6%], p=0.591). Only one patient in rivaroxaban group died from PTE. One patient on vitamin K antagonists and 2 patients on rivaroxaban fulfilled criteria for major bleeding on OAC. However, 5 (16.1%) and 6 (14.5%) patients had major bleeding related to thrombolysis before the OACs was introduced. Composite 30 days end point was similar between two groups (2 [5.9%] and 6 [14.6%], p=0.280), respectively. The average hospitalization stay was similar between two groups (10 [8–14] vs 8 [7–13] days, p=0.136).
Conclusion: There was no significant difference between major adverse events at 30 days between heparin plus Vitamin K antagonists compared to rivaroxaban group in PTE patients received thrombolytic therapy.

P6410 | BEDSIDE
Identification of normotensive patients with pulmonary embolism at high risk of adverse clinical outcome: comparison of two clinical scores

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Background: Recently two clinical scores (Bova score and TELOS score) have been proposed for the identification of normotensive patients with acute pulmonary embolism (PE) at high risk of haemodynamic collapse and death. The present study compared the accuracy of the two scores and investigated the prognostic utility of their combination.
Methods: Bova score, based on the presence of mild hypotension (systolic blood

pressure 90–100 mmHg), tachycardia (≥110/min), right ventricular dysfunction (RVD) and troponin elevation, categorized normotensive patients with PE into three groups: low, intermediate and high risk patients. TELOS score based on the presence of RVD, elevated troponin and plasma lactate (≥2mmol/L): when all three criteria are present, patients are considered at high risk of adverse outcome. We retrospectively applied the scores on a large cohort of patients derived from three prospective studies. The primary outcome was a composite of haemodynamic collapse and death within 7 days from diagnosis.
Results: Of 1276 screened patients, 21 patients with shock and 261 patients with missing values were excluded. Of the 994 (77.9%) patients included in the analysis, 63 (6.3%) reached the primary outcome. Bova score classified 775 (78.0%), 160 (16.1%) and 59 (5.9%) patients in low, intermediate and high-risk categories, with primary endpoint incidence of 3.7%, 14.4% and 18.6% respectively (c2 for trend P<001). Similarly to the Bova score, TELOS score identified 58 (5.8%) high-risk patients, with a primary outcome incidence of 20.7% (P<0.001 vs low risk). When we identified high-risk patients by using the combination of the two scores (high-risk patients according to Bova score together with high-risk patients according to TELOS score), patients included in the high-risk group increased to 91 (9.1%), without a reduction in the primary outcome incidence (18.7%).
Conclusions: Both Bova and TELOS scores identified a small group of normotensive patients at high risk of short-term adverse outcome, with no significant differences between scores. The combination of the two scores sensibly increased the proportion of high-risk patients.

P6411 | BEDSIDE
Filter thrombosis in patients with venous thromboembolism undergoing a temporary inferior vena cava filter insertion

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Background: About 40% of Japanese patients with acute venous thromboembolism (VTE) received an inferior vena cava (IVC) filter insertion. During temporary IVC filter replacement in patients with VTE, filter thrombosis is often observed even on unfractionated heparin (UFH) treatment. Argatroban is capable of inhibiting the action of both free and clot-associated thrombin. Predictors of temporary filter thrombosis in the treatment of acute VTE remain unknown.
Methods: After bolus injection of UFH, a temporary IVC filter (Neuhaus Protect, TORAY) was inserted in 99 patients with acute VTE. Patients with pulmonary embolism (PE) with shock or right ventricular (RV) dysfunction, or those with proximal deep vein thrombosis (DVT) were treated with a temporary IVC filter in the first 3 to 5 days after admission. Until 2012, 73 patients received continuous infusion of UFH (Gr-H). Since 2013, 26 patients received continuous infusion of argatroban (Gr-A) irrespective of heparin-induced thrombocytopenia (HIT). Patients with cardiac arrest on arrival were excluded. According to treatment regimen for HIT, argatroban was started at 0.7μg/kg/min and adjusted to reach an aPTT between 1.5 and 3 times baseline value. Massive IVC thrombosis was defined as development of stenosis ≥50% on the venogram at 3 to 5 days after insertion.
Results: Although the rates of female (35 vs 64%) and PE (85 vs 99%) were lower in Gr-A than in Gr-H (p<0.05, respectively), there were no differences in other patient characteristics between 2 groups. The incidence of massive IVC thrombosis (12 vs 21%, p=0.09) tended to be lower in Gr-A compared with Gr-H. On multivariate logistic regression analysis, independent predictors of massive IVC thrombosis were UFH use (odds ratio (OR) 4.29), duration of filter insertion ≥4 days (OR 3.92), and DVT alone or PE without shock nor RV dysfunction (OR 3.71) (p<0.05, respectively), whereas proximal DVT was not.
Conclusion: Argatroban use, short duration of filter insertion, and a restrictive filter strategy may be required to reduce massive IVC thrombosis in patients with acute VTE treated with temporary IVC filters.
Acknowledgement/Funding: none

ADULT CONGENITAL HEART DISEASE

P6412 | BEDSIDE
Depression and anxiety in adult Filipinos with congenital heart disease using the validated Filipino version of the Hospital Anxiety and Depression Score (HADS)

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Background: Congenital heart diseases (CHD) pose a major global concern due to its increasing survival trend in the adult stage; but data in our country is lacking. Despite improvement in management, formal assessment for anxiety and depression in patients with adult CHD is not routinely done. The Hospital Anxiety and Depression Scale (HADS) is a self-administered instrument highly reliable for detecting states of anxiety and depression. The HADS-P ("P" for Pilipino) is the validated Tagalog version of the HADS.
Objectives: We aim to determine the prevalence of anxiety and depression in adult CHD Filipino patients compared to healthy controls using the HADS-P questionnaire.
Methods: This is a cross-sectional study of adults with CHD at a tertiary center. A control group was also recruited. The HADS-P is a 14-item rating scale with independent subscales for anxiety and depression (7 items each) was administered to both the study and control groups. A cut–off score of >8 points on either of the depression and anxiety subscale was used to determine their respective prevalence.
Results: A total of 192 patients (92 patients with CHD and 100 controls) with a mean age of 33 years old were recruited. The proportion of cases with anxiety and depression were significantly higher among those with CHD (61% and 34% respectively, p-value <0.001), compared to healthy controls. Of the 92 patients with CHD, majority had an atrial septal defect, ventricular septal defect, and patent ductus arteriosus. Focusing on the CHD group, simple logistic regression identified employment status, a higher NYFC, low distance 6 minute walk test, uncorrected defects, and LV/RV failure as predictors of anxiety; whereas lower educational achievement, higher NYFC, right-to-left shunt or Eisenmenger physiology, low distance 6 minute walk test, and LV/RV failure were predictors of depression. Multiple logistic regression identified only employment status (ie. being unemployed) as a significant predictor of anxiety [OR 4.54, p 0.012]; while having a right-to-left shunt or Eisenmenger physiology was a significant predictor of depression [OR 6.44, p 0.004].
Conclusion: This cohort of adult Filipinos with CHD has higher HADS-P scores, suggestive of a higher prevalence of depression and anxiety. Factors associated with anxiety and/or depression were related to their underlying CHD and sociodemographic profile. Health care professionals should be alert for the possible need for psychological intervention for adult survivors of CHD, even among those that are seemingly emotionally well-adjusted.

P6413 | BEDSIDE
Survival Prospects and Circumstance of Death in Contemporary Adult Patients with Congenital Heart Disease: The Shifting Focus of Mortality from the Perioperative Period to Long-Term Complications

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Background: In the current era, over 90% of children born with congenital heart disease survive to adulthood. However, adult congenital heart disease (ACHD) patients have ongoing morbidity and reduced long-term survival. Recently the importance of specialized follow-up at tertiary ACHD centres has been highlighted. We aimed to assess survival prospects and clarify causes of death in a large cohort of patients at a single, tertiary centre.
Methods and results: We have included 6,969 adult patients (age 29.9±15.4 years, 49.9% female) under follow-up at our institution between 1991 and 2013. Causes of death were ascertained from official death certificates. Survival was compared with the expected survival in the general age and gender matched English population and standardized mortality rates (SMRs) were calculated. Over a median follow-up time of 9.1 years (IQR 5.2–14.5), 524 patients died. Leading causes of death were chronic cardiac failure (44%), pneumonia (10%), sudden-cardiac death (7%), cancer (6%) and haemorrhage (6%), while perioperative mortality was low. Isolated simple defects (ASD, VSD or PDA) exhibited mortality rates similar to those in the general population, while patients with Eisenmenger syndrome (SMR 12.8), complex congenital heart disease (SMR 14.1) and Fontan physiology (SMR 23.4) had much poorer long-term survival (P<0.0001 for all). The probability of cardiac death decreased with increasing patient's age (OR 0.90/decade [95% CI 0.82–0.98], P=0.02) whereas the proportion of patients dying from non-cardiac causes, such as cancer, increased (OR 1.34, [95% CI 1.1.2–1.63], P=0.002).
Conclusions: ACHD patients, as a whole, continue to be afflicted by increased mortality, as they grow older, compared to general population. Highest mortality rates were observed amongst patients with complex ACHD, Fontan physiology an Eisenmenger syndrome. Our contemporary data show a clear shift from perioperative to chronic cardiac mortality and non-cardiac death.

P6414 | BEDSIDE
How Doppler echocardiographic follow-up of aortic coarctation can be improved - a novel approach for the determination of pressure gradient using a refined equation

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Introduction and purpose: In patients with coarctation of the aorta (CoA) pressure gradients across the coarctation site obtained from transthoracic echocardiography are used as a noninvasive tool for quantification of CoA severity. However the assessment by Doppler velocity measurements (DVM) using the conventional Bernoulli equation is unreliable as it leads to an overestimation of the true stenosis. The purpose of this study was to determine a more accurate method for assessing the severity of CoA by a refined equation.
Methods: 25 patients with surgically repaired CoA were retrospectively enrolled. DVM of the precoarctic aorta (V1) and the site of the residual stenosis (V2) were made. The pressure gradients (PG) across the CoA was calculated using a novel equation, derived from the Bernoulli principle, the continuity and the linear momentum equations, including the ratio of the vessel area (VA) of the precoarctic

(Aprox) to postcoarctic (Adist) aorta (ΔP=4 (V2-V1 (Aprox/Adist))2). The calculated PG was compared to values yielded by the conventional Bernoulli equation (ΔP=4 (V22-V12)) and to the noninvasively measured blood pressure difference between the right arm and leg, which served as standard of reference. In 10 patients measurements of the pre- and poststenotic VA were taken from noninvasive angiographies (CT or MRI) and added to the calculation. In all other patients, a ratio of 1 for Aprox/Adist was applied (ΔP=4 (V2-V1)2).
Results: Calculation of the PG across the CoA with the refined equation showed better performance in regression analysis than with the conventional equation (corrected R2 of 0.664 versus 0.563), especially if measurements of the pre- and poststenotic VA were included in the calculations (corrected R2 of 0.887). Accordingly, Bland-Altman-limits of agreement showed smaller confidence intervals compared to the calculations by the conventional Bernoulli equation.
Conclusion: We found that this refined equation yielded more accurate results of the PG in CoA compared to the conventional Bernoulli equation, especially when adding measurements of the pre- and postcoarctic VA to the calculation. Moreover we can state that the pre- and poststenotic VA have to be different if the PG deviates from the blood pressure difference and can be estimated by the novel equation if not available by noninvasive imaging. Hence we recommend using the novel equation for assessment of severity in CoA and furthermore, considering additional noninvasive imaging for assessing VA in cases where the PG by DVM differs substantially from the blood pressure difference.

P6415 | BEDSIDE
Anomalous connections or the coronary arteries: a prospective observational cohort of 472 adults. The ANOCOR Registry

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Introduction: Anomalous connections of the coronary arteries (ANOCOR) are rare. Management of high-risk ANOCOR may be difficult in the lack of life-threatening cardiac events. Need of risk stratification model is recognized. Large-scale multicenter registries dedicated to these congenital abnormalities are lacking.
Purpose: The multicenter ANOCOR Registry provides prospective collection of contemporary data regarding the profile and the management of patients with ANOCOR.
Methods: The cohort population comprised consecutive patients presenting to French interventional cardiologists (n=71) during the recruitment period (January 2010-January 2013). ANOCOR was documented by selective coronary angiography or cardiac computed tomography angiography. Follow-up was planned at 5 years by the coordinating center.
Results: 472 patients (72% male) were enrolled with a mean age 63±13 years (16–95 years). Young patients (≤35 years of age) were few (n=11). First imaging modality was selective coronary angiography in 89.2% (n=421) and cardiac computed tomography angiography in 10.8% (n=51). Initial clinical presentation was confirmed or suspected coronary artery disease in 62.5% (n=295), cardiomyopathy or valvulopathy in 16.5% (n=78), atypical chest pain in 16.3% (n=77) and other causes in 4.7% (n=22). Twelve (2.5%) aborted sudden deaths were observed. Single ANOCOR was identified in 449 patients (95.1%) and multiple ANOCOR in 23 patients (4.9%). Among 496 ANOCOR, 235 (47.4%) involved the circumflex coronary artery, 165 (33.3%) the right coronary artery, 60 (12.1%) the left main coronary artery, 27 (5.4%) the left anterior descending coronary artery and 9 (1.8%) other arteries. Connection with opposite sinus or contralateral artery was noticed in 90.9% (n=451). Anomalous connections implied appropriate sinus in 4 cases (0.8%) and non coronary sinus in 2 cases (0.4%). A high take off above the sinotubular jonction was observed in 29 cases (5.9%). Six (1.2%) single coronary arteries and 4 (0.8%) connections with the pulmonary artery were noticed. Preaortic course, recognized as an anatomical high-risk feature, was present in 89.7% with ectopic right coronary artery, 5.7% with ectopic left main coronary artery or left anterior descending coronary artery and 0% with ectopic circumflex coronary artery.
Conclusion: Discovery of ANOCOR is often fortuitous in adult population. Ectopic right coronary artery associated with a preaortic course is not rare in >35 years of age. Analysis of the management of ANOCOR with preaortic course will be the next step of the ANOCOR Registry, a large ongoing multi-institutional study.
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P6416 | BEDSIDE
Uncertainties in insurances for adults with congenital heart disease

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Background: While life expectancy has greatly improved with often few physical restrictions, a substantial number of adults with congenital heart disease (CHD) still experiences restrictions in daily life in the areas of employment, insurances and mortgages. Despite increased scientific interest in long-term outcome of CHD, little about this is known.
Purpose: We studied the presence of constraints in health, life and disability insurances and mortgages applications in adults with CHD.
Methods: Patients were randomly selected from five hospitals from CONCOR (N=14.187), the Dutch national database of adults with CHD, and were send a questionnaire that included questions on demographic items (i.e., sex, age, educational, occupational and relational status) and on applications and potential constraints for a health, disability or life insurance or mortgage. All data were analyzed per defect (mild or moderate to severe) and compared to data from a reference group.
Results: Of the 406 randomly selected patients, 237 patients completed the questionnaire (response rate 58%). Median age was 41 (IQR 31–50) and 55% was female. Employment rates were significantly lower in patients with CHD compared to the reference group (65% versus 88%, p=0.002). Of patients with CHD, 40% had mild, 52% moderate and 8% severe CHD. Insurance and mortgage application rates were significantly lower for all patients with CHD compared to the reference group, but did not differ among the different CHD severity groups except for life insurances. The association of two clinical parameters, functional NYHA classification and left ventricular (LV) ejection fraction, with restrictions in insurance or mortgage applications was studied in 163 patients. After adjustment for several factors, restrictions were still not associated with clinical parameters. Only of 38% of all CHD patients medical information was requested; among patients with constraints this was the case in 70%. Additional medical information did not lead to different outcomes in constraints and CHD severity.
Conclusion: This study shows that additional clinical information or favorable prognostic clinical factors in patients with CHD as mild CHD, normal NYHA class and LV ejection fraction do not protect against constraints in insurance applications. Despite the overall improved morbidity and prognosis, adults with CHD still encountered more constraints than a reference group. Nowadays, accurate prognostication for most patients with CHD is possible, but there still seems to be an important gap between knowledge on CHD and transparency of insurance application processes.

P6417 | BEDSIDE
Multivariable mortality risk stratification in adult patients with eisenmenger syndrome

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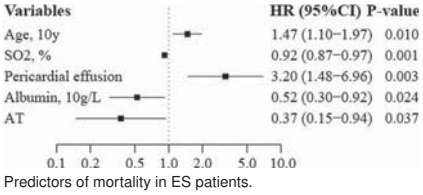
Background: Eisenmenger Syndrome (ES) is the extreme manifestation of pulmonary arterial hypertension (PAH) in patients with congenital heart disease, associated with high mortality. Several single parameters were proposed as predictors of mortality but risk stratification remains challenging, as multiple variables are available in the clinical setting.
Methods and results: In total 334 adult patients with ES were identified (62% female, 36% with Down syndrome), including 190 (57%) patients with post-tricuspid lesion, 29 (9%) with pre-tricuspid shunt and 115 (34%) with complex anatomy. Over a cumulative follow-up period of 1120 patient-years 78 patients died. On univariable Cox regression analysis several parameters were related to mortality, including age, oxygen saturation (SO2), 6-minute walk test distance, presence of sinus rhythm, QRS duration, presence of pericardial effusion on echocardiography, treatment with advanced therapy for PAH (AT for PAH) and several biochemical parameters. On multivariable Cox regression analysis (Figure) only age, SO2, pericardial effusion, albumin and AT remained in the mortality risk stratification model. This model remained stable after adjustment for missing values using multiple imputation as well as after adjustment for AT as a time dependent variable.



Predictors of mortality in ES patients.

Conclusions: Multivariable mortality risk stratification in feasible and may improve further management of patients with ES. Multicentre validation and adjustment of the risk stratification model is currently in progress and should enhance the risk stratification process and management of ES patients.

P6418 | BEDSIDE
Release of growth-differentiation factor 15 and associations with cardiac function in adults with congenital heart disease

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Background: Growth-differentiation factor-15 (GDF-15), an oxidative stress-induced cytokine with broad cardiac and non-cardiac activity, has diagnostic and prognostic value in acquired heart failure.
Purpose: We studied the release of GDF-15 in adults with congenital heart disease (ConHD), and assessed its association with cardiac function and functional capacity.
Methods: A total of 587 consecutive adults with ConHD (median age 33 [IQR 25–41] years, 59% men, and 90% NYHA I) underwent physical examination, electrocardiography, echocardiography, and venepuncture according to a standardised protocol. A subset of 143 patients underwent bicycle ergometry on the same day.
Results: Median plasma GDF-15 was 618 [IQR 487–867] ng/L. In 87 patients (15%), GDF-15 was above the reference value of normal (1109 ng/L). GDF-15 levels were higher in older patients ($r=0.367$, $p<0.001$). GDF-15 was higher in patients with elevated pulmonary pressure than in patients with normal pulmonary pressure (median 1114 versus 606 ng/L, $p<0.001$). GDF-15 was correlated with NT-proBNP ($r=0.445$, $p<0.001$). In multivariate analysis, adjusting for age, sex, and NT-proBNP, GDF-15 above the reference value was associated with NYHA class (odds ratio for NYHA$\geq$II: 3.5 [95% CI: 1.8–6.8],$p<0.001$), and decreased exercise capacity (odds ratio for workload$>$85%:0.2 [95% CI: 0.06–0.8], $p=0.018$), but not with systolic ventricular function or ECG rhythm.
Conclusion: GDF-15 was elevated above normal in a substantial number of stable ConHD patients and higher in those with elevated pulmonary pressures, regardless of underlying congenital diagnosis. GDF-15 is associated with NYHA class, NT-proBNP and exercise capacity, suggesting the marker has diagnostic and potential prognostic value in adults with ConHD.
Acknowledgement/Funding: None

P6419 | BEDSIDE
Long-term outcome of patients with ventricular septal defect: results from a national registry

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Background: Studies evaluating long-term outcome of patients with ventricular septal defect (VSD) are scarce but important to evaluate current VSD management and to inform patients about medical prognosis, professional and health insurance issues.
Purpose: This study aimed at determining the long-term outcome of patients with VSD included in the Belgian Registry on Adult Congenital Heart Disease.
Methods: Patients with VSD included in the national registry since 2005 were studied. Demographic, clinical, echocardiographic and invasive hemodynamic measurements were analysed.
Results: A total of 252 patients were studied for a median follow-up time of 19 (IQR 11–25) years. One hundred thirty-four (53%) patients were male. Median age at latest follow-up was 28 (IQR 24–34) years. Most VSDs (90%) were perimembranous. Median VSD size at baseline was 7 (IQR 5–10) mm. One hundred fourteen (45%) patients underwent VSD closure, 110 surgically and 4 percutaneously. Median age at VSD closure was 3 (IQR 0.5–6.7) years. Median Qp/Qs ratio was 2 (IQR 1.5–3).
At latest follow-up, 91% of the patients were in NYHA class I. No patient developed right heart failure. Eight patients (3%) presented with atrial arrhythmia during follow-up, of which 6 had undergone VSD closure. Left ventricular dilatation was present in 13 (5%) patients. No patient died during follow-up.
In the closed VSD group, five (4%) patients required pacemaker implantation for high degree atrioventricular block, 2 of which early postoperatively and 3 late after closure. A residual shunt was present in 16 (14%) patients. Five (4%) patients developed pulmonary hypertension. Interestingly, 20 (18%) patients developed some degree of (sub)valvular aortic stenosis (AS) during follow-up. Congenital aortic valve malformations (mainly bicuspid aortic valve) were only present in 8. The remaining 12 patients developed AS after VSD closure, potentially suggesting an association with surgery. Forty-four (39%) patients presented mild and 12 (11%) moderate to severe aortic valve regurgitation. No re-operations occurred.
In the open VSD group, six (4%) patients developed endocarditis. Nineteen (14%) spontaneous closures occurred.
Conclusions: Overall long-term survival in patients with VSD is excellent. Ninety-one percent of patients function in NYHA class I. Five patients needed pacemaker implantation after VSD closure. An important percentage of patients without congenital aortic valve malformations developed AS after VSD closure. A potential association with surgery needs to be further investigated.

P6420 | BEDSIDE
The advisability of atrial septal defect closure in patients older than 60 years

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Background: Transcatheter closure of secondary atrial septal defects (ASD) in adults is still unsolved, discussed and even controversial. Due to the fact that older patients the probability of successful treatment is greatly reduced due to the presence of different morphological features.
Purpose: The aim of our study was to investigate the effect of closing the ASD in older patients compared to younger.
Methods: During the period from May 2011 to May 2014, in the our Center transcatheter ASD closure using duble disk occluder was performed in 209 consecuitive patients (age from 18 to 82 years). A retrospective analysis based on the medical reports, functional status, degree of remodeling of the right ventricle (RV) and the right atrium (RA), as well as changes in systolic pulmonary artery pressure (SPAP) before and 12 months after procedure. To participate in the study selected 126 patients who were divided into two groups: group 1 (n=106) included patients younger than 35 years and group 2 (n=20) - 60 and older. The dimensions of the defect (median 18,17±23 mm) and the value of intracardiac left-right shunt (Qp/Qs ratio=1,69±0,22) did not differ between the groups.
Results: The study showed that a group of elderly patients ($>$60 years) had more severe symptoms of heart failure, compared with the younger group ($<$40 years). Level of SPAP, right ventricular size and atrium are related to the age. After 6 months postoperatively RV size decreased significantly in group 1 and group 2: from 41,68±8,22 mm to 33,73±5,13 mm; the size of the RA from 42,79±6,51 mm to 38,75±6,65 mm & from 52,79±8,13 mm to 43,53±7,06 mm and the SPAP from 34,33±7,06 to 26±4,56 mm Hg & from 52,05±14,55 to 38,68±11,47 mm Hg, respectively. The absolute changes of the SPAP and size of right chambers is not significantly different in the groups. Symptoms of heart failure (HF) noted 27% and 75% of patients before surgery in groups 1 and 2. After the procedure, reducing the symptoms HF noted 100% and 85% of patients in groups 1 and 2, respectively.
Conclusions: Closure of ASD is accompanied by improvement of clinical symptoms and decrease the size of the right heart chambers is not dependent on the age of the patient. However, the most beneficial results are obtained in patients with less severe symptoms HF, right chambers overload and initially less increased of pulmonary artery pressure. Closing hemodynamically significant ASD should be advised as soon as possible at an earlier date after the diagnosis, especially in older patients.

P6421 | BEDSIDE
Anticoagulation in adults with congenital heart disease and atrial arrhythmias. A report from a regional registry of congenital heart disease (RACCA)

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Patients with congenital heart disease (CHD) and atrial arrhythmias (AA) often do not have typical thromboembolic risk factors and typically present with arrhythmias other than non-valvular atrial fibrillation. The need for anticoagulation in intra-atrial re-entry tachycardia (IART) may be questioned, but the prevalence of intracardiac thrombi in this patients has been reported to be high. Thus, anticoagulation is recommended in high-risk patients. We sought to evaluate current practice on anticoagulation therapy and the accordance with existing guidelines.
Methods: A total of 2,384 patients $>$14 years were prospectively included over a period of 2 years in the regional RACCA registry. We addressed the use of anticoagulation or antiplatelet therapy in 258 patients with paroxysmal or chronic atrial flutter, atrial fibrillation or IART. Patients with previous intracardiac repair, cyanosis, Fontan palliation, mechanical valves or subaortic right ventricle or with CHA2DS2 VASc $>$1 were considered at high-risk.
Results: A total of 158 patients, which accounted for 60,8% of all cases with AA, were on antithrombotic treatment: warfarin 66,4%; new oral anticoagulants (NACO) 0,63%; and antiplatelets (ASA) 29%. Of high risk patients, only 50% were on anticoagulation with warfarin or NACOs. Fontan procedures were the underlying conditions more significantly treated with antithrombotic therapy ($p=0.025$). None of the patients with Fontan palliation were without therapy. However, despite European guidelines recommendations, in 11 Fontan patients, only 64% were on warfarin. The other 36% were on ASA. Six out of 15 patients with Senning repair for transposition were on VKA and 1 patient were on NACOS despite no data on pharmacokinetics or pharmacodynamics in CHD. In cyanotic patients with Eisenmenger syndrome or single ventricle physiology palliated with Glenn procedure, patients were more commonly treated with ASA (66%) than warfarin. According to the CHA2DS2 VASc score, patients with simple CHDs and no prosthetic valve or hemodynamically significant valve disease were significantly more likely receiving anticoagulation when they had experienced prior stroke or were hypertensive

(92% vs. 8%, p=0.011; 84% vs.16%, p=0.01, respectively). Finally, there was a trend toward no anticoagulation in female patients and in patients aged below 67 years (p=0.056).
Conclusions: The actual management of anticoagulation in adults with CHD and AA was in accordance with guidelines in 50 to 60%. In cyanotic patients, decisions were challenging and made on the basis of thrombogenic conditions and the increased risk of bleeding.

RISK REDUCTION – CLINICAL ASPECTS

P6422 | BEDSIDE
Metabolic syndrome given by different definitions and ten year (2001-2011) cardiovascular disease incidence in Greece; the ATTICA Study

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Background and purpose: To examine if the participants identified by different metabolic syndrome (MS) definitions shared the shame likelihood for cardiovascular disease (CVD) after 10-years of follow-up.
Methods: During 2001–2002, 1514 men and 1528 women (>18y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011–2012, the 10-year follow-up was performed in 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD was defined according to WHO-ICD-10 criteria. MS was defined using three definitions, provided by the National Cholesterol Education Program Adult Treatment panel III (revised NCEP ATP III), the International Diabetes Federation (IDF) or the Harmonized definition.
Results: The NCEP ATP III criteria for the MS were met by 20.0% of the sample, while 48.9% met the IDF criteria and 51.0% the Harmonized criteria using the IDF cut points for waist circumference. After adjustment for various potential confounding factors (i.e., age, sex, physical activity, smoking and eating habits, using the MedDietScore), history of MS using the revised NCEP ATP III definition, was associated with 83% higher likelihood (95% CI: 1.24–2.72) of 10-year-CVD incidence. Furthermore, using the IDF or the Harmonized definitions, insignificant results were observed (OR=0.91, 95% CI: 0.62–1.35 and OR=0.98, 95% CI: 0.66–1.47, respectively).
Conclusion: After 10 years of follow-up, participants with MS defined by the revised NCEP ATP III definition had increased likelihood of CVD.
Acknowledgement/Funding: Demosthenes Panagiotakos and Ekavi Georgousopoulou received research grants by Coca-Cola SA.

P6423 | BEDSIDE
Risk factors for cardiovascular and cerebrovascular diseases among 4,752 adult hypertensive subjects in the primary care setting in Guangdong province, China: a 5-year longitudinal analysis

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Background and introduction: In China, an increasing level of attention has been paid to the rising occurrence of disability and deaths caused by cardiovascular and cerebrovascular diseases (CCDs). Our previous study showed that the prevalence of hypertension was rising continuously, and more than one in ten of the general population had two or more chronic conditions simultaneously. The recent national health report showed that nearly 3 million people died from diseases related to CCD, accounting for 51% of the causes of total deaths annually in China.
Purpose: This longitudinal study aimed to explore factors associated with the presence of CCDs among an adult hypertensive population in the primary care setting in China.
Methods: The community health centres (CHCs) are the major primary care providers in mainland China. We selected six CHCs according to the geographic locations and population characteristics, wherein a national standardised protocol of community-based hypertension management strategy has been in place from August 2007 to July 2012. Information of adult hypertensive subjects enrolled in the care management of these CHCs were collected, and the prescription profiles of anti-hypertensive drugs were captured through face-to-face interviews as of August 2012. A multivariate Cox proportional hazards modelling analysis was performed.
Results: A total of 4,752 adult subjects with physician-diagnosed hypertension were included in the study with an overall follow-up rate of 92.9%. The age of the overall participants ranged from 23 to 98 years old, and there was a slightly higher proportion of females (58.4%, [2,774/4,752]). The mean survival time was 10.92 years (standard deviation 5.44 years). There were no significant differences (p=0.126) in the mean age years between males (67.02, standard deviation 11.23) and females (67.51, standard deviation 10.87). Factors associated with CCDs among hypertensive subjects included ageing (adjusted hazard ratio [aHR]=1.06, 95% CI 1.04 to 1.08), salty dietary preference (aHR=1.53, 95% CI 1.01 to 2.33), smoking behaviour (aHR=1.77, 95% CI 1.11 to 2.81), abnormal level of body mass index (aHR=1.07, 95% CI 1.01 to 1.12), and suboptimal blood pressure control (aHR=1.48, 95% CI 1.02 to 1.94).
Conclusion(s): Our study suggests that hypertensive patients in the primary care setting in China should be monitored closely for preventing secondary CCDs, especially for those who have risk factors of CCDs identified in the present study.

P6424 | BEDSIDE
Periodontitis - independent contributor to risk of myocardial infarction - a report from the PAROKRANK study

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Background: The relation between periodontitis (PD) and cardiovascular disease (CVD) is debated. Inflammatory activation accelerates the progression of atherosclerosis and increases the risk for plaque rupture and thrombotic occlusion leading to acute myocardial infarction (MI). PD, a tissue destructive inflammatory oral disease, is common in patients with CVD. The two conditions share many risk factors, but it has been postulated that PD per se is independently related to cardiovascular events.
The objective of the Swedish multicenter study PAROKRANK was performed to test this hypothesis.
Methods: A total of 805 patients (age <75 years) with a first MI and 805 age (mean 62±8), gender (male 81%) and geographically area matched controls without MI underwent a standardized dental examination including panoramic x-ray at 17 Swedish hospitals. Information on disease related risk and health factors (≈100 variables) were collected. Blood lipids, glucose and inflammatory biomarkers were analysed and participants without known diabetes were investigated with an oral glucose tolerance test. Saliva and microbial plaque samples were harvested. X-rays were analyzed at a core centre. Radiographic bone loss categorized participants as: healthy (≥80% remaining bone), mild to moderate PD (79–66%) or severe PD (<66%). Statistical comparisons were performed by t-test for continuous and Chi-square tests for categorical variables. Odds Ratios (95% CI) were calculated by logistic regression, crude and adjusted for confounders (smoking and marital status). A two sided $p<0.05$ was considered significant.
Results: PD was more common (42%) in patients than in controls (33%; $p<0.001$). There was an increased risk for MI among those with PD with a crude OR 1.5 (95% CI: 1.2–1.8; $p<0.001$). There were no significant baseline differences between the two groups apart from a family history of CVD in 38% of patients vs. 23% in controls ($p<0.001$) and smoking in 26 vs. 12% ($p<0.001$). The corresponding risk for MI after adjusting for confounders was 1.3 (95% CI: 1.0–1.6; $p<0.05$).
Conclusion: In this large, prospective case-control study of PD, verified by radiographic bone loss, the risk of a first MI was increased in subjects with PD and the risk remained after adjustment for confounding factors suggesting an independent relationship between PD and MI.
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P6425 | BEDSIDE
NT-proBNP as a predictor of calcified coronary atherosclerosis progression

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Background: Coronary calcium score (CCS) is a well validated index of subclinical atherosclerosis with high negative predictive value in patients with intermediate risk and low/absent CCS. Predictors of CCS progression are not well understood, as traditional coronary risk factors show a low relation with CCS progression. Cardiac natriuretic peptides have been recently indicated as possible biomarkers of vascular remodeling beyond the presence of cardiac anomalies and have been associated with the amount of CCS. We analyzed the hypothesis that NT-proBNP could be also a predictor of CCS progression.
Methods: We analyzed 601 middle aged subjects without previous cardiovascular events and a baseline value of CCS <100 Agatson Unit (A.U.) from the screening program of the Montignoso Heart and Lung Project. These subjects underwent a second computed tomography (CT) scan 3 years after basal CT, risk factor assessment, laboratory testing comprehensive of NT-proBNP, echocardiography. Glomerular filtration rate (GFR) was estimated with the Crockoft Gault formula. To evaluate predictors of CCS progression, subjects were divided according to CCS > or <100 at the follow-up CT.

Results: Mean age of our population was 64±6 (range 45–77) with a mean 10 years Framingham risk Score of 8.39±3.1% configuring an intermediate risk population. CCS progression occurred in 51 subjects (8%). Compared to participants without progression, those with CCS progression were older (66±6 y.o.vs. 63±6 y.o.) and had lower glomerular filtration rate (89.63±22.2 ml/min vs. 89.6±22.2 ml/min p<0.05) and higher NT-proBNP (94;49–117ng/L vs. 59; 31- 111 ng/L, p<0.05), without significant differences in mean Framingham risk score (9.14±3.4% vs. 8.3±3.1%, p=0.103). At multivariate analysis NT-proBNP predicted CCS (O.R. 1.613, 95% C.I. 1.060–2.60) independently by GFR, age, Framingham risk score and cardiac left ventricular indexed mass at echocardiography. The area under the curve for NT-proBNPat the ROC curve for CCS prediction was 0.610 (95% C.I. 0.54–0.71).
Conclusion: Among middle-aged subjects without previous cardiovascular events, NT-proBNP is a significant predictor of CCS over 3 years beyond traditional risk factors, suggesting the role of cardiac natriuretic peptides as a possible index of vascular remodeling.

P6426 | BEDSIDE
Impact of delay to reperfusion on infarct size and clinical outcomes in patients with ST-segment myocardial infarction

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Background: Longer delay from symptom onset to reperfusion has been associated with increased mortality and worse clinical outcome in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI). The mechanism underlying this association is not entirely clear. We aimed to evaluate the impact of the delay from symptom onset to reperfusion (<3h vs. ≥3h) on infarct size and clinical outcomes at 30 days in patients with STEMI treated with PPCI.
Methods: We analyzed 482 consecutive patients presenting to a tertiary care hospital with STEMI who underwent PPCI between July-2012 and April-2014. Peak CK, a measure of infarct size, and the incidence of major adverse events (defined as the composite of death, re-infarction or clinically driven target-vessel revascularization) and major bleeding (defined as BARC type≥3) at 30 days were compared between 2 groups of patients regarding time from symptom onset to reperfusion, classified as <3h vs. ≥3h.
Results: There were 249 (52%) patients with <3h delay and 233 (48%) with ≥3h delay. Patients with longer delay were significantly older; anticoagulant/antiplatelet treatment and baseline TIMI flow were similar in both groups. Patients with shorter delay had significantly smaller enzymatic infarct size, higher rates of final TIMI 3 flow and lower rates of the composite of major adverse events. Major bleeding rates were similar in both groups.

Impact of the delay to reperfusion

	Total (n=482)	Time to reperfusion <3h, n=249 (52%)	Time to reperfusion ≥3h, n=233 (48%)	p
Peak CK (UI/L)		1870	2290	0.02
Final TIMI 3 flow		229 (92%)	184 (79%)	<0.01
Ischemic MACE (death, re-MI, TVR)	42	16 (6.4%)	26 (11.1%)	0.06
Major bleeding BARC ≥3	19	8 (3.2%)	11 (4.7%)	0.5
Composite of major adverse events (ischemic and bleeding)	58	23 (9.2%)	35 (15%)	0.04

Conclusion: In patients with STEMI undergoing PPCI, longer delay to reperfusion negatively impacts clinical outcome. This effect appears to be mediated by less successful reperfusion and by a larger infarct size.

P6427 | BEDSIDE
Consistent reductions in atherogenic lipid parameters with the PCSK9 inhibitor alirocumab in patients not receiving background statin

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Background: The benefit of lipid-lowering therapy (LLT) on reducing cardiovascular (CV) risk is determined by the absolute reduction in atherogenic lipoproteins.
Objective: To determine pooled efficacy of alirocumab (ALI) in the absence of background statin on lipoprotein levels from two 24-week ODYSSEY trials.
Methods: Data were pooled from ALI and EZE groups in MONO (n=52 ALI, n=51 EZE) and ALTERNATIVE (n=126 ALI, n=125 EZE; atorvastatin control group was not included). MONO included patients with a SCORE 10-year calculated risk ≥1% and <5% of fatal CV events, not on any background LLT. ALTERNATIVE included patients with statin intolerance, and CHD/other CV risk factors; 37–44% of patients were on LLT other than statin/EZE. Mean baseline LDL-C levels were 3.6 mmol/L (139.7 mg/dL) and 4.9 mmol/L (191.3 mg/dL), respectively. Both studies compared ALI 75 mg (subcutaneous 1-mL injection) every 2 weeks (Q2W) vs. EZE 10 mg/day. ALI dose increased to 150 mg Q2W (also 1-mL) at Week (W) 12 in ALTERNATIVE if W8 LDL-C level was ≥1.81/2.59 mmol/L (≥70/100 mg/dL; depending on CV risk), and in MONO if W8 LDL-C level was ≥1.81 mmol/L.
Results: Alirocumab dose was increased from 75 to 150 mg Q2W at Week 12 in 49.5% of patients in ALTERNATIVE and 30.4% in MONO. Pooled data indicate statistically significant reductions in LDL-C, Apo B, non-HDL-C and Lp(a) (Table) for ALI vs. EZE. At W24, and vs EZE, ALI reduced LDL-C, Apo B, non-HDL-C, Lp(a) and fasting triglycerides from baseline by 30.9%, 25.3%, 25.7%, 14.4% and 4.3%, respectively. Treatment-emergent adverse event (TEAE) rates were generally similar between ALI and EZE patients. Common TEAEs in ALI-treated patients were influenza, headache and injection site reactions.
Conclusions: Alirocumab demonstrated substantial (>1.0 mmol/L [38.7 mg/dL]) reductions in atherogenic lipoproteins vs EZE in patients without background statin.
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P6428 | BEDSIDE
Cardio- and reno-protective effect of remote ischemic preconditioning in patients undergoing percutaneous coronary intervention. A prospective, non-randomized controlled trial

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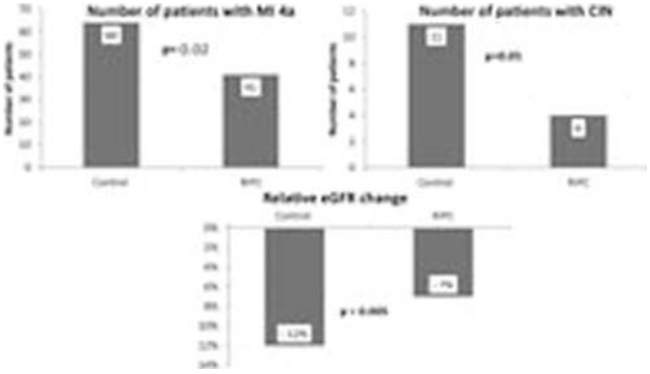
Background: Myocyte necrosis and contrast induced nephropathy (CIN) occurs frequently in elective percutaneous coronary intervention (PCI) and is associated with subsequent cardiovascular events.
Purpose: This study assessed the cardio- and reno-protective effect of remote ischemic preconditioning (RIPC) in patients undergoing elective PCI.
Methods: Two hundred consecutive patients undergoing elective PCI with normal baseline troponin-I (cTnI) values were recruited. Subjects were systematically allocated into 2 groups: 100 patients received RIPC (created by three 5-minute inflations of a blood pressure cuff to 200 mmHg around the upper arm, separated by 5-minute intervals of reperfusion) <2 hours before the PCI procedure, and the control group (n=100). The primary outcome was Incidence of PCI- related myocardial infarction (MI 4a) at 24 hours after PCI (defined as cTnI >0.20 ng/mL). Secondary outcome was incidence of CIN at 72 hours after contrast exposure.
Results: The incidence of MI 4a was lower in the RIPC group compared with the control group. Subjects who received RIPC had significant trend toward lower incidence of CIN and less chest pain during stent implantation compared to control group. No significant deference in the mean change of CRP was noted between both groups. At 3 month, the major adverse event rate was lower in the RIPC group (6 vs. 14 events; P=0.04).



Conclusions: The use of RIPC <2 hours before PCI, reduce the incidence of PCI-related MI 4a, tend to decrease the incidence of CIN and improve ischemic

Abstract P6427 – Table 1. Effect on mean lipoprotein levels

Absolute change, mmol/L [mg/dL]	Baseline ALI vs. EZE	W12 absolute change ALI vs. EZE	W12% change ALI vs. EZE	W24 absolute change ALI vs. EZE	W24% change ALI vs. EZE
LDL-C	4.6 vs 4.6 [176.5 vs 177.7]	–2.1 vs –0.8* [–82.8 vs –31.4]	–47.4 vs –16.7*	–2.1 vs –0.8* [–79.2 vs –29.8]	–45.6 vs –14.8*
Apo B	[131.5 vs 128.0]	[–47.7 vs –16.4*]	–36.5 vs –11.6*	[–47.8 vs –16.0*]	–36.5 vs –11.2*
Non-HDL-C	5.5 vs 5.5 [211.7 vs 210.8]	–2.3 vs –0.9* [–88.1 vs –36.2]	–41.9 vs –16.0*	–2.2 vs –0.9* [–84.8 vs –34.3]	–40.4 vs –14.7*
Lp(a)[a]	[31.6 vs 31.5]	[–3.9 vs –1.7*]	–20.1 vs –7.3*	[–6.1 vs –4.5*]	–23.3 vs –8.9*
Fasting triglycerides[a]	1.9 vs 1.8 [170.2 vs 156.3]	–0.2 vs –0.2 [–22.0 vs –20.6]	–9.3 vs –7.4	–0.3 vs –0.2 [–24.9 vs –20.3]	–10.3 vs –6.0

ALI, alirocumab; EZE, ezetimibe. [a]Medians shown for absolute change and adjusted means are shown for % change. *P<0.0001 vs EZE.

symptoms in patients undergoing elective PCI. The observed cardio- and renoprotection appears to confer sustained benefit on reduced MAE at 3 month followup.

P6429 | BEDSIDE
Prognostic value of coronary CT imaging in high-risk patients without symptoms of coronary artery disease

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Background: At present, traditional risk factors are used to guide cardiovascular management of asymptomatic individuals. Intensified surveillance may be warranted in those identified as high risk of developing cardiovascular disease (CVD).
Purpose: This study aims to determine the prognostic value of coronary CT angiography (CCTA) next to coronary artery calcium scoring (CACS) in high CVD risk patients without symptoms suspect for coronary artery disease (CAD).
Methods: A total of 665 high-risk patients (mean age 56±9 years, 417 males), having at least one important CVD risk factor (diabetes mellitus, or familial hypercholesterolemia) or a calculated European Systematic Coronary Risk Evaluation of >10% were included from outpatient clinics at two academic centres. Follow-up was performed for the occurrence of adverse events including all-cause mortality, non-fatal myocardial infarction, unstable angina or coronary revascularization.
Results: During a median follow-up of 3.0 (interquartile range 1.3–4.1) years, adverse events occurred in 40 (6.0%) individuals. By multivariable analysis, adjusted for age, gender and CACS, obstructive CAD on CCTA (≥50% luminal stenosis) was a significant predictor of adverse events (hazard ratio 5.9 [confidence interval 1.3 - 26.1]). Addition of CCTA to age, gender, plus CACS, increased the C-statistic from 0.81 to 0.84 and resulted in a total net reclassification index of 0.19 ($p<0.01$).
Conclusions: CCTA has incremental prognostic value and risk reclassification benefit beyond CACS in patients without CAD symptoms but with high risk of developing CVD. Whether CCTA based patient management will improve clinical outcome remains to be determined.

P6430 | SPOTLIGHT
Carotid intima-media thickness and aortic stiffness index are increased in normal healthy subjects with parental history of diabetes mellitus

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Background: Previous studies have shown that high HbA1c concentrations considered within the "normal range" may detect individuals with increased propensity for developing type 2 diabetes mellitus in the near future. Available information has also suggested that in the general population, high HbA1c concentrations may detect individuals at higher risk for cardiovascular mortality. However, little is known whether a non- diabetic subject with a family history of diabetes is at high risk for vascular damage or not. The aim of the present work was to evaluate the arterial status of healthy offspring of diabetic patients.
Methods: Fifty-six healthy subjects with parental history of diabetes were compared with fifty-six, age and sex-matched, healthy subjects without parental history of diabetes. Age, sex, body mass index, smoking habits, blood pressure, HbA1c, lipid profile were measured. Carotid intima-media thickness was measured by high-resolution B-mode ultrasound imaging, and aortic stiffness index was measured by M-mode echocardiography.
Results: HbA1c level, carotid IMT and aortic stiffness index were significantly higher in subjects with parental history of diabetes than in subjects without parental history of diabetes (5.6±0.38 vs. 5.42±0.33, P=0.009; 0.66±0.09 vs. 0.56±0.09, $P<0.001$; 5.12±2.36 vs. 3.52±1.51, $P<0.001$, respectively). In all healthy subjects, HbA1c level was positively correlated with Aortic stiffness index ($r=0.235$, P=0.013) and carotid IMT ($r=0.289$, P=0.002). Also we found a positive correlation between CCA IMT and Aortic stiffness index ($r=0.685$, $p<0.001$).
Conclusions: This study demonstrated that the CCA IMT and aortic stiffness index are significantly higher in subjects with parental history of diabetes compared with subjects without parental history of diabetes. Therefore, these findings suggest that glycemic control might have a pathophysiological relevance in the development of vascular disease, even in individuals without diabetes.

P6431 | BEDSIDE
Predictive and protective values of high-density lipoprotein cholesterol for cardiovascular events in statin-treated patients with acute myocardial infarction

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Purpose: A low level of high-density lipoprotein cholesterol (HDL-C) has been identified as a residual risk of cardiovascular events after lowering low-density lipoprotein cholesterol (LDL-C) in patients with stable coronary artery disease. Furthermore, a high HDL-C level is proven to have a protective effect for cardiovascular events in primary prevention studies. We evaluated whether the HDL-C level has predictive and protective values in patients with acute myocardial infarction (MI) following percutaneous coronary intervention (PCI) and statin treatment.
Methods: A total of 15,290 patients who had acute MI and statin treatment were selected from a nationwide MI registry. Baseline HDL-C level was used to identify patients with low HDL-C (Group A), normal HDL-C (Group B), or high HDL-C (Group C) levels according to the ATP-III criteria. The primary endpoint, defined as the composite of cardiovascular death and recurrent MI, was compared the between the groups both in the propensity adjusted and matched cohorts.
Results: At the median follow-up of 11.5 months, the primary endpoint occurred 2.7% (112/4098) in Group A, 1.4% (54/3910) in Group B, and 1.2% (8/661) in Group C. In the propensity adjusted cohort, low HDL-C level was associated with an increased risk of primary endpoint (hazard ratio [HR] 1.755, 95% confidence interval [CI] 1.274–2.417, p=0.001) and high HDL-C level was not associated with a reduced risk of primary endpoint (HR 0.562, 95% CI 0.275–1.146, p=0.113). In the propensity matched cohort, low HDL-C level was persistently associated with an increased risk of primary endpoint (HR 1.716, 95% CI 1.210–2.434, p=0.002) and high HDL-C level was associated with a reduced risk of primary endpoint (HR 0.449, 95% CI 0.214–0.946, p=0.035).
Conclusions: In acute MI patients treated with PCI and statins, a low HDL-C level was associated with an increased risk of cardiovascular death and recurrent MI. However, a high HDL-C level was possibly associated with a reduced risk of cardiovascular events, particularly in patients with ST-elevation MI.

P6432 | BEDSIDE
The efficacy of ischemic preconditioning for prevention of contrast medium-induced acute kidney injury

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Background: Contrast medium-induced acute kidney injury (CI-AKI) is a serious complication of angiography. Remote ischemic preconditioning (RPC) may prevent CI-AKI. In this study, we evaluated the effect of RPC for CI-AKI.
Methods: Patients with impaired renal function (serum Cr (s-Cr) >1.4 mg/dL or eGFR <60 mL/min/1.73m^2) undergoing elective angiography were divided to standard care (continuous intravenous saline infusion 12 hours before to 12 hours after angiography 1mL/kg/hr), with (n=34) or without RPC (n=31). RPC was accomplished by performing 4cycles of alternating 5-minute inflation and 5-minute deflation of a standard upper-arm blood pressure cuff. RPC was started before angiography and the time between last inflation and the start of angiography was <45 minutes. The primary end point was the incidence of CI-AKI, defined as an increase in s-Cr ≥25% or ≥0.5 mg/dL above baseline at 48 hours after angiography. We also measured serum cystatin C (s-cysC) at baseline and 48 hours after angiography. More than 60 mL of contrast medium was used in all patients.
Results: There were no significant difference of amount of contrast medium between control group and RPC group (control group 105±51mL versus RPC group 89±22mL). CI-AKI occurred in 4patients (6%), 4 (13%) in the control group and 0 (0%) in the RPC group ($P<0.05$). The change of s-cysC from baseline to 48hours after angiography was not different between 2groups. No major adverse events were related to remote ischemic preconditioning.
Conclusions: RPC before angiography prevents CI-AKI in high-risk patients.

P6433 | BEDSIDE
Long-term anti-hypertensive treatment with amlodipine/perindopril results in lower carotid IMT at 3.5 years than with atenolol/bendroflumethiazide

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Introduction: Carotid Intimal Medial Thickness (CIMT) can identify patients at elevated risk of cardiovascular disease. It is an independent predictor of risk of myocardial infarction, stroke and cardiovascular death. The Anglo Scandinavian Outcomes Study (ASCOT) enrolled 19,257 patients in seven countries (UK, Ireland, Norway, Sweden, Denmark, Finland and Iceland) with elevated cardiovascular risk without established cardiovascular disease. Participants were randomly allocated to receive combination anti-hypertensive therapy with atenolol ± bendroflumethiazide or amlodipine ± perindopril. Its Hypertension-Associated Cardiovascular Disease (HACVD) sub-study collected detailed cardiovascular phenotypic data from 1,006 participants at two centres in London and Dublin.
Purpose: We hypothesised that anti-hypertensive therapy with the amlodipine ± perindopril-based regimen would result in a lower burden of carotid atherosclerotic disease evidenced on CIMT.
Methods: Data were collected in two phases, ~1.5 years and ~3.5 years post-randomisation to treatment assignment at each HACVD site. Participants allo-

cated to either regimen underwent conventional CIMT measurement following a standardised study protocol.
Results: Nine hundred and nineteen patients had complete data available for analysis at the point of completion. Baseline characteristics were evenly matched across each of the treatment groups. Treatment with amlodipine±perindopril resulted in lower CIMT than in the atenolol±bendroflumethiazide group at 1.5 years (0.801mm ± 0.185 SD vs. 0.844mm ± 0.196, P<0.001) and subsequently at 3.5 years (0.873mm ± 0.192 vs. 0.823±0.183).
Conclusion: Long-term treatment with an anti-hypertensive regimen using amlodipine ±perindopril results in significantly lower CIMT than with atenolol ± bendroflumethiazide.

UPCOMING RISK FACTORS

P6434 | BEDSIDE
Prevalence and determinants of exercise oscillatory ventilation in a population at cardiovascular risk enrolled in the EUROEX trial

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Background: Cardiopulmonary exercise testing (CPET) with gas exchange analysis allows functional evaluation of cardiopulmonary diseases and definition of ventilatory and metabolic parameters that may add to define the level of cardiovascular (CV) risk. Among CPET-derived variables, the occurrence of exercise oscillatory ventilation (EOV), a pathological ventilatory pattern, in the general population at risk for CV diseases is not described in literature. We aimed at assessing the prevalence of EOV in a general population enrolled in the EUROEX study.
Methods: 599 healthy subjects (60±14 years; male 48.4%; BMI 28±6 kg/m^2) underwent a maximal CPET with personalized incremental ramp protocol. Subjects had different CV risk factors, but no previous CV events. A subgroup (n=230; 62±13 years; male 48.7%; BMI 29±5 kg/m^2) also underwent echocardiography within 6 months.
Results: A prevalence of 15.9% EOV was observed. The EOV group showed higher prevalence of diabetes (25 vs 14%, p<0.05) and female sex (71 vs 47%, p<0.05). EOV patients showed reduced exercise tolerance (workload 109±46 vs 121±49 W, p<0.05), impairment of oxygen consumption (VO2)-related variables (peak VO2 15.1±3.8 vs 20±7.2 ml/min/kg, p<0.01) and worse ventilator efficiency (VE/VCO2 slope: 27.7±4.6 vs 25.7±3.6; peak PETCO2: 36.5±4.5 vs 39.1±4.3 mmHg, p<0.01); a lower heart rate at peak exercise (125±21 vs 135±23 bpm, p<0.01) and heart rate recovery (14±9 vs 16±9 beats, p<0.05). Echocardiographic data showed a reduction of end-systolic dimensions of both ventricles (LV ESVi: 13.5±4 vs 15.5±6 ml/mq, p<0.05; RV ESA: 6.9±1.6 vs 7.8±2 cmq, p=0.01)and right atrial area (14.8±4 vs 16.8±4 cmq, p<0.01) in the EOV group. At a multivariate analysis the EOV determinants were TAPSE, E/A and BMI.

EOV determinants	OR	P value
TAPSE, mm	0.16	0.03
BMI, kg/mq	0.07	0.04
E/A	1.12	0.09

Conclusion: EOV subjects exhibited a higher prevalence of diabetes, worse exercise performance and ventilation efficiency. EOV determinants in this population were an index of RV systolic function, LV diastolic function and BMI. These findings may provide the bases for a more in-depth definition of abnormal exercise phenotypes in the prediction of CV risk.

P6435 | SPOTLIGHT
New indexes of cardiovascular risk: relationship between epicardial and pericardial fat thickness

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Purpose: It is well known the role of epicardial fat thickness in the stratification of cardiovascular risk. Little is reported in literature about pericardial fat. We aimed to establish a relationship between pericardial and epicardial fat and cardiovascular risk stratification.
Methods: We enrolled 177 patients (mean age 44) without significant valvular disease, with normal ejection fraction (FE >55%) and acoustic window suitable for the evaluation of epicardial and pericardial fat. All patients were subjected to an anamnestic and clinic evaluation for the detection cardiovascular risk factors and previous cardiovascular events. The epicardial and pericardial fat was evaluated in end-systole in the parasternal long axis view in three consecutive cardiac cycle. The whole population was divided in two group, similar for age and gender, basing on thickness of epicardial fat (EFT) according with literature. Group A (n=89) with normal EFT <7 mm and group B (n=88) with altered EFT>7 mm.
Results: In group B average value of pericardial fat thickness was 8,1 vs 5,5 mm in group A, average EFT was 8,3 mm in group B and 5,1 mm in group A (r=0,444; p<0,001) demonstrating a direct correlation between epicardial and pericardial fat thickness. average body mass index was 33 in group B and 26 in group A (p=0,02). group B presented a higher prevalence of cardiovascular risk factors compared to group A. Hypertension was 40,4% vs 27,2% (p<0,01). Diabetes was 11,2% vs 4,5% (p=0,03), dyslipidemia was 34% vs 17% (p<0,01); presence of at least one risk factor was 40,5%vs 28,4% in group B and group A respectively (p=0,005) Left ventricular diastolic dysfunction was also evaluated (E ' <8 and atrial enlargement). in group B 72% of patients presented this alteration vs 45% in group A (p<0,001).
Conclusions: Our study confirms that the epicardial fat, a simple parameter to be measured during a standard echocardiographic examination, adds information about cardiovascular risk. Nevertheless pericardial fat shows to be similar to EFT in evaluation of risk profile, with the same increase and similar cut-off; the association with left ventricular diastolic dysfunction could play an important role in early stratification of these patients.

P6436 | BEDSIDE
Simultaneously measured inter-arm & inter-leg systolic blood pressure differences and cardiovascular risk stratification: A systemic review and meta-analysis

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Background: Association of inter-arm systolic blood pressure difference (IASBPD) with cardiovascular (CV) morbidity and mortality remains controversial.
Purpose: We aimed to thoroughly examine all available evidence on inter-limb blood pressure difference and its association with CV risk and outcomes.
Methods: We searched PubMed, Embase, CINAHL, Cochrane library and Ovid for studies reporting bilateral simultaneous blood pressure measurements in arms or legs and risk of peripheral arterial disease (PAD), coronary artery disease (CAD), cerebrovascular disease, subclavian stenosis or mortality. Random effect meta-analysis was performed to compare effect estimates.
Results: Twenty seven studies met inclusion criteria but only 17 studies (18 cohorts) were suitable for analysis. IASBPD of 10 mmHg or more was associated with PAD (RR 2.22, 1.41–3.5; p=0.0006; sensitivity 16.6%, 6.7–35.4; specificity 91.9%, 83.1–96.3; 8 cohorts; 4,774 subjects), left ventricular mass index (SMD 0.21; 0.03–0.39; p=0.02; 2 cohort; 1,604 subjects) and carotid and brachial-femoral pulse wave velocities (SMD 0.25, 0.03–0.47; P=0.03; 3 cohorts; 2649). Association of PAD remained significant at cut off of 15 mmHg (RR 1.91; 1.28–2.84; p=0.001; 5 cohorts; 1,914 subjects). We could not find statistically significant direct association of CAD, cerebrovascular disease, CV and all-cause mortality in subjects with IASBPD of 10 mmHg or more, 15 mmHg or more and inter-leg systolic blood pressure difference of 15 mmHg or more. Inter-leg blood pressure difference of 15 mmHg or more was strong predictor of PAD (P=0.0001) and brachial-ankle pulse wave velocity (P=0.0001). Two invasive studies showed association of IASBPD and subclavian stenosis (estimates couldn't be combined).
Conclusions: Inter-arm and leg blood pressure differences are associated with PAD, subclavian stenosis, high left ventricular mass effect and higher brachial-ankle pulse wave velocities. A BP difference of more than 10 or 15 mmHg is predictive of occlusive vascular disease, however lack of BP difference is less informative. Inter-arm and inter-leg BP difference measurements are inexpensive tools which can help clinicians in cardiovascular risk stratification of the patients.

P6437 | BEDSIDE
Surgical and pharmacological reassignment influence on transsexuals cardiovascular risk profile

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Aim: To evaluate the cardiovascular effects and to stratify early cardiovascular risk in transsexual subjects undergone pharmacological and/or surgical gender reassignment. We stratified early cardiovascular risk in transsexual patients who underwent sexual reassignment surgery or only hormone replacement therapy.
Methods and results: We enrolled 56 transsexual patients: 6 undergone female-to-male (FtM) reassignment surgical therapy, 16 not-operated FtM, 13 operated male-to-female (MtF) and 21 non-operated MtF subjects. All underwent anthropometric, laboratory and instrumental [carotid artery intima-media thickness (C-IMT) and flow mediated vasodilation (FMD) of brachial artery] evaluations. We compared operated versus hormone replacement therapy (HRT) patients. We distinguished: group 1-transsexual patients who underwent gonadectomy (orchiectomy for MtF subjects and hystero-annessiectomy for FtM subjects); group 2- transsexuals only treated with HRT (estrogens and anti- androgens for MtF subjects and androgens for FtM subjects). Our results showed a statistically significant difference (p<0.0001) between group 1 and 2 patients according to FMD values. FMD percentage (%) in patients who underwent gonadectomy was lower than not- surgically treated patients, who take only hormone replacement therapy (5.711 in Group 1, 7.339 in Group 2, respectively). Mean C-IMT values were higher in gonadectomized patients than in no-operated patients one (0.733 in Group 1; 0.582 in Group 2). The duration of hormone therapy correlates positively with mean C-IMT (B=0.001) and negatively with FMD (%) (B=–0.007).
Conclusions: Cardiovascular risk, which is expressed in terms of endothelial (FMD) and morphological (C-IMT) dysfunction, increases in subjects undergoing gonadectomy as compared to those receiving cross sex reassignment therapy

alone. Previous sex does not affect the results. Therefore, a protective role of the gonads might be suggested.

P6438 | BEDSIDE

The mediating effect of adherence to Mediterranean diet on the association between fibrinogen and 10-year cardiovascular disease risk: Results Of The 10-year Follow-up of the ATTICA study (2002-2012)

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Objective: Thrombosis markers such as fibrinogen have been associated with increased cardiovascular disease (CVD) risk and are usually managed with pharmaceutical ways. On the other hand, adherence to Mediterranean diet is a widely accepted protective habit against CVD, but mainly though the management of CVD risk factors. Few studies have recently revealed a potential antioxidant and antithrombotic role of Mediterranean diet that needs further research. The aim of the present study was to investigate this role under the prospective design of the ATTICA study.
Methods: The study sample were the volunteers of the ATTICA study (that included information from 1514 men and 1528 women). At baseline, the fibrinogen levels were measured, as well as assessment of dietary habits was based on the MedDietScore, that evaluates adherence to Mediterranean diet. In 2012, the 10-year follow-up was performed in 2009 participants and development of CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria.
Results: The 10-year incidence was 19.7% in men and 11.7% in women ($p<0.001$). Unadjusted analysis showed that increased fibrinogen levels increased CVD risk (Relative Risk (RR) per 1 mg/ml = 1.006, 95%Confidence Intervals (CI):1.003, 1.008). After adjusting for age, gender, history of diabetes mellitus, hypertension and hypercholesterolemia, smoking, family history of CVD the association remained significant (RR=1.003, 95% CI: 1.000,1.006, p=0.05), but when adherence to Mediterranean diet was included, the association regained significance (RR=1.002, 95% CI: 1.000,1.004, p=0.045), and thus, stratified analysis according to MedDietScore tertiles revealed that increased fibrinogen levels were significantly promoting CVD only among subjects that were away of the Mediterranean dietary pattern, but lost significance as regards to subjects that were close and very close to Mediterranean diet.
Conclusion: Adherence to Mediterranean dietary pattern might have an important antithrombotic effect apart from other beneficial effects against CVD risk. Promotion of Mediterranean diet could be an important target for public health strategies, especially under the emerging need for reducing the CVD prevention cost.

P6439 | BEDSIDE

Living alone and depressive symptoms are associated with major cardiovascular events in patients with chronic coronary heart disease

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Background: There is evidence from population-based and observational studies linking psychosocial stress, such as emotional stress and depression, to risk of coronary heart disease (CHD) and mortality. Patients with previous myocardial infarction report a higher degree of depressive symptoms, stress at work and at home, and financial strain. However, most studies evaluating psychosocial stress have assessed its association with risk for CHD in the general population.
Purpose: The aim of the analysis was to describe the association between patterns of self-reported psychosocial stress and cardiovascular (CV) outcomes in patients with chronic CHD.
Methods: The STabilization of Atherosclerotic plaque By Initiation of darapLadIb TherapY (STABILITY) trial randomized 15,828 patients with chronic CHD in 39 countries. At baseline, data on CHD risk factors were obtained from 15,456 patients completing a lifestyle questionnaire with specific information on: level of (never, sometimes, often, always) depressive symptoms; home, work and financial stress; home- and work-related sense of control; and if the subject was living alone. Psychosocial stress variables were analysed with multivariable Cox proportional hazards models, per category change, related to major adverse cardiovascular event (MACE; CV death, non-fatal myocardial infarction, non-fatal stroke) during a median of 3.7 years of follow-up, adjusted for CV risk factors, co-morbidities, prior diseases and education.
Results: Increased risk of MACE occurred in patients reporting feeling down (HR 1.14, 95% CI 1.06–1.23), lost interest in hobbies (HR 1.11, 95% CI 1.04–1.18) or experienced financial stress (HR 1.11, 95% CI 1.04–1.18). No significant evidence of a relationship was observed for home-related stress (HR 1.06, 95% CI 0.99–1.14), home- (HR 0.99, 95% CI 0.94–1.04) or work-related lack of control (HR 0.96, 95% CI 0.81–1.13). Of the patients, 52.4% were working and 47.6% were retired or did not work for other reasons such as unemployment. Among employed patients, stress at work was associated with a lower risk of MACE (HR 0.82, 95% CI 0.69–0.98) compared to those reporting no stress. Patients living alone had a higher risk of MACE (HR 1.28, 95% CI 1.11–1.48).
Conclusion: Financial stress, depressive symptoms and living alone were associated with an increased risk for ischaemic events and death. These findings suggest a need for additional support in patients with chronic CHD. Conversely to prior data, self-reported work-related stress was associated with improved prognosis. This finding warrants further investigation.
Acknowledgement/Funding: The STABILITY study was funded by GlaxoSmithKline

P6440 | BEDSIDE

Marital status is associated with a prevalence of metabolic syndrome in men based on the 2013 Korean National Health Examination and Nutrition Survey

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Objective: This study aims to investigate the gender-specific associations between socioeconomic status and metabolic syndrome (MetS) in Korean adults.
Methods: We examined the relationship between socioeconomic status and the prevalence of MetS in 4,689 Korean adults aged 20 to 79 years (2,024 men and 2,665 women) who participated in the 2013 Korean National Health Examination and Nutrition Survey. Occupation status was classified as none, manual, nonmanual based on a self-reported questionnaire. Marital status was classified as single, married, divorced, and widowed. A modified Asian criterion based on a harmonized definition of MetS was adopted. Adjusted odds ratios (ORs) for MetS were calculated using multiple logistic regression models.
Results: The prevalences of MetS in men and women were 30.9% and 24.8%, respectively. Significant differences in the association between marital status, occupational status, household income, education, and MetS were found between males and females. Compared with the married men, the ORs (95% CIs) for MetS in single and divorced men were 0.447 (0.310–0.645) and 1.612 (1.018–2.554), respectively after adjusting for covariates such as age, smoking status, alcohol drinking, and exercise status. However, in women, there was no significant association with marital status and MetS. Compared with the lowest household income group and the lowest educated group (<7 years) in women, the ORs for MetS in the highest income and the highest educated group (>12 years) were 0.631 (0.461–0.864) and 0.460 (0.315–0.670), respectively.
Conclusions: Marital status was significantly related to the prevalence of MetS in men, but not in women. Economy and education status was related to the prevalence of MetS in women, but not men. These findings suggest that gender-specific public health interventions that consider socioeconomic status are needed for targeting MetS prevention and treatment.
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P6441 | BEDSIDE

The role of uric acid as early marker carotid atherosclerosis in subjects without cardiovascular disease

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Recent studies have suggested that hyperuricemia is a risk factor for cardiovascular disease in the general population. Carotid intima-media thickness (C-IMT) measured noninvasively by ultrasonography is now widely used as a surrogate marker for atherosclerotic disease and directly associated with increased risk of cardiovascular disease.
Objective: We aimed to investigate whether elevated serum uric acid (SUA) concentrations are associated with higher risk of carotid atherosclerosis in patients without cardiovascular disease.
Methods: The study included 136 participants, without manifested cardiovascular disease (mean age 66,07±11,2 years, 82 (60%) women). For all patients was determined: presence of risk factors for cardiovascular disease (hypertension, hyperlipidemia, smoking, diabetes, obesity, age), SCORE risk, laboratory analysis and anthropometric measurements. The carotid artery intima-media thickness (C-IMT) and carotid atherosclerotic plaques were measured by B-mode ultrasound.
Results: The patients were divided into 2 groups according to level serum uric acid. The first group (I) consisted of subjects with normal SUA, n=95 (69,85%), the second (II) group patients with elevated level SUA, n=41 (30,15%). The average value of SUA level was 289,86μmol/L ±55,24 in the first group vs. 443,41μmol/L ±58,77 in the second group ($p<0,0001$). Patients with high SUA had significantly higher maen age (p=0,058), average number of risk factors (p=0,03), SCORE risk (p=0,005), body mass index (p=0,002), the prevalence of diabetes ($p<0,005$). C-

IMT were significantly higher in the second group compared to the first group (1,00±0,21 vs 0,81±0,16, p<0,0001). The high C- IMT values (>0.90mm) were observed in 68% patients in II group vs 20% in I group, p<0,0001. Patients with elevated SUA had more frequently one or more carotid plaques (p=0,003). Also, they had a higher average number of carotid plaques (p<0,0001) and percentage of stenosis ((p<0,0001). In the first group, plaques were mostly fibrous (30.0%), followed by fibrocalcified (17%) and calcified (7%), in the second plaques were mostly fibrocalcified (36,6%). After multiple linear regression analysis, SUA levels were identified to be independently correlated with C-IMT (R=0.34; p<0.001); number of carotid plaques (R=0.25; p=0.003); percentage of stenosis (R=0.22; p=0.017); characteristic of plaque (R=0.26; p=0.024).
Conclusions: There is an association between elevated serum uric acid concentrations and subclinical carotid atherosclerosis in patients without clinically evident cardiovascular disease.

P6442 | BEDSIDE
Relation between parameters of arterial stiffness and endothelial function among patients with and without severe periodontal disease

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Introduction: Periodontal disease has been described as playing a role in the atherosclerosis process, and its relation with intimal thickness and vascular endothelial function has been investigated.
Purpose: To determine whether there are differences in parameters of arterial stiffness and endothelial function between patients (P) with and without severe periodontal disease (SPD).
Methods: Patients referred to School of Dentistry, University of Buenos Aires-Argentina were assessed. All P gave their informed consent to participate in the study. Demographic characteristics, atherogenic risk factors, and concomitant pathologies were determined. P with known cardiovascular pathology were excluded from the study. Previously calibrated dentists determined gingival-periodontal indexes. Using carotid Doppler ultrasound, a single operator assessed arterial stiffness parameters: compliance (COP), elastic modulus (EM) and β stiffness index (β SI). Vascular endothelial function (EF) was assessed by brachial artery flow-mediated dilatation. The patients were divided into two groups: with and without SPD. Statistical analysis was performed by ANOVA and Pearson's correlation coefficient with an alpha error <0.05 and 95% confidence intervals, using SPSS 20.
Results: Sixty P were included; 60% were women; 25 P were in the group with SPD, and 35 in the group without SPD. Respective results of the studied variables were: age 56.53±17.58 vs 51.12±12.97 years (p:NS), diabetes 8% vs 8.57% (p:NS), hypertension 68.29% vs 54.28% (p:NS), tobacco 8% vs 11.42% (p:NS), hypercholesterolemia 12% vs 14.28% (p:NS), probing depth (PD) 2.53±1.30 (CI95% 1.81–3.25) vs 1.25±0.51 (CI95% 1.31–1.73) p=0.02, clinical attachment level (CAL) 4.80±2.00 (IC95% 3.69–5.91) vs 1.72±0.93 (CI95 1.33–2.11) p=0.001, intimal thickness (IT) 0.10±0.17 (CI95% 0.095–0.11) vs 0.82±0.18 (CI95% 0.074–0.98) (p:NS), COP 2.41±1.32 vs 3.08±1.02 (p=0.004); EM 48.33±12.53 vs 38.86±7.69 (p=0.005); βSI 4.21±1.03 vs 3.64±1.02 (p=0.004); EF 16.13±5.02 vs 22.76±4.50 (p=0.0003). Correlation between: COP and CAL r=–0.60 (p<0.001), EM and CAL r=0.58 (p<0.001), βSI and CAL r=0.66 (p<0.001), EF and CAL –0.59 (p<0.001).
Conclusions: Parameters of arterial stiffness and endothelial function were worse in P with severe periodontal disease, and correlated moderately with clinical attachment level. Correlation with compliance and endothelial function was negative.

P6443 | BEDSIDE
High protein intake supplementation to compensate changes in ventricular repolarization due to 21-days of bedridden immobilization

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Prolonged inactivity induces reduction of lean body and bone mass, glucose intolerance, and weakening of the cardiovascular system. Increased protein intake has been proposed to counteract some of these effects. We aimed at assessing the effects on ventricular repolarization (VR) of supplementing high protein intake (1.2 g/kg/d plus 0.6 g/kg/d whey protein) and alkaline salts (90 mmol KHCO3/d) as countermeasure (CM) during 21-days of head-down (–6°) bed-rest (BR).
Methods: 8 healthy men (mean age 30±5) were enrolled at DLR (Germany) as part of the European Space Agency BR studies in a cross-over design and randomly assigned to dietary CM or isocaloric control (CTRL) first, with wash-out of 4 months between repetitions. High fidelity (1000 Hz) Holter 12-leads ECG was acquired before (PRE), the last day of BR (HDT21), and 4 days after its end (POST). The night period (23:00–06:30) was selected for analysis and vectorcardiogram computed from X,Y,Z leads derived using inverse Kors regression. Selective beat averaging was used to obtain averages of P-QRS-T complexes preceded by the same stable heart rate (10 msec bin amplitude, range 900–1200 msec). For each average, T-wave amplitude (Tmax) and area, RTapex and RTend, R/T amplitude ratio, ventricular gradient (VG) and QRST angle were measured.
Results: BR induced RTapex and RTend shortening, T-wave amplitude and area decreasing, higher R/T and lower VG. At HDT21, when nutritional CM was given, most of the effects seemed reversed. At POST, all parameters restored to their control values.

Results with and without nutritional CM

	PRE	HDT21 CTRL	HDT21 CM
Tmax (microV)	567±118	464±127*	563±186#
T wave area (mV·msec)	71.4±10.7	60.5±21.7*	69.5±22.3#
R-Tapex (msec)	275±17	264±21*	259±20
R-Tend (msec)	383±27	366±22*	359±23#
R/T (a.u.)	2.84±0.42	3.87±1.37*	3.25±0.94#
VG (microV)	77±26	60±28*	98±28#
QRST (angle)	49±28	54±27	50±27

*p<0.05 paired t-test vs PRE, #p<0.05 paired t-test CTRLvs CM.

Conclusions: Sustained reduced gravitational stimulus and immobilization affected VR during the night period. High protein intake supplementation appeared to reverse the majority of the changes, thus decreasing ventricular heterogeneity and arrhythmic risk.
Acknowledgement/Funding: This study has been funded by the Italian Space Agency (contract 2013-033-R.0, recepient E.G. Caiani)

P6444 | SPOTLIGHT
Trajectories of body mass index before the diagnosis of cardiovascular disease

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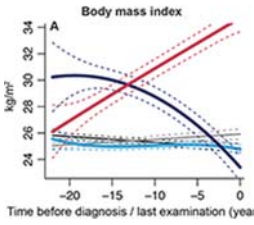
Background: Individuals at the time of diagnosis for cardiovascular disease (CVD) might have different levels of body mass index (BMI). Our aim was to characterize patterns of BMI and other cardio-metabolic risk factors among middle-aged and elderly individuals before CVD diagnosis.
Methods: We included 6126 individuals free of CVD at baseline from the population-based Rotterdam Study. Individuals were followed from 1989–2012 with clinical examinations every 4 years. Latent class trajectories of incident CVD cases were used to identify patterns of BMI before CVD diagnosis. Additionally, mixed-effect models were used to characterize trajectories of other cardio-metabolic risk factors.
Results: During follow-up (median 16.7 years) 1748 participants developed CVD. Among the CVD patients, we identified 3 patterns of BMI. The "stable overweight" group compromised 87.8% of patients with steady BMI levels over time accompanied by a decrease in high density lipoprotein (HDL) cholesterol and an increase in waist circumference. Two other groups which compromised 6.4% and 5.8% of CVD patients were termed "progressive weight gainers" and "progressive weight losers". The progressive weight gainers experienced an increase in BMI levels over time accompanied by increases in diastolic blood pressure and glucose and a decrease in HDL cholesterol. The progressive weight losers experienced a decrease in BMI levels 10 years before CVD development. Despite the decrease in their cardiovascular risk factors over time, this group experienced an increase of predicted CVD risk.



Body mass trajectories before the event

Conclusion: Our findings highlight a substantial heterogeneity in BMI development prior to CVD diagnosis accompanied by different trajectories of other cardiovascular risk factors. Most of the CVD patients were in the stable overweight category.

P6445 | BEDSIDE
Statin is associated with lower incidence of deep vein thrombosis confirmed by CT angiography in patients undergoing total knee replacement arthroplasty

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Background: Statin has potential to reduce the occurrence of venous thromboembolism in apparently healthy persons.
Purpose: To investigate whether statin is associated with lower incidence of deep

vein thrombosis (DVT) in patients undergoing total knee replacement arthroplasty (TKRA).
Methods: We retrospectively enrolled consecutive 414 patients who received TKRA from Feb. 2006 to Jan. 2015. All the patients received computed tomographic angiography (CT-angio) of both low extremities at 7 days after index surgery and some patients received pulmonary artery CT-angio. DVT and/or pulmonary thromboembolism were confirmed by expert blinded to the study group. They were analyses according to state of their chronic use of statin of any kind.
Results: One hundred and ten patients are satin users and 304 are non-stain users. The occurrence of DVT is significantly higher in statin naïve patients as compared in statin users, 33.5% vs. 10.5%, (HR 0.35, CI 0.151–0.752, p=0.035). By multiple regression analysis, statin use was an independent risk factor for the occurrence of DVT (HR 3.02, CI 1.536–6.382, p=0.021). Age and smoking were also independent predictors for DVT. Pulmonary thromboembolism (PTE) did not occur in statin group (0%) but occurred in 20 patients (8.2%) in non-statin users with significant difference (HR 0.60, CI 0.385–0.852, p=0.041). No mortality was found during hospitalization in both groups.
Conclusion: Statin may be associated with lower occurrence of DVT and PTE in high risk patients who are undergoing TKRA. This results warrant further prospective randomized studies to evaluate the statin as prophylactic measures against DVT.

INTERVENTIONS IN PRIMARY AND SECONDARY PREVENTION

P6446 | BEDSIDE
A critical appraisal of safety and efficacy of statins for primary prevention in HIV patients

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Background: Statins are largely prescribed in HIV patients on highly active antiretroviral therapy (HAART) for primary prevention, but their clinical benefit is to date far from being clearly established in this peculiar population.
Purpose: To assess the effectiveness and safety of various dosages of different statins in HIV patients on HAART.
Methods: Studies including HIV patients on HAART treated with statins for primary prevention were included. Total cholesterol reduction was the primary end point; LDL cholesterol, HDL cholesterol, triglycerides and discontinuation related to adverse events the secondary ones. Impact of age, CD4 cell counts, length of disease and HAART regimens and duration on these end points were tested at meta-regression analysis.
Results: Seventeen studies were included accounting for 719 patients (20.5% female, 44.2±4.7 years, baseline CD4 count 497±109 cells/mm^3). For total cholesterol, Rosuvastatin 10 mg and Atorvastatin 10 mg were the most efficacious treatments ([–1.67] mmol/l, 95% CI [–1.99]–[–1.35] and [–1.44] mmol/l, 95% CI [–1.85]–[–1.02], respectively), for LDL Rosuvastatin 10 mg ([–1.12], 95% CI [–0.83]–[–1.40]), Atorvastatin 80 mg ([–2.10], 95% CI [–0.81]–[–3.39]) and Simvastatin 20 mg ([–1.57], 95% CI [–0.47]–[–2.67]). Higher decreases in HDL were reported for Pravastatin 10–20 mg, Rosuvastatin 10 mg and Atorvastatin 10 mg, while triglycerides were reduced more decisively by Rosuvastatin 10 mg, Atorvastatin 10 and 80 mg and Simvastatin 20 mg. Discontinuation rate was 3.1%, with the higher incidence occurring with Atorvastatin 10 mg (8.5%). At meta-regression, nucleoside reverse transcriptase inhibitors (NRTI) sparing regimens reduced the efficacy for total cholesterol and triglycerides, while that for HDL was deceased with non-NRTI containing regimens
Conclusion: Statin therapy significantly lowers cholesterol values in HIV patients with a satisfying safety profile. HAART may significantly interact with statin therapy but it doesn't affect its lipid-lowering efficacy.

P6447 | BEDSIDE
Correlations between subclinical cardiovascular disease and periodontal disease

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Background: There is a universally recognized need to explore additional cardiovascular risk factors and risk markers and to attain an enhanced correlation between statistical risk assessment and the presence of subclinical cardiovascular disease.
Objective: We intended to examine the relationship between subclinical cardiovascular disease evaluated by cardiac and vascular ultrasound examination and the periodontal disease (PD) status, assessed through a simple clinical exam.
Methods: We screened 190 individuals during a cardiovascular primary prevention program. Data on risk factors were collected using an individual evaluation sheet and through determination of laboratory parameters (lipid profile, glucose) in a period of ±3 days from the baseline clinical and ultrasonography evaluation. Ultrasound data was collected on three examinations made in same day: echocardiography, brachial artery flow mediated dilatation and carotid artery intima media thickness. Data on PD status were collected through a simple clinical exam performed in a period of ±7 days from the baseline clinical and ultrasonography evaluation and categorized the study group in a subgroup of normal periodontal status (N=69 persons; 36,3%) and periodontal disease subgroup (N=121; 63,7%).
Results: After data collection we divided the study group according to PD status and compared the mean values for ultrasound measurements. There are significant variances between the groups, regarding both the structural and functional cardiovascular parameters, the only parameters that have not been different being LV systolic and diastolic diameter dimensions, LV shortening fraction and LV ejection fraction.There is widespread presence of subclinical cardiovascular disease in the subgroup of persons with abnormal PD status, 110 (91%) persons out of 121 having at least one type of subclinical injury. The presence of PD is associated with a relative risk RR=2,98 (CI 2,08–4,28) for any type of subclinical cardiovascular damage. Oppositely, a normal periodontal status is highly indicative for a reduced occurrence of subclinical lesions. We calculated concordance coefficient for group classification based on subclinical cardiovascular impairment status compared with classification based on PD status and we found Kappa=0.624, p<0,001 (high concordance).
Conclusions: A normal periodontal status is indicative of low probability for the presence of subclinical cardiovascular disease and an abnormal periodontal status is highly indicative for the occurrence of subclinical cardiovascular disease.

P6448 | BEDSIDE
One-year follow-up from the CUT-IT trial: a randomized trial comparing a low energy diet with aerobic exercise in overweight individuals with coronary artery disease

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Background: Physical inactivity and overweight are major risk factors in coronary artery disease (CAD) and physical activity and weight loss are central in secondary prevention. The objective of this study was to evaluate a low energy diet (LED) combined with aerobic interval training (AIT) and intensive AIT as secondary preventive strategies.
Methods: 70 participants with CAD, BMI >28 kg/m^2 and no diabetes were randomized (1:1) to 12 weeks' supervised AIT at 90% maximal heart rate 3 times/week or weight loss using a LED (800–1000 kcal/day). Both groups continued supervised AIT 2 times/week for 40 weeks following the initial intervention. The intervention was evaluated by a cardiopulmonary exercise test, dual X-ray absorptiometry to assess body composition, body weight and waist/hip-ratio.
Results: 57 (81.4%) participants were men, median age was 63 (IQ range 58–67) years, median BMI was 31.3 kg/m^2 (IQ range 29.7–33.7) and mean VO2peak was 21.0 ml/min/kg (SD 5.1). No between-group difference on relevant baseline data was seen. 29 participants in the LED and 26 in the AIT group completed 1-year follow-up. Results of the intervention are presented in table 1 (mean and SD). The combination of LED and training led to significantly greater weight loss without loss of lean body mass and similar improvement in exercise capacity as the AIT only
Conclusion: The results indicate that a LED regimen followed by AIT may be a superior prevention strategy for overweight CAD patients. Further analyses will evaluate the effects on cardiovascular and metabolic risk markers.
Acknowledgement/Funding: Danish Heart Foundation and the Danish council for independent research

Abstract P6448 – Table 1. Results of the intervention (mean and standard deviation)

	LED+AIT (n=29)			AIT only (n=26)			Between group difference
	Baseline	1 year	p-value	Baseline	1 year	p-value	p-value
VO_2 peak$_{BW}$ (ml/min/kg)	20.5 (4.9)	23.7 (6.7)	0.0001	21.0 (4.9)	22.5 (5.8)	0.0524	0.0977
VO_2 peak$_{FFM}$ (ml/min/kg fat free mass$^{(2/3)}$)	126.5 (25.4)	135.2 (34.4)	0.0245	126.8 (24.7)	132.4 (29.2)	0.1908	0.5602
Weight (kg)	95.6 (10.7)	88.4 (11.3)	<0.0001	96.2 (13.8)	94.6 (14.7)	0.0135	<0.0001
Body fat (%)	36.7 (6.8)	32.0 (8.3)	<0.0001	34.6 (6.5)	33.0 (7.7)	0.0046	0.0001
Waist/hip-ratio	0.98 (0.07)	0.97 (0.06)	0.4266	1.00 (0.07)	1.00 (0.05)	0.5437	0.3193
Lean body mass (kg)	56.3 (8.3	55.8 (8.7)	0.1716	58.4 (9.1)	58.6 (9.2)	0.5935	0.1710

LED, low energy diet; AIT, aerobic interval training.

P6449 | BEDSIDE
Effects of resveratrol and caloric restriction on serum levels of norepinephrine in healthy subjects

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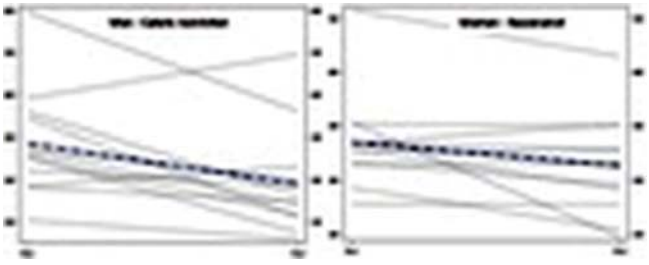
Background: Norepinephrine (NE) plays an important role in the pathophysiology of cardiovascular disease. High levels are associated with coronary events and cardiac arrhythmias. Animal studies suggest benefits of calorie restriction (CR) and resveratrol on cardiovascular system and controversial results on the catecholamine levels. This study examined the effects of resveratrol and CR on serum NE levels in healthy subjects and its relationship to metabolic and inflammatory markers.
Methods: Study randomized 48 healthy subjects (24 women), aged 55 to 65, to 30 days of resveratrol (500 mg/day) or CR (1000cal/d). Blood samples were collected at baseline and at 30 days. Laboratory data analyzed were: NE, triglycerides, total cholesterol, HDL, VLDL, LDL, apolipoprotein A1 (apoA1) and B (apoB), lipoprotein (a), non-esterified fatty acids (NEFA), glucose, insulin, oxidative stress (antioxidant), and C-reactive protein (CRP).
Results: NE decreased in the resveratrol group (269±120 224±94 pg/ml, p=0.037) and in CR group (347±160 254±171 pg/ml; p=0.008). The largest reduction of NE occurred in men of CR group of 286±127 to 190±125 pg/ml (p=0.021) and in women of resveratrol group from 271±89 to 228±92 pg/ml (p=0.027) (Figure). total cholesterol increased with resveratrol (208±33 to 218±45 mg/dl; p=0.03) and decreased with CR (216±44 to 203±40 mg/dl; p=0.01). HDL, LDL, apoAI, apoB decreased in the CR group. ApoB increased in the resveratrol group. Glucose, insulin, NEFA, lipoprotein (a) and antioxidant capacity did not change in either group. Serum levels of NE correlated with total cholesterol (0.44; $p<0.01$) and LDL (0.33; $p<0.01$).



Conclusion: Both interventions reduced serum levels of NE. Long-term benefits should be assessed.

P6450 | SPOTLIGHT
Impact of cardiovascular risk factors management on long-term all-cause and cardiovascular mortality: an observational study

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Background: In clinical trials, lowering cardiovascular risk factors (RF) reduce cardiovascular (CV) morbidity and mortality. Nonetheless, few data exist on general population.
Purpose: We assessed the impact of the control of RF at baseline on long-term all-cause and CV mortality in French general population.
Methods: Analysis was based on the Third French MONICA population-based survey on RF (1995–1996). Participants aged 35–64 were randomly recruited from the general population of three French areas. Vital status and causes of death were obtained 18 years after inclusion. Statistical analysis was based on multivariable Cox modelling. We assessed the impact of the control of high blood pressure, high LDL-cholesterol, diabetes and smoking. For the assessment of high blood pressure, high LDL-cholesterol and diabetes we used the threshold recommended in the guidelines for cardiovascular risk factors management currently used at the time of recruitment.
Results: In our study, 3402 subjects were included. Half were men and 2.5% had history of Coronary Heart Disease. Moreover 569 (17%) subjects presented 2 or more non-controlled RF, 1194 (35%) presented 1 non-controlled RF, 770 (23%) presented all RF controlled under treatment (or were former smokers) and 869 (25%) presented none RF. During the follow-up, 389 deaths occurred (76 due to a CV cause). Considering all-cause mortality, after adjustment for centre, age, gender, educational level, gamma-glutamyl transpeptidase and mean corpuscular volume (as proxies of alcohol consumption) plus medical history of chronic disease (i.e. atherosclerotic disease, cancer, chronic renal failure, respiratory insufficiency, heart failure or liver disease), the hazard ratio (HR) for subjects presented 1 non-controlled RF and for subjects presented 2 or more non-controlled RF was 1.38 [1.03–1.83](p=0.029) and 1.80 [1.33–2.43](p<0.001), respectively, as compared to subjects presented all RF controlled. For subjects presented none RF, adjusted HR was 0.66 [0.44–0.98](p=0.042). Considering CV mortality, adjusted HR for subjects presented 1 non-controlled RF and for subjects presented 2 or more non-controlled RF was 1.70 [0.84–3.42](p=0.138) and 3.67 [1.85–7.29](p<0.001), respectively, as compared to subjects presented all RF controlled or none RF (adjusted HR for subjects presented none RF as compared to subjects presented all RF controlled was not significant (0.56 [0.17–1.83]; p=0.338)).
Conclusions: Failing to control RF (high blood pressure, high LDL-cholesterol, diabetes and smoking) increases significantly long-term all-cause and cardiovascular mortality.

P6451 | BEDSIDE
Effect of multidisciplinary educational programs delivered to scholar children on cardiovascular risk profile of their relatives- systematic review and meta-analysis

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Background: Multidisciplinary educational programs involving scholar children and their relatives could be an easy and scalable preventive measure to face the increasing burden of cardiovascular diseases. Nevertheless such programs are not common in our context.
Objective: To identify, summarize and analyze studies reporting multidisciplinary educational programs involving scholar children and the reported effect on cardiovascular risk factors in their relatives.
Methods: A pre-defined protocol in accordance with the PRISMA was used. Electronic searches in Medline, Pubmed, Embase, Cochrane Library, IBECS, SciELO and LILACS were conducted through March 2014 involving multidisciplinary educational programs with parallel groups design. Reported outcome variables were high density cholesterol (HDL), low density cholesterol (LDL), triglycerides, systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured in children's relatives before and after interventions. Random effect was used to summarize pooled effects and heterogeneity was analyzed by I2. Quality of studies was evaluated with the Cochrane risk of bias tool.
Results: Of 4253 studies found, four reached the inclusion criteria for the systematic review and two were included in the meta-analysis contributing with three separate samples. Included studies involved 787 children (3–11 years) and 711 relatives. Interventions lasted 5–12 months and the pooled effects (95% CI) in relatives were: HDL 1.78 (0.10; 3:47) mg/dL (I2=0%, p=0.819), LDL 5.53 (1.52, 9.55) mg/dL (I2=70.4%, p=0.034), triglycerides –4.45 (–18.69, 9.78) mg/dL (I2=47.1%, p=0.151), SBP –2.60 (4.43, –0.86)mm Hg (I2=0.0%, p=0.956), DBP –2.02 (–3.23, –0.82) mm Hg (I2=54.4%, p=0.095). Methodological criteria was low and risk of bias was high across studies.
Conclusion: Evidence on scholar programs involving LM is weak. Paucity of studies and the absence of some methodological criteria indicate that research in cardiovascular primary prevention invloving scholars and their relatives is warranted.

P6452 | BEDSIDE
Patients' understanding of chronic antithrombotic therapy in the era of direct oral anticoagulant therapy

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Background: Patients' warfarin understanding is generally poor and contribute to suboptimal anticoagulation and subsequent complications.
Purpose: To investigate knowledge of antithrombotic therapy among a population of patients receiving chronic anticoagulation therapy with vitamine K antagonists (VKA) or direct oral anticoagulants (DOA)
Methods: We conducted a prospective study among 193 patients consecutively admitted in a cardiology unit for various causes and receiving anticoagulant therapy for more than 3 months. All patients were invited to independently fill in a questionnaire (10 questions) with specific focus on indication, side effects, precautions and risks of under/over dosing of anticoagulation therapy. The questionnaire was handed out by a nurse in a face-to-face interview. Patients with severe cognitive impairment or psychiatric desorders were excluded.
Results: Mean age was 73 y, 135 patients were male (70%), 67 (35%) of them had sociocultural level medium or high. Atrial fibrillation was the main indication of therapy (n=128; 66%). VKA and DOA concerned respectively 68% (n=132, group 1) and 32% (n=61, group 2) of the patients.
While the vast majority patients were aware of the anticoagulant therapy (n=173; 90%), most of them did not know risks and precautions needed with these drugs

Table 1. VKA vs DOA knowledge

	Group 1 (VKA; n=132)	Group 2 (DOA; n=61)	p
Need (VKA) or absence (DOA) of biological control	n=108 (82%)	n=55 (90%)	0.06
Food interaction (VKA) or not (DOA)	n=39 (30%)	n=18 (30%)	0.95
Drug interaction (VKA) or not (DOA)	n=46 (35%)	n=15 (25%)	0.21
Bleeding risk	n=42 (25%)	n=43 (75%)	<0.001
Embolic risk	n=18 (14%)	n=10 (16%)	0.60

(table 1). Bleeding risk was better understood with the AOD but the potential embolic risk in case of underdosing was poorly understood in the two groups.
Conclusion: Patients' anticoagulant therapy knowledge, regarding both vitamin K antagonists and direct oral anticoagulants, is poor, especially concerning the risk of under/over anticoagulation. With the increasing use of DOA with short half life and no biologic control to assess compliance, improving patient education and physician involvement in therapeutic education, is crucial.

P6453 | BEDSIDE
Predictors of permanent work disability in patients under 50 years old undergoing percutaneous coronary intervention

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Introduction: This study describes the incidence and predictors of permanent disability pension (PWD) in patients <50 years old who underwent percutaneous coronary intervention (PCI).
Materials and methods: 910 patients undergoing PCI at 4 hospitals in 2002–2012. Patients records were reviewed for baseline and procedural data and late adverse events. Data on permanent work disability (PWD) pension allocation were acquired from the national Centre for Pensions, which governs the statutory pension security in the country.
Results: Mean follow-up was 41±31 months. Altogether 103/910 (11.3%) of patients were on PWD by the end of follow-up, 60 (58.3%) for cardiac diagnoses. Independent predictors of PWD were postprocedural stroke (HR 4.67, 95% CI 1.84–11.87), postprocedural MI (HR 3.28, 95% CI 1.80–5.96), diabetes (HR 1.99, 95% CI 1.06–3.72), discharge diuretics (HR 3.506, 95% CI 2.095–5.868) and increasing age (HR 1.15, 95% CI 1.06–1.25). Predictors of PWD for cardiac diagnoses were postprocedural stroke and MI, discharge diuretics and Ca-blockers, diabetes and age.
Conclusions: Patients ≤50 years old undergoing PCI are at a high risk for subsequent permanent disability for cardiac diagnoses. This finding underscores the need for reinforcing adherence to secondary prevention by cardiac rehabilitation and early collaboration with occupational health care professionals.
Acknowledgement/Funding: Finnish Foundation for Cardiovascular Research

P6454 | BEDSIDE
Adults with congenital heart disease: individualized structured patient education to improve patients' knowledge on infective endocarditis

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Introduction: Adults with congenital heart disease (CHD) are at increased risk of infective endocarditis (IE). Previous studies have shown that they have a poor understanding of this disease and its preventive measures. Two years ago, we implemented a transition program (TP) for youth and young adults led by an advanced practice nurse, offering individualized patient education on IE and dental hygiene. This study aims to assess the level of IE knowledge and the level of dental hygiene in everyday life in CHD adults with and without TP participation.
Methods: From 11/2012 to 02/2014, a descriptive cross-sectional study among adults with CHD and regular follow-up at our Center has been carried out. 187 consecutive CHD patients with current or former indication for IE prophylaxis according to the European Society of Cardiology Guidelines were included. Demographic and clinical variables were obtained from the medical records. IE knowledge was assessed using the "Leuven Knowledge Questionnaire for Congenital Heart Disease" (by P. Moons, 2009). Adjustments to the questionnaire with respect to oral hygiene and dental visits were made. The answers were scored according to their accuracy (maximal score 40).
Results: Out of the 187 patients (39% female), 54 visited the TP. TP patients were younger (mean age 21±4 vs. 40 year ± 14 years) than the remaining CHD patients. There was no difference in gender, CHD complexity and history of previous valve replacement or previous IE between patients with and without TP participation. TP patients were less likely to have a college or university degree (TP 4% vs 35%). Despite a lower educational background, TP patients achieved a significantly higher IE knowledge score (TP 26±8 vs 21±10, $p<0.001$) compared to adults without structured IE education. The IE knowledge score remained high (26±8) even in patients with TP participation only the year before the current visit (n=26). All patients had good results regarding dental hygiene (i.e. brushing their teeth at least twice a day; TP 85% vs. 80%) and dental visits (at least once a year; TP 81% vs. 81%).
Conclusions: Systematic patient education as part of a TP improves IE knowledge independent of the patients' educational background. This knowledge was sustained in the year after participation in the TP. All patients showed fairly good results regarding dental hygiene and dental visits. More emphasis could be put on early patient and parent education, as well as on regular repetition.

P6455 | BEDSIDE
Visualization of coronary artery calcification: influence on preventive therapy and lifestyle modification in patients with a new diagnosis of coronary artery disease

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Background: Direct health provider to patient presentation of coronary computed tomography angiography (CTA) findings may increase adherence to preventive therapy and risk modification. The purpose of this study was to assess the influence of visualization of coronary artery calcification (CAC) and lifestyle recommendations on cholesterol concentrations and other risk variables in symptomatic patients with hyperlipidaemia and non-obstructive coronary artery disease (CAD).
Methods: Prospective two-centre randomized controlled trial. Patients were randomized 1:1 to intervention or standard follow-up in general practice. The primary end-point was change in plasma total-cholesterol concentration at 6-months follow-up.
Results: We included 189 patients (mean [± SD] age 61 [12] years, 57% males). Median (IQR, range) Agatston score was 166 (101–334, 70–2054). The reduction in plasma total-cholesterol concentrations tended to be higher in the intervention than in the control group, 1.32 mmol/L vs. 1.18 mmol/L (P=0.181). In a subgroup analysis including patients continuing statin therapy during follow-up (n=147), the reduction in plasma total-cholesterol concentrations was more pronounced in the intervention than in the control group, 1.71 mmol/L vs. 1.44 mmol/L (P=0.027). More patients in the control group continued smoking (22% versus 9%, P=0.014) and unhealthy dietary behaviour (64% versus 44%, P=0.005). A weight loss was seen in the intervention group (–1.5 kg versus +0.5 kg, P=0.001) and furthermore there was a tendency towards a higher degree of statin adherence in the intervention group (P=0.056).
Conclusion: Visualization of CAC and brief recommendations about risk modification after coronary CTA in symptomatic patients with hyperlipidaemia and non-obstructive CAD may have a favourable influence on plasma total-cholesterol concentration, adherence to statin therapy and risk behaviour. Further investigations are needed to delineate the findings.
Acknowledgement/Funding: This study received financial support from Lillebaelt Hospital-Vejle Research Foundation (U-08-01), the Novo Nordisk Foundation (1-01-5087), and the T

P6456 | BEDSIDE
Closing the treatment gap: coaching patients on achieving cardiovascular health (COACH)

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Background: In 2011 almost one third of all deaths in the Australian population were attributable to cardiovascular disease, of these 80% were preventable. Telephone coaching programs are flexible, multifaceted and integrated with the patient's primary health care provider.
Purpose: This study aimed to measure changes in cardiovascular risk factors among patients with coronary heart disease (CHD) and/or type 2 diabetes enrolled in a centralised state-wide telehealth coaching program in the public health sector in the Australian state of Queensland.
Methods: A population-based analysis of cardiovascular risk factor data collected prospectively as part of The COACH Program delivered through Queensland Government's Health Contact Centre. Participants were patients with CHD (n=1962) and type 2 diabetes (n=707), of whom 145 were Indigenous. Changes in fasting lipids, fasting glucose, glycosylated haemoglobin (HbA1c), blood pressure, body weight, body mass index (BMI), waist circumference, alcohol consumption and physical activity, as measured at entry to, and completion of, the program were analysed using pair-wise comparison.
Results: Improvements in cardiovascular risk factor status, from entry to completion of the program, were found across all biomedical and lifestyle factors in patients with CHD and/or type 2 diabetes. For both diseases, reductions in serum lipids, blood glucose, smoking habit and alcohol consumption combined with increases in physical activity were the most notable findings. Those most clinically significant were: a decrease in mean LDL-cholesterol from 2.4 mmol/L to 1.8 mmol/L (CHD) and from 2.5 to 2.0 mmol/l (diabetes); a decrease in mean alcohol ingestion from 1.4 to 1.1 (CHD) and 1.3 to 0.9 (diabetes) standard drinks; and an increase in mean physical activity from 142 to 229 minutes (CHD) and from 127 to 182 minutes (diabetes) per week; and a decrease in mean HbA1c from 8.2% to 7.4% for diabetes patients ($p<0.001$ for all comparisons). Similar differences were found in mean change scores in cardiovascular risk factors between Indigenous and non-Indigenous participants.
Conclusion: A centralised state-wide telehealth coaching program overcomes obstacles of distance and limited access to health services and facilitates guideline concordant decrease in cardiovascular risk.

P6457 | SPOTLIGHT
Women's awareness, perceptions and knowledge of heart disease - three country comparison

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Background: A critical step towards improving the uptake of cardiovascular disease (CVD) prevention and treatment strategies in women is ascertaining their awareness of CVD, including the barriers to taking preventive action.
Purpose: To undertake a cross-sectional survey in New Zealand women aged ≥25 years looking at their CVD awareness, perceptions and knowledge, and compare the findings to those from corresponding studies undertaken in the USA (2012) and Austria (2011).
Methods: Participants were recruited via "citizen panels" managed by an on-line survey research company. Panel membership was broadly representative of the New Zealand population. Participants completed an on-line questionnaire previously developed by the American Heart Association and adapted for the New Zealand environment.
Results: A total of 724 women completed the survey. CVD was identified as the leading cause of death by only 21% of women, compared to 56% in the USA and 75% in Austria. Between 40–50% of women were aware of the atypical signs of a heart attack (i.e. fatigue and nausea), compared to 10–18% in the USA. Over 70% of women were aware of the leading risk factors for CVD (smoking, high blood pressure, high cholesterol, being overweight, and having a family history of CVD). Almost 50% of women correctly identified type 2 diabetes as a risk factor (compared to 28% in Austria). The main barriers to taking preventive actions were similar to those reported by women in the USA and Austria, and included not perceiving themselves to be at risk, lack of time/family commitments, lack of money and lack of confidence. Age and ethic differences were observed.
Conclusions: Clear differences exist between countries in terms of women's awareness, perceptions and knowledge of CVD. These findings highlight the importance of undertaking country-specific surveys so that heart health messages and interventions for women can be targeted appropriately.
Acknowledgement/Funding: Heart Foundation of New Zealand (Project Grant, Douglas Senior Fellowship, Māori Cardiovascular Fellowship, and Chair in Heart Health)

P6458 | BEDSIDE
Usefulness of carotid ultrasonography for prevention of cerebral infarction

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Carotid plaques in neurologically asymptomatic subjects have been reported to be both markers of generalized atherosclerosis and sources of thromboemboli. Then,we evaluated association between carotid plaque and cerebral infarction.
Methods: We evaluated 184 patients who were suspected of cerebral infarction and underwent head MRI and carotid ultrasongraphy (US) (120 males of 67.8±7.8 years old, 64 females of 69.8±8.2: mean±standard deviation). Carotid plaque score (PS) was calculated by US, and MRI findings were classified as follow CI scores: 0: WNL, 1:leukoaraiosis 2: lacunar infarction, 3: atherosclerotic cerebral infarction. Cardio-Ankle Vascular Index (CAVI) was measured for evaluation of arterial stiffness. CAVI, which is calculated based on the stiffness parameter thus obtained, is theoretically independent of changes in blood pressure. Risk factor (RF) included hypertension, dyslipidemia, diabetes mellitus, smoking history (SMH).
Results: CI or lacunar infarction was observed in 6 (27.2%) out of 22 patients without plaque,28 (41.1%) out of 68 patients with PS of less than 5 (mild), 29 (48.3%) out of 60 patients with PS between 5 and 10 (moderate), and in 23 (67.6%) out of 34 patients with PS of more than 10 (marked). Incidence of CI or lacunar infarct was greater in patients with PS than in those without. CI score was 1.32±1.3 in patients without plaque, 1.50±1. 41 in mild, 1.61±1.36 in moderate, and 2.32±1.22 in marked (P=0.34 vs cases without plaque). CAVI was 10.86±1.39 in cases with CI or lacunar infarct and 8.66±1.12 in those without ($P<0.001$). Out of 42 cases with atherosclerotic cerebral infarction, max thickness of internal carotid plaque in the artery responsible for infarction was 1.86±0.94 ($P<0.05$ vs 1.25±0.82 in contralateral artery). No plaque was observed in 8 internal carotid arteries for infarction. PS was greater at contra lateral carotid artery in 14 patients. Mean number of risk factor was 2.0±1.01 in patients with marked CA, 1.8±0.9 in those with moderate CA, 1.68±1.1 in those with mild CA, and 1.31±0.8 without plaque (P=0.009 vs marked CA,P=0.021 vs moderate CA).
Conclusions: In general, carotid arteriosclerosis is associated with degree of cerebral ischemia and aortic stiffness, however, cerebral infarction may occur in patients with none or mild carotid arteriosclerosis. Internal carotid plaque or CAVI may also be associated with development of CI in most of patients, but not in all. Increase of RF or CAVI may predict CI in patients without severe carotid arteriosclerosis.

SURVEILLANCE OF RISK FACTORS AND INTERVENTIONS

P6459 | BEDSIDE
Management of overweight and obesity in patients with coronary heart disease across Europe: results from EUROASPIRE IV survey

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Introduction: Four cross-sectional surveys were conducted between 1999 and 2013 under the auspices of European Society of Cardiology, Euro Heart Survey and subsequently the EURObservational Research Programme. The most recent EUROASPIRE IV was a cross-sectional survey carried out in 78 centres from 24 European countries.
Purpose: To describe the prevalence and management of overweight and obesity in patients with coronary heart disease in Europe.
Methods: Consecutive patients aged <80 years after CABG, PCI and acute coronary syndrome were identified from hospital records and interviewed and examined at least 6 months after their coronary event.
Results: In total, 16,426 medical records were reviewed and 7998 patients (24% females) interviewed on average 16 months after having a coronary event. Overall, 82% were overweight (BMI ≥25 kg/m^2), 38% were obese (BMI ≥30 kg/m^2) and 58% centrally obese (waist circumference ≥102 cm in men, ≥88 cm in women). Obesity was more prevalent in women and was a major health problem across all 24 countries (26% in Serbia up to 49% in Slovenia). Similar variations were observed for central obesity (47% in Bosnia & Herzegovina up to 73% in Cyprus). Nearly 20% of the obese patients claimed to have never been told to be overweight, only 50% of them tried actively to lose weight during the past month and 62% intended to do so next month. Since their hospital discharge, less than half of the obese patients had followed dietary recommendations to lose weight and/or tried to engage in more physical activity and nearly 10% were not aware of their weight. The comparison with the previous two surveys demonstrated persistent increasing obesity and central obesity rates with comparable trends in both sexes.
Conclusions: The management and the raising prevalence of obesity and central obesity in coronary patients across Europe is a cause of concern. More intensive preventive cardiology programmes, appropriately adapted to medical and cultural settings in each country, focusing on diet and especially physical activity are urgently required for all patients with established coronary or other atherosclerotic disease.
Acknowledgement/Funding: Unrestricted research grants to the ESC from AstraZeneca, Bristol-Myers Squibb/ Emea Sarl, GlaxoSmithKline, F. Hoffman-La Roche, MSD and Amgen

P6460 | BEDSIDE
Secular changes in cardiovascular risk factors of 50-year-old men over a period of 50 years. The study of men born 1913, 1923, 1933, 1943, 1953 and 1963

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Background: A downward trend in the incidence and mortality of cardiovascular diseases has been reported in Western Europe during the last decades. These changes have apparently related to the improvement of the risk factors over time. However, an escalating pandemic of overweight and obesity is taking over and the improvement of the risk factors may not be sustained.
Purpose: The aim of the present study was to study the trends in secular cardiovascular risk factors in 6 separate series cohorts of 50-year-old men over a period of 50 years in Sweden.
Methods: From 1963,men sample of living in Sweden,were random and examined with respect to cardiovascular risk factors. With 10-year intervals, six random population samples of men, totally 3563 50-year-old men were investigated between 1963 and 2013. The trends of variables were analysis. Hypertension, diabetes, smoking, high cholesterol and obesity were analysis as the 5 secular cardiovascular risk factors, OR of people with one, two, three, four, five risk factors was analysis compare with man 1913.
Results: The average weight increased from 75.9 kg in 1963 to 87.2 kg in 2013 ($p<0.001$). A continues increase in body mass index from 24.8 to 27.1kg m^{-2} ($p<0.001$) and s-trigycerids increase from 1.26 to 1.49 mmol/L ($p<0.001$) was also seen. In contrast s-cholesterol decreased from 6.4 mmol/L to 5.3 mmol/L ($p<0.001$) and the proportion of smokers fell markedly from 56% to 11% of the population ($p<0.001$). The prevalence of hypertension tended to plateau while diabetes increased slightly. The cumulative risk assessment (hypertension, diabetes, smoking, high cholesterol and obesity) showed that the proportion with ≤1 risk factor increased significantly whereas considerably fewer had ≥4 risk factors.
Conclusion: Middle age men based on population had s-cholesterol decreased and smokers fell. Despite a weight increase of 11 kg and a slight increase in diabetes, the total cardiovascular risk factor pattern was still improved in 50-year old men in Sweden over the last 50 years.

P6461 | BEDSIDE

The burden of cardiovascular diseases in Europe - results of the global burden of disease study 2013

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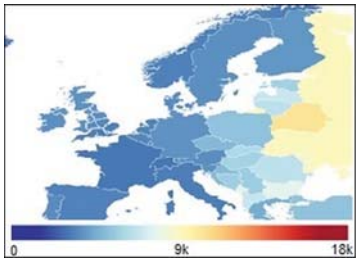
Purpose: To better examine patterns in cardiovascular disease (CVD) in Europe, we analyzed results from the Global Burden of Disease (GBD) 2013 Study. GBD is a multinational study of disease burden by age and sex for 188 countries from 1990 through 2013, using all available data for risk factors, death and disability.
Methods: GBD produces consistent and comparable results over age, sex, time and space. Total health loss due to premature death plus disability is reported as a disability-adjusted life year (DALY). CVD burden is the aggregate of separate mortality and disease prevalence estimates created for ischemic heart disease, ischemic stroke, hemorrhagic stroke, atrial fibrillation, peripheral vascular disease, aortic aneurysm, hypertensive heart disease, endocarditis, rheumatic heart disease, and a category for other CVD conditions.
Results: In Western Europe, the 5 lowest CVD-specific DALY rates, standardized for age, are found in Andorra, Switzerland, France, Iceland, and Italy while the 5 highest rates are in Ireland, Malta, Germany, Finland, and Greece. Significantly higher DALY rates are found in Central and Eastern Europe, with the highest rate found in Belarus. The figure below shows age-standardized CVD DALY rate per 100,000 in 2013. There is a distinct west-to-east gradient for CVD health across Europe that is only partially explained by the distribution of known CVD risk factors and health system performance.



DALYs per 100,000 Lost to CVD, 2013

Conclusion: The burden of CVD varies widely across Europe. Increased attention must be paid to CVD health within Europe since disparities will likely increase as the European population ages.
Acknowledgement/Funding: The Bill and Melinda Gates Foundation

P6462 | BEDSIDE

Trends in clinical profile, medical treatment and risk factors control in patients with stable coronary heart disease in Spain between 2006 and 2014

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Introduction: Patients with stable coronary heart disease are considered as high-risk patients and deserve the highest medical treatment intensive to control risk factors. Medical treatments have evolved
Methods: We compared to nationwide registries performed in Spain in 2006 (n: 2897) and 2014 (n: 1110) that included stable patients with coronary heart disease from outpatient clinics. Optimal medical treatment was considered the sum of antiplatelet, statin, ACE or ARB and betablockers. Atovastatin 40–80 mg/daily and rosuvastatin 20–40 mg/daily were considered intensive statin treatment.
Results: 4007 patient were included, mean age 67.2 (11.2) years and 74.1% males. No differences were found in mean age between both registries but patients included in the 2014 registry had significantly lower prevalence of hypertension (48.1% vs. 68.6%), diabetes (34.5% vs. 38.8%), stroke (6.0% vs. 9.9%) and concomitant heart failure (9.3% vs. 18.6%). Nonetheless, the percentage of current smokers increased form 10.7% to 15.4% ($p<0.01$). Patients from the 2006 registry had significantly lower mean heart rate systolic (132.7±18.7 vs. 136.7±18.8) and diastolic (75.2±11.1 vs. 77.7±11.1) blood pressure and slightly higher mean heart rate (69.6±10.1 vs. 66.1±11.4). Patients from the 2014 registry had lower total cholesterol (175.5±10.1 vs. 187.2±40.1), low-density lipoprotein cholesterol (LDLc) (98.0±43.7 vs. 111.3±34.9), lower fasting glucose (111.1±28.9 vs. 120.5±44.6) as the only statistically significant differences in blood test parameters. Patients from the 2014 registry received significantly more statins (96.0% vs. 68.3%), beta-blockers (70.3% vs. 58.2%), ACE or ARB (73.3% vs. 59.1%) and antiplatelets (89.2% vs. 80.3%). Relevant increases in intensive statin treatment (9.7% to 42.5% vs; $p<0.01$) and optimal medical treatment (26,9% to 47.8% $p<0.01$) were observed between both registries. The use of insulin in diabetic patients remained the same in both registries (25.9% vs. 21.3%; p=0.14) but the use of oral antidiabetics increased from 62.6% to 81.1% ($p<0.01$). The percentage of patients with LDLc <70 mg/dl was almost three times higher in the 2014 registry (27.3% vs. 9.5%; $p<0.01$) but the rate of blood pressure <140/90 mmHg decreased (66.3% vs. 74.6%; $p<0.01$).
Conclusions: Relevant improvements in medical treatment implementation in stable coronary heart disease patients attended by cardiologists in outpatient clinics were observed. LDLc control has improved but blood pressure control and smoking abstinence remain as clinical challenges in these patients.

P6463 | BEDSIDE

Prevalence, recognition and treatment of atherosclerotic cardiovascular disease in Korea: from 2002 to 2010 Korea Health Insurance Sample Cohort Database (KHISCDB)

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Background: Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of cardiovascular morbidity and mortality. However, nationwide epidemiologic data about of ASCVD in Korea are limited.
Methods: Using the 2002–2010 Korea Health Insurance Sample Cohort Database (KHISCDB), we performed a nationwide population-based epidemiologic study. KHISCDB is sampled from administrative enrollment and claims data (national health insurance information DB) and is composed of a representative population cohort of 1,025,340 people. We considered people to have a chronic, specific medical condition if KHISCDB administrative data have a claim indicating that people received a medical service or treatment for the condition, using CCW chronic condition algorithm of US CMS (For example, to identify a person with DM in 2004, at least 1 inpatient claim or 2 outpatient claims had to include any of the following diagnosis codes from ICD 10: E10,E11,E12,E13,E14 from 2003 to 2004). Considering longitudinal nature of data, a patient is classified into two groups. A person who diagnosed with a chronic condition for any year from 2004 is "Diagnosed person" and a person who diagnosed with a chronic condition for any year from 2004 and treated afterward is "Treated person".
Results: From KHISCDB, there are a total of 1,025,340 people in 2002. The baseline study population in 2004 included 724,379 people, aged 20 and over and enrolled continuously and followed from 2004 to 2010 (Fig A). The diagnosed prevalence of ASCVD risk factors and ASCVD steadily increased during the study period. In 2010, it was 25.7% of hypertension, 29.2% of dyslipidemia, 20.1% of DM, 3.8% of cerebrovascular disease (CVD), 6.6% of peripheral artery disease (PAD) and 10.2% of coronary heart disease (CHD). However, treated prevalence was not increased to that extent. In 2010, it was 17.7% of hypertension, 14.0% of dyslipidemia, 9.2% of DM, 1.1% of CVD, 2.2% of PAD and 3.5% of CHD. (Fig B)
Conclusions: The prevalence of ASCVD risk factors and ASCVD was increased but remained undertreated. This epidemiologic study offers an opportunity to provide to a better understanding of the prevalence of ASCVD in Korean populations and results of the study will be of practical relevance to physicians, health care organizations, and those who issue clinical guidelines for the reduction of ASCVD risk.

P6464 | BEDSIDE

Treatment withdrawals and their implications on the success of cardiovascular outcome studies

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Background: Treatment withdrawals can jeopardize the interpretability and success of long term cardiovascular (CV) outcome trials. Understanding the implications of withdrawals on study power and duration will raise awareness for the need of improved retention efforts. Identifying subgroups of patients at higher risk of withdrawal may allow for more focused retention strategies.
Methods: We examined rates and predictors of withdrawal from treatment in dal-OUTCOMES (clinicaltrials.gov NCT00658515), a trial that compared an HDL cholesterol-raising agent (dalcetrapib) with placebo in 15,871 patients with acute coronary syndrome who were followed for a median of 31 months. We used Monte-Carlo simulation to investigate the dependence of study power on baseline CV risk, anticipated risk reduction, and treatment withdrawal rate. Proportional hazards regression was used to assess dependence of treatment withdrawal on clinical and demographic characteristics and prior occurrence of CV endpoint events.
Results: Annualized treatment withdrawal and primary endpoint event rates in dal-OUTCOMES were 8.8% and 3.4%, respectively, with no differences between treatment groups. Simulation indicates that under such assumptions loss of study power can be up to 20%. Twenty-five variables related to study logistics (country, participation in substudy), age, gender, CV history, and baseline lipids were investigated; those with $p<0.002$ (= 0.05/25) were considered significant predictors of treatment withdrawal. The strongest predictor was occurrence of a non-fatal CV event after randomization (HR=2.3; 95% CI [1.9, 2.7], $p<0.001$). Other predic-

tors for treatment withdrawal included country (HR=5.5 for most vs least), gender (HR=0.83 for males), eGFR (HR=1.04 per 10 mL/(min×1.73m^2)), age (HR=1.01 per year), total cholesterol (HR=1.04 per 10 mg/dL), smoking (HR=1.24), and BMI (HR=0.98 per kg/m^2). The risk of withdrawal from treatment decreases with time (50% lower in 3rd vs 1st year of dal-OUTCOMES).
Conclusion: Even within an "expected" range for large clinical trials, treatment withdrawals have a strong, adverse influence on study power. Occurrence of non-fatal CV events significantly increases the likelihood of subsequent treatment withdrawal. Clinical and demographic factors may identify patients more likely to withdraw from treatment and hence allow targeted strategies for patient retention. Independent confirmation of our results from other trials is desired.
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P6465 | BEDSIDE
Estimating the reduction in 10-year atherosclerotic cardiovascular disease risk with statin therapy: a VOYAGER meta-analysis

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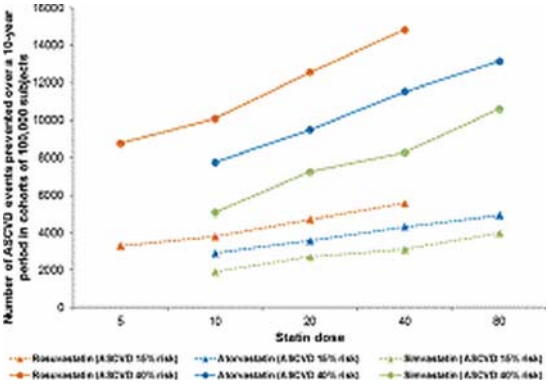
Aim: To estimate the potential reduction in 10-year atherosclerotic cardiovascular disease (ASCVD) risk with statin therapy using data from VOYAGER.
Methods: The VOYAGER meta-analysis database includes data from 32,258 patients included in 37 randomised trials. This analysis included 29,486 patients considered candidates for high-intensity statin therapy according to the 2013 American College of Cardiology/American Heart Association (ACC/AHA) blood cholesterol guideline. Using patient's total cholesterol and HDL-C levels, together with the 2013 ACC/AHA assessment of cardiovascular risk guideline, the change in ASCVD risk was calculated as a ratio of on-treatment to baseline risk for each patient. The least-squares mean (LSM) ratios of 10-year ASCVD risk were calculated for atorvastatin 10–80 mg, rosuvastatin 5–40 mg and simvastatin 10–80 mg. Hypothetical cohorts of 100,000 patients each, with baseline risks of 15 and 40%, were created. The potential numbers of ASCVD events prevented were estimated for each statin and dose within each cohort.
Results: LSM ratios of 10-year ASCVD risk were 0.80–0.67, 0.78–0.63 and 0.87–0.74 for atorvastatin 10–80 mg, rosuvastatin 5–40 mg and simvastatin 10–80 mg, respectively. The predicted number of ASCVD events prevented over a 10-year period increased with increasing statin dose and increasing baseline risk (Figure).



Conclusion: In patients with ASCVD risk, especially those with high baseline risk, effective statin therapy can potentially prevent a clinically significant number of ASCVD events. The number of ASCVD events prevented thus depends on baseline risk, as well as on choice and dose of statin.
Acknowledgement/Funding: Analysis and medical writing support funded by AstraZeneca.

P6466 | BEDSIDE
Muscle related complaints, serious adverse events vents and drug discontinuations in 17,706 subjects randomized to simvastatin or ezetimibe/simvastatin in the IMPROVE-IT study

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Background: Statin side effects include rare serious muscle related events (SMRE) such as rhabdomyolysis and less serious but more ambiguous muscle related complaints (MRC) such as myalgia. Given that musculoskeletal complaints are common in older individuals, we incorporated a proactive plan to evaluate SMRE and MRC in the IMPROVE-IT trial where 18,144 post ACS subjects were randomized to either simvastatin 40mg (S) or ezetimibe/simvastatin 40mg (EZ/S).
Purpose: To ascertain the rate and consequences of MRC drug during a long term follow up trial in subjects who took at least one dose of study.
Methods: To evaluate MRC we screened for unexplained myalgia, weakness or tenderness at each visit and provided a management strategy. Suspected SMRE, muscle related adverse or serious adverse events or abnormal laboratories possibly related to SMRE that met predefined criteria were sent for adjudication.
Results: Of those randomized, 17,706 received > one dose of study drug and 11,622 were statin naïve at entry. These subjects had 71,637 years of exposure to S or EZ/S. After 8 months in the trial the dose of S in either arm could be increased to 80mg if LDL-C was >79 mg/dL. During the trial, 28% in the S arm and 6% in the EZ/S arm were titrated to 80mg. SMRE were rare and did not differ between S or EZ/S groups. Screening for MRC, done for up to 8.75 years with a 52 month median drug exposure time, was positive in ~1/5 of subjects but was associated with a low incidence of drug discontinuation (Table 1).
Conclusion: Ezetimibe did not appear to increase the risk of SMRE on top of simvastatin. Discontinuation rate due to MRC was low and equally distributed between groups.
Acknowledgement/Funding: This study was funded by Merck & Co., Inc.

P6467 | SPOTLIGHT
Influence of medical follow-up on the quality of preventive therapy and ACS outcomes, according to registry data

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Purpose: To assess the relationship between regularity of visiting doctor, quality of medical therapy 1 year prior to acute coronary syndrome (ACS) and ACS outcomes.
Methods: We used the data of the LISS (Liubertsy Infarct Survival Study) registry. In this part of the study we included all patients hospitalized with ACS to the local Liubertsy hospital from 01.11.2013 to 31.1.2014. 17 patients died during first 4 days of hospitalization and were excluded from the study. All other patients after obtaining informed consent were asked to fulfill a specially designed checklist containing questions about regularity of medical follow-up 1 year prior to ACS, medical therapy and adherence to it. Then, all the patients were divided into two groups: those who never visited primary care doctor 1 year prior to ACS (group A, n=107) and those who visited primary care doctor 1 time or more 1 year prior to ACS (group B, n=108). The primary end point (PEP) of the study was the development of myocardial infarction (MI) during reference hospitalization.
Results: Patients of groups A and B were comparable by the prevalence of main cardiovascular risk factors, incidence of ischemic heart disease, prior MI, presence of chronic heart failure. However, they differed in age (57 and 70 years, consecutively) and sex (68% of males in group and 40% of males in group B). There were significant differences in the frequency of receiving antiplatalets (11% vs 44%), ACE-inhibitors (17% vs 36%), ARA (1% vs 17%), beta-blockers (14% vs 53%), Ca antagonists (2% vs 15%), statins (6% vs 27%). The PEP was registered in 50% of patients in group A and in 27% of patients in group B ($p<0.01$).
Conclusion: Patients adherent to medical follow-up significantly more often received evidence-based primary and secondary preventive medications. It seems that due to this fact they had significantly better outcomes.

P6468 | BEDSIDE
Long term adherence to evidence-based cardioprotective medications after acute myocardial infarction and its impact on mortality

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Background: Guidelines for the secondary prevention and management of acute

Abstract P6466 – Table 1. Key outcomes for SMRE and MRC

	Overall subjects			Statin naive subjects		
	Simva (n=8,855)	EZ/Simva (n=8,851)	p value	Simva (n=5,831)	EZ/Simva (n=5,791)	p value
All rhabdomyolysis*	0.2%	0.1%	0.273	0.2%	0.1%	0.643
– with renal dysfunciton*	n=9	n=9		n=6	n=6	
– w/o renal dysfunction*	n=9	n=3		n=4	n=2	
Myopathy*#	0.1%	0.2%	0.393	0.1%	0.2%	0.434
"Yes" to possible MRC	19%	19.6%	0.263	18.9%	20.4%	0.039
MRC "Yes" led to stopping study drug at same or next visit	2.4%	2.3%	0.808	2.6%	2.6%	0.973

*Adjudicated by independent blinded muscle clinical events committee. #MRC with CK >5x ULN on repeated measures or >10x once and not rhabdomyolysis.

myocardial infarction (AMI) recommend, as an adjunct to lifestyle modification, aspirin, beta blockers (β-blockers), angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), and statins as lifelong treatment.
Purpose: To investigate potential determinants of long-term adherence to these evidence-based cardioprotective medications (EBCMs) in patients with AMI, and to estimate the effect of adherence on all-cause mortality.
Methods: Patient-based retrospective cohort study of 1-year survivors of AMI, members of a health organization in Israel, between 2005 and 2010. Adherence was measured using the proportion-of-days-covered (PDC) metric, and defined as PDC≥80%.
Results: Of 4655 patients prescribed at least one medication, 864 died during an 8-year follow up (median 4.5 years). Nonadherence to each EBCM approximated 50%, and 80% for combined therapy of all EBCMs. In multivariable analyses, adherers to at least one EBCM were more likely to be of Jewish origin (adjusted odds ratio [AOR], 2.11; 95% confidence interval [CI], 1.60–2.78), and attending a cardiologist at least once during the first year of follow up (AOR, 1.26; 95% CI, 1.05–1.51). Increasing number of outpatient visits to primary physicians and cardiologists was associated with improved adherence and followed a significant dose-response gradient. Factors significantly associated with reduced adherence were presence of comorbid conditions, and readmissions within the first year of follow up (AOR, 0.65; 95% CI, 0.55–0.78). Results were consistent when evaluating adherence of each EBCM separately.
Except for β-blockers, medication nonadherence was significantly associated with increased all-cause mortality risk for aspirin (Adjusted hazard ratio [AHR], 1.28; 95% CI, 1.11–1.47), statins (AHR, 1.36; 95% CI, 1.18–1.57), and ACEIs/ARBs only among ischemic heart disease patients with documentd heart failure (AHR, 1.57; 95% CI, 1.16–2.14). Multidrug combined therapy exerted incremental survival benefit in a dose-response gradient, exceeding that of single component treatment, with the highest risk of mortality observed in patients adherent to none of the EBCMs as compared to adherents to all EBCMs (AHR, 1.38; 95% CI, 1.06–1.80).
Conclusions: Mortality risk profile for nonadherents to EBCMs will not improve unless strategies are implemented to improve long-term adherence. Further research is needed to elucidate the role of ACEI/ARB in patient subgroups.

P6469 | BEDSIDE
Coaching care model in patients with high cardiovascular risk: lessons from the EuroASPIRE database

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Introduction: The EuroASPIRE III survey primary care arm, carried out in 66 general practices in 12 European countries, was one of the largest epidemiological trials focused towards uncovering unhealthy lifestyles.
Purpose: The aim of our study was to create a coaching care model implemented on high-risk patients followed over 18 months, in order to improve cardiovascular prevention and risk management according to the ESC guidelines.
Methods: Study population was selected from the 489 subjects who had previously participated in EuroASPIRE III – Primary Care Arm. We enrolled 325 individuals who met inclusion criteria: antihypertensive and/or lipid-lowering and/or anti-diabetes medication started, age less than 80 years, without history of coronary heart disease. An 18 months intervention trial was conducted in primary care settings by general practitioners (GP).
Results: Out of the 325 subjects enrolled in our study 62% were women and the mean age of the patients was 55.9 years. 80% of the subjects had systolic hypertension while 66% diastolic hypertension. Out of the entire population who had total cholesterol over 190 mg/dl 78% were men. However, 75% of the women had increased LDL-cholesterol as compared to low HDL-cholesterol where 80% were men. High triglycerides were present in 58% of the men and 42% of women. 16% of the patients enrolled in our study were dysglicemic. At the 18 months follow-up we observed that hypertension was the best controlled risk factor (p<0.001), as well as total cholesterol and LDL-cholesterol which had improved significantly (p<0.001).

Trend of BP parameters and lipid profile

Parameters	Baseline	18 months	p
SBP (mmHg)	146±18.3	136.9±11.7	<0.001
DBP (mmHg)	86.19±11.7	77.76±7,6	<0.001
Total cholesterol (mg/dl)	214.39±44.17	203.8±42.26	<0.001
LDL cholesterol (mg/dl)	127.78±37.51	118.5±35.51	<0.001
HDL cholesterol (mg/dl)	56.14±15.38	54.20±14.48	0.098
Triglycerides (mg/dl)	128.5*	140.0*	0.6

SBP, systolic blood pressure; DBP, diastolic blood pressure.

Conclusion: Primary prevention needs a multidisciplinary approach, which addresses lifestyle and risk factor management by general practitioners, nurses and other allied health professionals, in order to improve guidelines adherence.

P6470 | BEDSIDE
Impact of PPI treatment on gastrointestinal bleeding associated with NSAID use among post-myocardial infarction patients on antithrombotic therapy - A nationwide study

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Background: Bleeding complications have been associated with both antithrombotic therapy and with non-steroidal anti-inflammatory drugs (NSAID) therapy, but preventive effect of proton-pump inhibitors (PPI) treatment is unresolved.
Purpose: We examined the impact of PPIs on the risk of gastrointestinal bleeding in post-myocardial infarct (MI) patients on antithrombotics who were prescribed concomitant NSAID therapy.
Methods: Using nationwide Danish registries, we included patients aged ≥30 years admitted with first-time MI and on antithrombotic treatment, 1997–2011. We estimated the effect of PPIs on the risk of gastrointestinal bleeding according to NSAID plus antithrombotic therapy using adjusted time-dependent Cox regression models.
Results: Of 82,955 post-MI patients (mean age 67.4, 64% men), all of whom were taking single or dual antithrombotic therapy, 42.5% filled at least one NSAID prescription and 45.5% received PPIs. Over a mean follow-up of 5.1 years, 3,229 gastrointestinal bleeds occurred. The crude incidence rates of bleeding (events/100-person-years) on concomitant antithrombotic and NSAID therapy were 1.8 on PPIs versus 2.1 off PPIs. The adjusted risk of bleeding was lower with PPI use (hazard ratio (HR) 0.72 [95% CI 0.54–0.95]) regardless of antithrombotic treatment regimen, type of NSAID and type of PPI used, Figure.

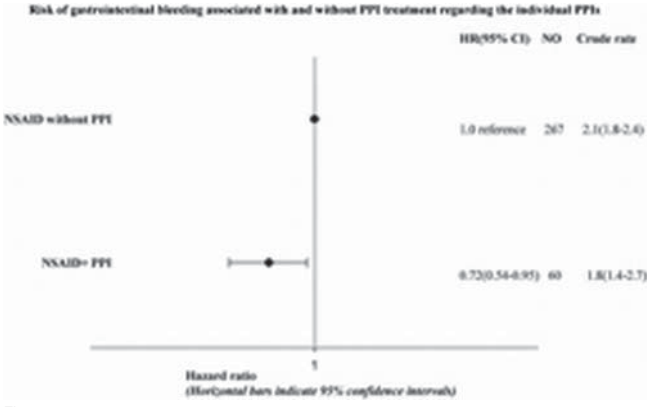

Figure 1

Conclusion: The use of PPIs was independently associated with decreased risk of gastrointestinal bleeding in post-MI patients using NSAID concomitantly with antithrombotic treatment. All post-MI patients in whom NSAIDs are judged necessary might benefit from PPI therapy as well.

DIET AND EXERCISE: PREVENTION BEGINS HERE

P6471 | BEDSIDE
Randomized study of 30 days of resveratrol and caloric restriction on serum levels of sirtuin-1 in healthy subjects

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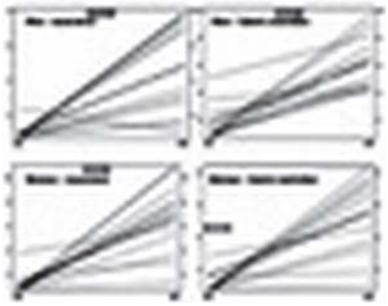
Sirtuin-1 (Sirt1) plays an important role in vascular biology, and regulates aspects of age-dependent atherosclerosis. In animals, the system of sirtuins is strongly influenced by resveratrol (RSV) and caloric restriction (CR), but its expression in humans is controversial. This study examined the effects of RSV and CR on serum levels of Sirt1 and vascular biomarkers in healthy subjects.
Methods: Study randomized 48 healthy subjects (24 women), aged 55 to 65, to 30 days of RSV (500 mg/day) or CR (1000cal/d). Blood were collected at baseline and at 30 days. Laboratory data analyzed were: triglycerides, total cholesterol (TC), HDL, VLDL, LDL, apolipoprotein A1 (apoA1) and B (apoB), lipoprotein (a), non-esterified fatty acids (NEFA), glucose, insulin, oxidative stress, C-reactive protein (CRP), and Sirt1. Expression of Sirt1 gene was analyzed by real-time polymerase chain reaction (RT-PCR).
Results: RSV and CR increased serum levels of Sirt1, respectively from 1.06±0.71 to 5.75±2.98 ng/ml (p<0.0001) and from 1.65±1,81 to 5.80±2.23 ng/ml (p<0.0001). Increase occurred in women (1.40±1.39 to 6.04±2.61 ng/ml, p<0.0001) and in men (1.36±1.41 to 5.78±2.62 ng/ml, p<0.0001) and for each intervention (Figure). TC increased with RSV (208±33 to 218±45 mg/dl; p=0.03)

and decreased with CR (216±44 to 203±40 mg/dl; p=0.01). HDL, LDL, apoAI, apoB decreased in the CR group. ApoB increased in the RSV group. Glucose, insulin, NEFA, lipoprotein (a) and antioxidant capacity did not change in either group. Expression of Sirt1 gene by RT-PCR was higher in the CR group (11.00±1.24 to 12.48±1.29; p<0.001) but not in the RSV group (11.07±1.44 for 11.24±1.57; p=0.93).



Conclusion: CR and RSV increased plasma levels of Sirt1. Long-term impact of these interventions on atherosclerosis must be assessed.

P6472 | BEDSIDE
Can we LEARN to be effective in reducing obesity-related cardiovascular risk in women? Conventional vs internet-based program administration: interim analysis

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Background: The LEARN (Lifestyle-Exercise-Attitudes-Relationships-Nutrition) program is an established weight management program that may have positive impact on cardiovascular disease (CVD) risk, but is limited in application due to physical requirement of weekly face-to-face sessions.
Purpose: To study the efficacy of a novel electronic format of the LEARN program compared to a traditional face-to-face format in achieving both weight loss and reduction of CVD risk factors in women.
Methods: Subjects include women (n=90) with ≥2 CVD risk factors prospectively randomized to either weekly face-to-face LEARN classes or weekly online podcasts of LEARN classes with an online message board. Baseline, 3- and 12-month studies include body composition, cardiopulmonary exercise, endothelial function, and laboratory testing. Analysis was done by ANOVA and matched pairs analysis.
Results: The first 34 women (mean age 53±9.1 years, mean BMI 34.3±5.5, 68% dyslipidemic, 41% hypertensive, 41% glucose intolerant) to complete baseline and 3 month testing are included in this interim analysis. Mean weight loss was 4.2 kg (p<0.0001), with similar weight loss between each group (p=0.6011). All subjects experienced significant reductions in body fat (mean –1.4%) and body volume (mean –4.5 L). Although there was a trend for improved exercise capacity and respiratory exchange rate (RER), no significant differences were observed (Table 1).

Table 1. Matched pairs analysis at 3 months

	All patients (n=34)	Face-to-face (n=14)	Online (n=20)
Weight Lost (kg)	–4.2 (p<0.0001)	–3.6 (p=0.0088)	–4.6 (p=0.0019)
% Fat	–1.4 (p=0.0015)	–1.0 (p=0.0177)	–1.6 (p=0.0172)
Body Volume (L)	–4.5 (p=0.0003)	–4.3 (p=0.0331)	–4.6 (p=0.0026)
RER	0.06 (p=0.0536)	0.09 (p=0.1252)	0.03 (p=0.2670)
Peak VO2 (mL/kg/min)	–0.4 (p=0.6359)	–1.05 (p=0.5295)	0.70 (p=0.8849)
% HR Achieved	2.5 (p=0.2630)	2.1 (p=0.1784)	2.7 (p=0.4559)
Reactive Hyperemic Index	–0.05 (p=0.7335)	0.03 (p=0.8851)	–0.1 (p=0.5916)

Conclusions: In women with CVD risk exposed to 3 months of LEARN program, online lessons appear to be as effective as traditional face-to-face classes in initial achievement of body weight, fat and volume loss. We await the final results of this year-long study regarding longer term maintenance and physiologic effects of weight loss upon CVD risk in women.
Acknowledgement/Funding: Internal Funding – Mayo Clinic Foundation – CV Prospective Study Grant

P6473 | BEDSIDE
J-shaped curve relationship of daily salt excretion and electrocardiographic left ventricular hypertrophy in first-visit outpatients

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Background: High dietary salt intake is a well-known risk factor for developing hypertension and left ventricular hypertrophy (LVH). However, there is no report investigating the relationship between daily salt excretion and LVH in first-visit outpatients.
Purpose: The aim of this study is to clarify the relationship between daily salt excretion and electrocardiographic LVH in first-visit outpatients.
Methods: Four hundred eight consecutive patients aged 40 to 80 years, visiting outpatient cardiology clinic for their first time were recruited. Patients with advanced renal dysfunction, congestive heart failure, myocardial infarction and other confounding electrocardiographic abnormalities were excluded. The relationship between daily salt excretion and Sokolow-Lyon voltage criterion or other clinical variables was examined.
Results: The patients were classified into four groups according to the quartiles (Q) of daily salt excretion (Q1: ≤8.0, Q2: 8.0–9.8, Q3: 9.8–11.5 and Q4: ≥11.5 g/day). Both the prevalence of LVH assessed by Sokolow-Lyon criterion and the mean value of the Sokolow-Lyon voltage showed J-shaped curve with the lowest in Q2 of daily salt excretion among the group. (Q1: 3.0±1.0mV, Q2: 2.5±0.7mV, Q3: 2.9±0.9mV, Q4: 2.8±0.9mV, p=0.002). After adjusting for age, sex, and other clinical variables, Sokolow-Lyon voltage again demonstrated J-shaped curve with the lowest in Q2 of daily salt excretion.
Conclusions: Not only high daily salt excretion but also lowest daily salt excretion were correlated with the high prevalence of LVH. Low daily salt excretion in first-visit outpatients may suggest LVH.

P6474 | BENCH
Plasma levels of c-type natriuretic peptide in normal, overweight and obese young population

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Purpose: In recent years natriuretic peptide (NP) entered in the "lipolytic arena" and novel physiological functions have been discovered. The role of atrial NP (ANP) and B-type NP (BNP) during lipolysis/lipogenesis was largely defined, while the action of C-type NP (CNP), the third member of the NP family, was not. Recent evidence suggested CNP as an important, natural regulator of adipogenesis. Aim of the study was to evaluate plasma levels of CNP in normal (N), overweight (OW) and obese (O) young population.
Methods: CNP plasma levels were measured in 82 subjects (age:13.0±2.3; BMI-N=20.3±0.5; BMI-OW=25.3±0.0.5 BMI-O=30.3±0.6) by a specific radioimmunoassay. To better describe the neuroendocrine profile, NT-proBNP and MR-proANP were also measured in the same samples. Biochemical parameters were also evaluated. Advanced glycated endproducts (AGEs) dependent skin autofluorescence was measured by the AGE reader apparatus.
Results: CNP plasma levels resulted progressively reduced in OW=8.8±3.5, n=10 and O=6.7±0.9, n=43 with respect to normal (N=10.4±1.6 pg/ml, n=25; p=0.04 N vs. O) while NT-proBNP (N=36.2±5.9; OW=62.1±30.9 O=54.4±6.4 pg/ml) and MRproANP (N=29.1±1.7; OW=31.8±5.4 O=30.5±1.7 pmol/l) resulted similar in all groups. Insulin (p<0.0001), cholesterol (p=0.003), triglycerides (p=ns) and LDL (p=0.0005) were progressively higher in O and OW in comparison with N subjects. Higher amounts of AGEs were observed in OW (1.74±0.4) and O (1.45±0.06) in comparison with normal (1.28±0.04 AF, p=0.02 N vs. OW). Visceral trunk fat was also measured and resulted significantly higher in OW (36.1±2.39) and O (39.4±0.69) with respect to N (23.3±1.6, p<0.0001 respectively). CNP correlated significantly with age (p=0.001), fat mass (p=0.007), insulin (p=0.01), cholesterol (p<0.0001), LDL (p=0.0006), NT-proBNP (p=0.01) and MRproANP (p=0.01). Circulating CNP values were similar in males and females. A significant correlation (r=0.313, p=0.006) was observed between AGEs and trunk fat.
Conclusion: In the population studied we observed lower plasma CNP levels confirming previous data. The correlations observed suggested that these alterations might be in part due to endocrine-metabolic deregulation. AGEs being involved in oxidative stress at vascular level, contributed to endothelial damage. The direct relationship between visceral trunk fat and skin AGEs confirms the increased risk of vascular disease due to accumulation of abdominal fat in our population, while the relationship between skin AGEs and circulating levels of total cholesterol and LDL reflects an incorrect food eating.
Acknowledgement/Funding: Unique Project Code B55E09000560002, supported by the Regione Toscana (Tuscany Region) under the Research Call "Innovation in Medicine 2009".

P6475 | BEDSIDE
Real-time longitudinal monitoring of patients diet, exercise and weight loss has substantial positive effects on metabolic syndrome parameters

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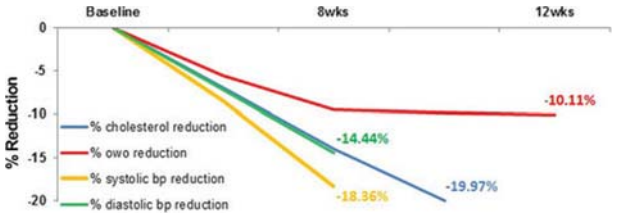
Background: Intensive lifestyle change programmes are utilised in cardiovascular disease prevention, but their efficacy is variable. Real-time monitoring of patients is feasible.
Purpose: To evaluate the efficacy of real-time adherence monitoring of pa-

tient's diet and exercise plan, in targeting metabolic syndrome parameters of weight/BMI, blood pressure (BP), and total cholesterol (TC) in overweight/obese (OWO) individuals.
Methods: 28 OWO (BMI >25 & <40) persons were enrolled. At entry, 16 had elevated BP (>140/90), 12 elevated TC (>5 mmol/l). Baseline resting metabolic rate (RMR) and BMI was calculated. Participants had a reduced daily calorie intake (~300–500 Kcal below RMR) and increased daily exercise (10,000–12.500 steps). Phone app training tracked caloric intake, while a wireless weighing-scale and pedometer, enabled daily weight tracking and exercise adherence monitoring. Non-adherents received motivational emails, SMS or phone-calls. Participants were met weekly, either face to face or via video-link. The primary aim was to assess the effects on weight loss; also, BP and TC were analysed at specific time points.
Results: Significant weight loss was achieved at weeks 4 (n=28), 8 (n=21), and 12 (n=12) with an average weight reduction of 5.6%, 9.6% and 10.1% ($P<0.01$ for each time point). In 16 hypertensive subjects, by week 8 average systolic BP declined 17.1% and diastolic BP by 14.7%. Average TC in 12 hypercholesterolaemic subjects reduced from 6.21 mmol/l to 4.97 mmol/l or 19.94% by week 10, (see Figure).



Conclusion: Intense lifestyle and behavioural intervention, coupled with real-time remote monitoring of patients diet, exercise and weight has a substantial positive effect on metabolic syndrome parameters and may have a seminal role to play in cardiovascular disease prevention.

P6476 | BEDSIDE
Increased consumption of fat and carbohydrates is associated with severe coronary artery disease

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Background: The association of dietary pattern with cardiovascular disease is well established.
Purpose: To examine the association between different dietary patterns and the severity of coronary artery disease (CAD).
Methods: The study population consisted of 188 consecutive symptomatic CAD patients recruited from the outpatient cardiology department of our Hospital. All patients underwent coronary angiography and they were categorized in subjects with one, two or three vessel disease (1VD, 2VD, 3VD respectively) and in subjects with left main (LM) disease. Patients with LM disease (stenosis≥50%), 3VD, or 2VD marked by stenosis of the proximal left anterior descending artery ≥70% were characterized as having angiographically severe CAD. Among several other demographics and clinical characteristics all subjects were tested with a validated semi quantitative food frequency questionnaire. Univariate and multivariate (principal components analysis) analyses were used in order to evaluate the relationship between dietary habits and the severity of CAD, adjusting for potential confounders.
Results: After adjusting for all traditional risk factors (diabetes mellitus, hypertension, hyperlipidemia, family history of CAD and smoking habits), an increase in red meat consumption lead to a 47% increase in the probability of having severe CAD ($p<0.01$). Body mass index did not differ between patients with severe and non-severe CAD (p=0.11). Moreover, dietary pattern consisting of high consumption of red meat, sweets, pasta, potatoes and low consumption of fruits and vegetables (western type diet) was associated with higher probability of having severe CAD ($p<0.01$). This association between "Western type" diet and severe CAD was also evident even after adjustment for several cardiovascular risk factors (OR=1.9, p=0.022).
Conclusion: Dietary patterns affect the progression and severity of CAD. Western type diet is associated with the extent of CAD independently from traditional cardiovascular risk factors. Further studies are needed to elucidate the impact of different dietary patterns on cardiovascular health.

P6477 | BEDSIDE
Aerobic high-intensity exercise training improves coronary flow reserve velocity and endothelial function in individuals with chest pain and normal coronary angiogram

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Purpose: Patients with impaired coronary flow reserve and chest pain despite normal coronary angiogram constitute a therapeutic problem with considerable residual morbidity associated with functional limitation and reduced quality of life. Exercise training has been shown to improve endothelial function and symptoms in coronary artery disease. The aim of the current study was to assess the effect of high intensity aerobic exercise training on coronary flow reserve, endothelial function and functional capacity in this population
Methods: Sixteen patients with typical exercise induced chest pain and normal coronary arteries assessed by coronary angiography at our university hospital were included. Twelve patients underwent a 3 months high intensity aerobic exercise-training program with 1 to 1 monitored exercise session on treadmill in a 4 min x 4 manner 3 times a week. Four patients served as controls. Coronary flow velocity reserve (CFVR) was measured using adenosine-induced hyperemia in the mid to distal segments of the left anterior descending coronary artery and the posterior descending coronary artery with trans thoracic color Doppler mapping. Adenosine was administered by intravenous infusion (0.14 mg/kg/min over 2 min) to record spectral Doppler signals during hyperemia. Peak diastolic flow velocities were measured, and coronary flow reserve calculated as the ratio of hyperemic to basal peak coronary flow velocities. Flow mediated endothelial function, measured as relative changes in brachial artery diameter (FMD), was measured with 2D brachial artery imaging using a 12 MHz linear-array transducer connected to a VIVID 7 ultrasound machine. Peak VO2 was measured with a maximal treadmill test and breath by breath ergo spirometry.
Results: After 3 months of exercise training CFVR increased from 2.45±0.53 to 2.85±0.43 (p=0.004) whereas FMD increased from 4.0±2.0% to 7.8±2.7% ($p<0.001$). This was associated with an increase in Peak VO2 which increased from 27.4±5.7 ml/kg/min to 31.2±6.6 ml/kg/min (p=0.003). There were no statistical significant changes for peak VO2, CFVR or flow mediated vasodilation in the control group: CFVR 2.6±0.4 vs 2.7±0.5, Peak VO2 (ml/kg/min) 26.5±4.1 vs 27.2±3.5, FMD % 4.3±2.1 vs 4.6±2.1
Conclusion: A 3 month program of high intensity aerobic exercise training improved coronary flow reserve, peak VO2 and flow mediated vasodilatation in patients with chest pain and normal coronary angiogram.

P6478 | BEDSIDE
Acute effects of energy drink consumption on endothelial function

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Background: Energy drink consumption is increasing especially among adolescents and young adults. Cases of fatal arrtyhmia linked to energy drink consumption have been reported. Vascular effects of energy drinks are not known.
Purpose: This study investigates the effects of energy drinks on endothelial functions in healthy volunteers assessed by flow mediated dilation (FMD) of the brachial artery.
Methods: 30 healthy volunteers (15 male) aging 19 to 46 years were included in the study. Demographic variables, baseline heart rate and blood pressures were recorded. Flow mediated dilation measurements of the brachial artery were performed and recorded per protocol. FMD values were calculated. The volunteers were asked to drink 355 ml of energy drink containing 53,25 mg caffeine after baseline measurements, and all measurements were repeated 60 minutes later. Baseline and post energy drink values were compared.
Results: Systolic blood pressure (P=0,59), diastolic blood pressure (p=0,71), and heart rate values (p=0,056) were similar before and after energy drinks. Baseline arterial diameters (p=0,24) and peak arterial diameters (p=0,79) in hyperemia also did not change after energy drink consumption. There was a 1,58% absolute decrease in FMD levels after energy drink consumption (9,7±4,6% at baseline vs 8,1±4,7% after energy drink) but the difference did not reach statistical significance (p=0,176).

Baseline and post-energy drink parameter

Parameter	Baseline	Post energy drink	p value
Systolic blood pressure (mmHg)	111±12	114±13	0,59
Diastolic blood pressure (mmHg)	72±8	73±8	0,71
Resting heart rate (beat/min)	73±10	70±10	0,056
Baseline arterial diameter (mm)	3,7±0,7	3,8±0,6	0,24
Peak arterial diameter (mm)	4,1±0,7	4,1±0,7	0,79
Flow mediated dilation (%)	9,7±4,6	8,1±4,7	0,176

Values are expressed as mean ± SD.

Conclusion: Energy drinks containing 53,25 mg of caffeine/355 ml did not have any significant influence on blood pressure, heart rate or endothelial functions in healthy volunteers.

P6479 | BENCH

Previous exercise training improves the lipid profile and the autonomic modulation in a model of menopause

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Purpose: Exercise training has been indicated as a intervention non pharmacological for attenuation of metabolic and cardiovascular dysfunctions triggered by the advent of menopause. However, lipid metabolism and the cardioprotective effects of previous exercise training (PT) are unknown in this condition. Thereby, the aim of the present study was to investigate the effects of previous exercise training on cardiovascular autonomic control and lipid profile in ovariectomized rats.
Methods: Female Wistar rats were divided into 4 groups (n=8 each): control (C), sedentary ovariectomized (SO), trained ovariectomized (TO) and previously trained ovariectomized (PTO). The training was performed on a treadmill, in which were 4 weeks before ovariectomy and more 8 weeks after ovariectomy for PTO (5d p/w, 40–60%), and 8 weeks after ovariectomy for TO (5d p/w, 40–60). Arterial pressure (AP) and heart rate (HR) were directly recorded and and autonomic modulation was evaluated by frequency-domain. The parametrial, retroperitoneal and subcutaneous adipose tissues were removed and weighed after euthanasia. Lipolysis was assessed in adipocytes and in content extracted from glycerol of parametrial adipose tissue. The level of plasma triglycerides (TG) was measured.
Results: The ovariectomy induced rising in AP (CS: 103.03±6.3; SO: 117.95±3.80; TO: 110.00±2.9; PTO:114.00±2.72 mmHg), increase of body weight (CS: 294.38±10.6; SO: 349.29±6.6; TO: 345.5±4.8; PTO: 336.43±2.9) and parametrial fat, subcutaneous fat and lipolysis parametrial. Both trained groups induced bradycardia (TO: 355.32±14 and PTO: 331.14±17.92 bpm) in compared to SO (374±6.8 bpm) with an additional reduction in the PTO. The trained groups reduced AP, increased variability of the pulse interval and the high frequency band in relation to SO and CS, but only PTO group reduced low frequency band of the pulse interval compared to SO and CS, maintaining the sympatho-vagal balance. The PTO reduced the weight of fat (subcutaneous, retroperitoneal and parametrial), the diameter of adipocytes (parametrial and retroperitoneal) in compared to the other groups. Lipolysis in PTO group was similar to the CS, with decreased plasmatic TG in relation to the other groups.
Conclusion: In this sense, the results of this study demonstrated that exercise training performed prior ovariectomy induced an improvement in autonomic modulation and lipid profile, suggesting a beneficial role of this approach in the prevention of damage caused by the menopause in this experimental model.
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P6480 | BEDSIDE

Natural antioxidant ice-cream improves vascular function and exercise performance in healthy subjects

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Diet is a major lifestyle factor in primary and secondary prevention of cardiovascular diseases. Epidemiological investigations revealed an inverse correlation between the intake of polyphenols-containing foods and coronary artery disease mortality. Cocoa and nuts are polyphenol-rich nutrients which elicits artery dilatation by reducing oxidative stress and increasing nitric oxide generation. We hypothesized that an antioxidant ice cream, product with a selected blend of cocoa, hazelnut and other ingredients from organic farming, could improve vascular function and exercise performance in healthy subjects via an oxidative stress-mediated mechanism. Thus, we performed an interventional study in which we measured the acute effect of natural antioxidant ice cream, on oxidative stress and artery dilatation in a population of healthy subjects. 14 subjects (7 male,7 female), mean age 38 years, were randomly allocated to a treatment sequence with 100 mg of antioxidant ice cream or milk ice cream in a cross-over, single-blind design. Total polyphenol content (mg/100g) was significantly higher in antioxidant ice cream compared to milk ice cream (1817 vs 96). There was at least 1 week washout between the 2 phases of the study. Flow mediated dilatation (FMD), oxidative stress (assessed by measuring plasma hydroperoxides, analytic method d-ROMs), exercise test (exercise double product: blood pressure x heart rate) were assessed at baseline, after a 24 hours abstinence from food rich in polyphenols, and 2 hours after ingestion of ice cream. Compared to baseline intake of antioxidant ice cream showed a decrease of the average values of oxidative stress by reducing plasma hydroperoxides (331±47 vs 281±38,p±≤0,01),while no effect was observed with milk ice cream (302±43 vs 308±50). Compared to baseline FMD increased significantly after intake of antioxidant ice cream (2,55±0.6 vs 6,3±1,3,p≤0,001) but not after milk ice cream intake (2,45±0,9 vs 2,34±0,5).The exercise test performed 2 h after intake of antioxidant ice cream showed compared to baseline a clear improvement of physical performance, characterized by a reduction of the double product on the peak effort for the same load reached (26.055±2646 vs 21.501±2351,p≤0.01) while no difference was observed with milk ice cream (26.055±2646 vs 25.264±2739). Our results suggest that short term administration of a natural antioxidant ice cream improves vascular function and physical activity with a mechanism involving its high content of polyphenols mediated by an oxidative stress mechanism. This may be a novel approach in prevention of cardiovascular disease.

P6481 | BEDSIDE

Does statin therpy unfavourably influence healthy lifestyle? The results of the lipidogram survey

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Introduction: Recently it has been suggested that statin therapy might have an unfavourable effect on healthy lifestyle, including diet, physical activity, weight and smoking, compared with statin non-users.
Purpose: We assessed the differences in the temporal trends of healthy lifestyle parameters between statin users and non-users among Polish adults included to the LIPIDOGRAM survey.
Methods: Through 675 primary care centres in 444 Polish cities, 17,065 individuals were included to cross-sectional nationwide population-based survey in 2004 (LIPIDOGRAM 2004 survey). A separate prospective randomized sample of 1,842 individuals recruited in 2004 had a 5-year follow-up (LIPIDOGRAM 5-YEARS survey). The parameters of healthy lifestyle – changes in diet, physical activity, body mass index (BMI) and waist circumference (WC), as well as smoking habits - were evaluated 3 times (in 2004, 2006 and 2010).
Results: 1190 patients (65%) completed the LIPIDOGRAM 5-YEARS study in 2010. Within this group there were 520 patients with dyslipidaemia (43.7%) in 2004, of whom 189 (36.3%) were treated non-pharmacologically, and for the rest (n=331; 63.7%) statins were administered. In 2010 (compared with 2004) there were almost 2 times fewer patients on diet in the group of statin users compared with statin non-users (25.7 vs 49.2%; p<0.001). At study baseline (2004) regular physical activity was declared by 40.2% dyslipidaemia patients without statin therapy and by 23.9% by statin users (p<0.001). After 5-year follow-up, regular physical activity was continued only in 3.7% statin non-users and 6.3% of patients on statin therapy (p=0.199). In 2010 there were numerically less individuals with BMI <25 kg/m^2 (who kept a normal BMI compared with 2004) in statin users than patients without statin therapy (15.4 vs 21.2%; p=0.097). Similarly there were significantly more patients who kept the correct values of WC in the group of statin non-users (47.1%) compared with statin users (36.6%; p=0.019). Opposite results were observed for smoking habits, as significantly more statin users stopped smoking after 5-year follow - there were 6 vs 12.2% smoking patients in 2010 in statin users and non-users, respectively (p=0.015).
Conclusions: A small proportion of patients with dyslipidaemia, both on and not on statin therapy, complies with a healthy lifestyle; a great challenge for physicians. The application of healthy diet and the number patients with correct BMI/WC was reduced among statin users over time. Statin therapy does not seem to affect physical activity and might positively influence quitting smoking.
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MITRAL SURGERY

P6482 | BEDSIDE

Unfractionated vs. low-molecular weight heparin immediately after heart valve surgery

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Introduction: A number of studies have suggested that low molecular weight heparin (LMWH) may be used for early anticoagulation after heart valve surgery, as unfractionated heparin (UFH) is used, but yet, there is no consensus which LMWH is better to use.
Purpose: We wanted to investigate efficacy and safety of early anticoagulation by using the UFH vs. two different LMWHs, immediately after heart valve surgery.
Methods: In this prospective study, we evaluated the intensity and safety of early anticoagulation after heart valve surgery of 170 consecutive patients (pts) by measuring the activated partial tromboplastine time (aPTT) and anti-Xa activity on the first, second and the last day of the therapy by UFH (55/170 pts) and two LMWHs, dalteparin (58/170 pts) and enoxaparin (57/170 pts). We evaluated early postoperative mortality and morbidity, especially hemorrhagic and thromboembolic events, as well as hematologic parameters, chest tube output, and the need for transfusion and reexploration. Independent samples t-test, one-way-ANOVA, chi^2 test and Kruskal-Wallis test, were performed in the statistic analysis.
Results: There was no difference between the groups in terms of demographic and other baseline characteristics (p=NS). UFH had a tendency to over-anticoagulate (aPTT>70s) patients at the beginning of treatment but not

in the middle, nor at the end of therapy, when majority of patients were optimally anticoagulated (aPTT 45–70s) ($p<0.0001$). Patients treated with enoxaparin were steadily optimally anticoagulated (anti-Xa 0.5–1 IU/ml) during the follow-up ($p<0.0001$). On the other hand, dalteparin treated patients were constantly under-anticoagulated (anti-Xa<0.5 IU/ml), predominately on the first day ($p<0.0001$), which was also evident on the second ($p=0.028$) and the last day of treatment ($p=0.024$). There was no difference between the groups in terms of thromboembolic and major bleeding events rate (p=NS). UFH treated patients had more pleural and pericardial hemorrhagic effusions (5/55), comparing with enoxaparin treated (0/57) and dalteparin treated patients (1/58) ($p=0.022$). Overall mortality was 5.3%. Mortality rate was similar in all groups, 2/55 among UFH treated patients, 3/57 among enoxaparin treated patients and 4/58 among dalteparin treated patients (p=NS).

Conclusions: Using the LMWH for early anticoagulation after heart valve surgery is as safe and effective as using the UFH, but there is a difference between level of anticoagulation achieved by enoxaparin and dalteparin, that could be attributed to their different low-molecular characteristics.

P6483 | BEDSIDE
Conventional mitral surgery in patients with left ventricular dysfunction: a single centre experience

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Background: Left ventricular (LV) dysfunction is often underestimated in patients with severe mitral regurgitation. Even in the presence of "normal" LV function, volume or pressure overload can lead to adverse consequences affecting survival. Decision making for these high-risk patients poses a real dilemma in the daily practice since trans-catheter treatments are rapidly expanding as alternative to conventional surgery.

Purpose: To evaluate the early and mid-term outcomes of patients undergoing conventional mitral surgery with a moderate/severe ventricular dysfunction.

Methods: From 2004 to 2014, 178 patients (115 males, mean age 66,9±10,6 years) with an ejection fraction (EF) less than or equal to 45% underwent mitral valve repair (50) or replacement (128). Mean preoperative EF was 37±6,2%. Mean PAPs was 48,9±13,8 mmHg while mean creatinine was 1,24±0,88 mg/dl. Thirty-eight patients had diabetes and 92 had an associated coronary disease. Variables with a P value <0,10 at univariate analysis entered the multivariate logistic regression to determine predictors of in-hospital death. Kaplan–Meier estimates were calculated and compared using a log-rank.

Results: Operations were performed in urgent/emergent conditions in 9,3% of cases. Cardiopulmonary-bypass and cross-clamp times were 168±60 and 118±42 minutes. CABG was performed in 61 patients. Forty-seven patients (26,4%) required IABP. Eleven patients died in hospital (6,2%). Two patients had a stroke. Five required a continuous veno-venous hemofiltration. Median postoperative stay was 14 days (range 6–158). Median FU-time was 16.2 months (IQR 4–50). Nine patients died and 9% was lost at FU. Survival rates were 92,6 at 1y and 87,9 at 5 and 8 years. Freedom from mitral reoperation was 95,6 at 1y and 93,4 at 5 and 8 years. Age (P=0,04; OR 1,32, C.I. 1,015–1,73), CPB time (P=0,04; OR 1,019, C.I. 1.001–1,038) and preoperative creatinine (P=0.03; OR 3,04, C.I.1,11–8,3) were independent predictors of in-hospital death. Type of surgery (repair vs. replacement) didn't impact on death as well as the presence of coronary disease (P=0.54) and EF <30% (P=0.69). Mean EF didn't change at discharge (37,7±9,2%) and at last FU (38,5±10,5%).

Conclusions: Conventional mitral surgery still represents a satisfactory option in very complex patients with moderate/severe myocardial dysfunction. A lower EF doesn't affect early outcomes while age, creatinine and cardiopulmonary bypass time are independent predictors of in-hospital deaths. Older patients with a combined cardio-renal impairment can probably benefit from alternative/trans-catheter therapies.

P6484 | BEDSIDE
Effects of concomitant MAZE procedure in patients with functional mitral regurgitation undergoing isolated mitral valve annuloplasty using the HeartPort technique

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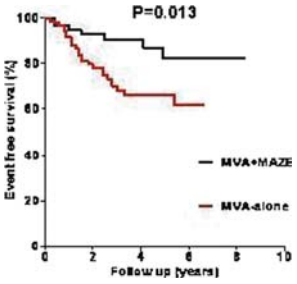
Backgroud: Significant functional mitral regurgitation (FMR) is frequently associated with atrial fibrillation (AFIB). The HeartPort technique is a minimally invasive endoscopic video-assisted approach via the right chest avoiding sternotomy.

Objective: To study effects of concomitant MAZE procedure in patients with FMR undergoing isolated mitral valve annuloplasty (MVA) using the Heartport technique.

Methods: The study population consisted of 139 patients (age 67±12y, 60% males, 47% coronary artery disease, 69% AFIB) with FMR undergoing isolated MVA between 2005 and 2012. Concomitant MAZE procedure was performed in 56 (40%) patients (the MVA+MAZE group). The remaining patients underwent MVA alone (the MVA-alone group).

Results: The performance of MAZE was not associated with increased 30-day mortality (0% in both groups, NS). During a median follow-up of 3.6 y (IQR 2.2–4.9 y), the cummulative rate of death from any cause was similar in the MVA+MAZE (13%) and the MVA-alone (19%) group (HR, 0.49; 95% CI 0.21–1.16; p=0.11). In contrast, the MVA+MAZE group showed significantly lower rate of hospitalizations for heart failure than the MVA-alone group (13% vs 30%; adjusted HR, 0.41; 95% CI 0.20 - 0.83; p=0.014) (Figure). In addition, reverse left ventricular remodeling was observed only in the MVA+MAZE group (Δ end-systolic volume, –18 ml vs + 4 ml; $p<0.05$; Δ ejection fraction, +5.5% vs –2.2%; $p<0.05$).



Hospitalizations for worsening HF

Conclusions: In patients undergoing minimally invasive MVA, concomitant MAZE procedure was associated with improved long-term outcome and reverse left ventricular remodeling.

P6485 | BENCH
Do we bring down long-term survival in patients with severe ischemic mitral regurgitation when replace mitral valve: propensity-matched analysis?

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Background: Severe ischemic mitral regurgitation (IMR) is associated with reduced long-term survival and optimal treatment still remains controversial. Our study focused on patients with severe compromised ischemic left ventricle and functional IMR to understand how mitral valve replacement versus repair affects survival and provide the predictors of long-term mortality.

Methods: 1068 patients (mean age 57,9±8,3 years) with coronary artery diseases and ischemic mitral regurgitation were operated – in 989 patients mitral valve (MV) repair and in 79 patients MV replacement were combined with CABG. Groups were matched by propensity score using LV remodeling, MR grade by quantitative echocardiography, demographics dates and co-morbidity. Survival (with mean follow-up 7,34±1,8 years) and NYHA class were compared. Uni- and multivariate analyses were performed and the predictors of long-term mortality were identified.

Results: Before matching 10-year survival was significantly worse in replacement group (HR– 2,14; 95% CI 1,43–3,21; p=0,001). After propensity matching 1:1 we've received cohort of 138 patients with severe compromised LV (EDD 71,1±7,9 mm, ESD 59,1±9,7 mm, iEDV 126±33,9 ml/m^2 with EF 31,5±5,7%) and severe MR (ERO PISA 0,43±0,18 mm^2). In matched cohort four patients who underwent mitral valve repair died at 30 days postoperatively and five patients died after valve replacement (p=0,5). The fact of mitral valve replacement versus repair did not impair long-term survival (HR: 1,35; 95% CI 0,82–2,29; p=0,26) and overall in 1- and 5-year were 91,8±0,14% and 57,2±0,48% respectively (long-rank p=0,251). Distribution of NYHA functional class in follow-up improved (Wilcoxon signed-ranks test p=0,001 for both group) and was comparable between matched groups (with mean 2,38±0,68 after MV replacement vs. 2,25±0,92 for MV repair, χ^2: 5,29, p=0,49). In multivariate Cox regression LV ESD (HR: 1,038, 95% CI 1,004–1,072, p=0,013) and advanced NYHA (HR: 2,55, 95% CI 1,57–6,1, p=0,037) were found as independent risk factors for an increased long-term mortality after surgery.

Conclusion: The mitral valve chordal-sparing replacement versus repair did not take down survival in patients with severe damaged ischemic LV. The functional status of patients is comparable between repair and replacement group in long-term follow-up. Survival mostly depends on factors related to the patient's condition at the time of surgery.

OPTIMISING TECHNIQUES AND OUTCOME AFTER CARDIAC SURGERY

P6486 | BENCH
Should Ross procedure be considered a feasible alternative for adult patients who require AVR? Single centre 357 patients long-terms outcome, clinical and echocardiographic study

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Aim of the study is to evaluate clinical and echocardiographic characteristic and mid-long term results of Ross operation in different groups of age with emphasis

on durability of the aortic autograft and pulmonary homograft and on the risk factors for re-operation.
357 pt underwent Ross procedure (247 M, mean age 29.4±11.1 years) and had complete clinical and echocardiographical follow up (mean f-u 13.4±3.9 years). The cohort was divided into 2 age groups at the time of surgery. Group 1 consisted of 202 (57%) pt less than 18 years old (141 M, mean age at f-u of 22.7±4.5 years), whereas group 2 consisted of 155 (43%) pt older than 18 years of age (106 M, mean age at f-u of 33.2±7.4 years). Mean age at surgery was 10.3±6.3 years in group 1 (range 1 week-18 years) and 25.8±6.9 years in group 2 (range 19–63 years), ($p<0.0001$). In group 1, 71 patients (36%) had a redo procedure or surgery vs. 45 patients (29%) in group 2 (p=NS). Mean time for redo surgery was 6.4±4.1 years in group 1 and 6.7±4.2 years in group 2 (p=NS). Homograft survival was 11.4±4.9 years in group 1 vs. 13.2±4.4 years in group 2, p=NS. The need for a second redo surgery was 3% in group 1 and 3% in group 2, (p= NS). Delay from previous surgery was 6.5±5.5 years in group 1 vs 13.2±3.6 years in group 2, ($p<0.0001$). Freedom from surgery after 10 years was 66% in group 1 and 81% in group 2 (p=0.0025), after 20 years 62% vs 72% (p=0.06) respectively.

Freedom from redo surgery

	Group 1 (202 patients)	Group 2 (155 patients)	p
After 1 year	94%	98%	0,1128
After 5 years	79%	86%	0,1179
After 10 years	66%	81%	0,0025
After 15 years	63%	75%	0,0219
After 20 years	62%	72%	0,0625

Ross procedure should be considered a feasible alternative for adult patients who require AVR, especially for people with an active lifestyle and young women who plan to become pregnant. Technical expertise is required to ensure optimal benefits and enhanced durability for the patients.

P6487 | BEDSIDE
Systemic inflammation and oxidative stress contribute to acute kidney injury after transcatheter aortic valve implantation

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Background: AKI is common after conventional valve surgery with cardiopulmonary bypass (CPB) and has been linked to preexisting comorbidities, periprocedural hypotension and systemic inflammation. TAVI does not require CPB but post-procedural AKI is still common. The extent of systemic inflammation and the mechanism of AKI after TAVI is not fully understood.
Objective: To characterize the inflammatory response after trans-catheter aortic valve implantation (TAVI) and evaluate its contribution to the mechanism of post-procedural acute kidney injury (AKI).
Methods: 105 consecutive patients undergoing TAVI at our institution were included in this study. We analysed the peri-procedural inflammatory and oxidative stress responses by measuring a range of biomarkers (including C-reactive protein [hsCRP], cytokine levels and myeloperoxidase [MPO]), before TAVI and 6, 24 and 48 hours post-procedure. We correlated this with changes in renal function and patient and procedural characteristics.
Results: We observed a significant increase in plasma levels of pro-inflammatory cytokines (hsCRP, Il6, TNFa receptors) and markers of oxidative stress (MPO) after TAVI. The inflammatory response was significantly greater after trans-apical (TA) TAVI compared to trans-femoral (TF). This was associated with a higher incidence of AKI in the TA cohort compared to TF (42% vs 8%, respectively, $P<0.0005$). The incidence of AKI was significantly lower when the reactive oxygen scavenger N-Acetylcysteine (NAC) was given peri-procedurally (11% vs 39%, $P<0.001$) with a 3x lower relative risk of developing AKI with NAC (RR 4.7; 1.4–18.3). In multivariate analysis only the TA approach and no use of NAC before the procedure were independent predictors of AKI.
Conclusion: TAVI creates a significant post-procedural inflammatory response, more so with the TA approach. The mechanisms of acute kidney injury after TAVI are complex. Inflammatory response, hypoperfusion and oxidative stress may all play a part and may therefore be therapeutic targets to reduce/prevent AKI in the future.
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P6488 | BENCH
A tailor made valve surgery with a novel autologous bioprosthesis

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Purpose: We are developing a novel autologous heart valve prosthesis (Biovalve) with a unique in-body tissue engineering method. This enables us to select a tailor made valve replacement to fit the each patient and keep biocompatibility. In this study, we made 3 types of heart valve and tested the feasibility of them in a large animal model.
Methods: We created many kinds and sizes of molds for Biovalves using plastic rods with 3D printer easily and quickly considering the recipient character. In this study, we selected 3 types (a conventional type, a full-root type and a valve with a metalic stent for transcatheter implantation) and embedded them in the subcutaneous spaces of adult goats for 1–2 months. After extracting the molds with the tissue and removing the plastic rods only, Biovalve with tri-leaflets similar to those of the native valves were constituted from completely autologous connective tissues and fibroblasts.
Five cases of conventional Biovalves were implanted in the aorta under cardiopulmonary bypass, 8 cases of full-root type were implanted in the apico-aortic bypass, and 22 stent valve type were implanted with transcatheter technique into in situ the aortic and pulmonary valves (15 and 7, respectively).
Results: In each type, Biovalves were successfully implanted and showed smooth movement of the leaflets with a little regurgitation in angiogram, and the maximum duration reached to 2 months in full-root type and 6 months in stent valve type. Histological examination of the Biovalves showed the autologous cells covering the laminar surface of the valve leaflets and also getting into the connective tissues.
Conclusion: The Biovalves have a potential to be used for tailor made therapy in valve surgery and satisfy the higher requirements of the systemic circulation maintaining the histological character as autologous tissues.

P6489 | BEDSIDE
Conventional aortic valve replacement in medium/high risk patients

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Introduction: Medical treatment of aortic stenosis is associated with a poor prognosis and the advent of transcatheter valve implantation (TAVI) seems to be a good option to those ineligible for surgery. However, its use in medium and high risk patient still able to go for surgery is still under debate.
Purpose: To evaluate short and long-term results of high/medium risk patients who underwent conventional aortic valve replacement (AVR).
Methods: From January 2006 to December 2010, 125 patients with isolated or predominant aortic stenosis, logistic EuroSCORE >10 (mean 17.2±7.8; range10–50.8; 23.2% with EuroSCORE>20), from a total of 798 (15.7%) were submitted to conventional AVR. Mean age 77.0±5.5 years (62–90); female 87 (67%); 84 (67%) were in NYHA III-IV; COPD in 33 (26.4%); reoperation in 15 (12%); moderate to severe LV dysfunction in 36 (29%); 9 (7.2%) patients with cerebral vascular disease; mean aortic valve area 0.6±0.2cm 2 and mean transaortic gradient 57.2±16.1 mmHg. Mean systolic pulmonary artery pressure 54.6±17.6 mmHg.
Results: A bicuspid valve was found in 15 (12%) and calcified aorta in 33 (25.4%) (one case of porcelain aorta). Biological valves implanted in 115 (92%), mean size 21.8±1.2mm. Septal myectomy performed in 102 (82%) and aortic root enlargement in 39 (31.2%). Thirty-day mortality was 1.6% (2 patients), comparable to that observed in those with EusoSCORE <10 (0.6%; P=0.232). Inotropic support used in 23 cases (18%). Complications included pacemaker implantation in 6 cases (4.8%) and major stroke in 2 (1.6%). Mean postoperative creatinine 1.6±1 mg/dL. Mean hospital stay was 8.8±6 days. No significant paraprosthetic leak was detected at discharge. Survival at 1, 3 and 6 years was 93.4±2.3%, 86.0±3.2% and 65.3±5.2%, respectively, which was significantly lower than the 673 patients who had EuroSCORE <10 (98.2±0.7%, 96.0±1.1% and 87.7±1.8%, respectively for the same periods; $P<0.001$)
Conclusion: Despite the growing trend towards the use of TAVI in patients considered to be at high/medium risk for surgery, conventional AVR, when feasible, remains the best option, as it can be performed with low early mortality and morbidity, comparable to lower risk populations, but with impaired late survival, probably because of associated comorbidities.

P6490 | BEDSIDE
Ross operation: is it possible to identify the ideal candidate?

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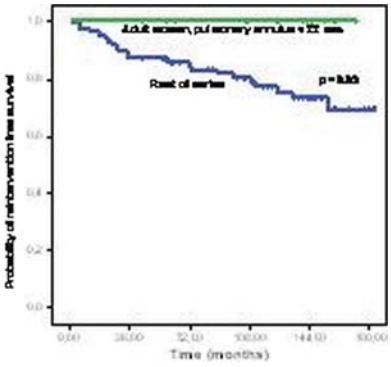
Purpose: Autograft and homograft reintervention are possible complications after Ross operation. Our aim was to identify, in a prospective series of a reference cardiovascular surgery hospital, the variables that identify those patients free of reintervention in any valvular substitute in the long term.
Methods: Since November 1997 to July 2009, a total of 107 patients diagnosed of severe aortic valve disease requiring surgical treatment underwent Ross surgery (mean age 30±11 years, 71 male, 86 patients≥18 years). In all of them, a comprehensive clinical and echocardiographic evaluation was performed before the intervention and at discharge, at 6, 12 months and annually after surgery.
Results: After up to 15 years of follow up (median 11 years, interquartile rank 8–13 years) 21 patients (20%) required surgical or percutaneous reintervention, 11 on the autograft and 10 on the homograft. Probability of survival free from reintervention of both valve substitutes at 5 and 10 years was 88% and 81%,

respectively. Women had better reintervention-free survival at median follow-up (85% versus 75%), as well as adult patients (≥18 years, 80% versus 67%) and the 34 patients with pulmonary annulus <22 mm in the echocardiogram previous to surgery (82% versus 76%), but none of these differences were statistically significant. However, the subgroup of 16 adult women with pulmonary annulus <22 mm had a significantly better reintervention-free survival at median follow-up (100% versus 73%, p=0.04, figure).



Conclusion: In our series, none of the adult women with pulmonary annulus <22 mm required reintervention of the autograft or homograft in the long-term. Further confirmation of this finding in larger series could be useful to identify the ideal candidate for Ross surgery.

P6491 | BEDSIDE
Impact of small annulus on valve hemodynamic and mid-term outcome following transcatheter aortic valve implantation compared with surgical aortic valve replacement

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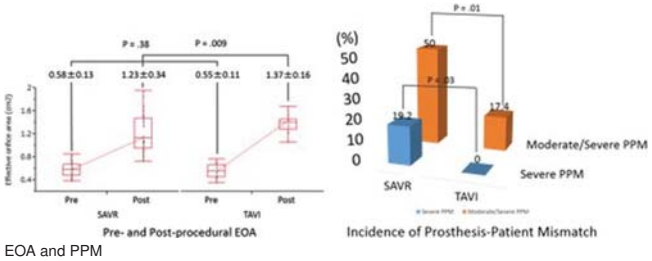
Purpose: The aim of this study was to investigate the impact of small annulus on valve hemodynamic and mid-term outcome in patients with severe aortic stenosis (AS) following transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement (SAVR).
Methods: From Jan. 2013 to Aug. 2014, a total of 206 consecutive patients underwent aortic valve replacement in our institute were retrospectively enrolled. We defined annulus with 20mm or less measured by pre-procedural transesophageal echocardiography as small annulus. We compared the post-procedural valve hemodynamics including prosthesis-patient mismatch (PPM) and mid-term outcome between TAVI and SAVR patients.
Results: The age of the 75 severe AS patients with small annulus ranged from 63 to 95 years (mean±SD, 80.7±7.0 years, SAVR [n=52] 78.4±6.1 years vs TAVI [n=23] 85.9±6.1 years, P<0.0001)). Post-procedural transaortic peak velocity (peakV), mean aortic pressure gradient (mPG), and effective orifice area (EOA) were significantly better in the TAVI group than in the SAVR group (peakV, SAVR 2.81±0.55m/sec vs TAVI 2.51±0.37m/sec, P=0.007; mPG, SAVR 17.0±6.6mmHg vs TAVI 13.2±4.4mmHg, P=0.005: EOA, SAVR 1.23±0.34cm^2 vs TAVI 1.37±0.16cm^2, P=0.046). Severe PPM defined as EOA ≤0.65cm^2 was seen in the SAVR group (26 cases, 50%) while no severe PPM was occurred in the TAVI group (P=0.03). In the light of these results, device success rate was significantly higher in the TAVI group (78.3%) than in the SAVR group (53.9%, P=0.045), whereas 1-year mortality was similar between the two groups (P=0.80)



EOA and PPM

Conclusion: In the severe AS patients with small annulus, TAVI was hemodynamically superior to SAVR and significantly reduced the incidence of PPM, though it did not affect 1-year mortality.

P6492 | BEDSIDE
Type 2 diabetes and prosthesis-patient mismatch are associated with faster structural valve degeneration in bioprosthetic aortic valves

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Introduction: Bioprosthetic aortic valves have been progressively more frequent due to excellent hemodynamic properties and freedom from warfarin. The main problem is long-term durability that is limited by structural valve degeneration (SVD). The patients that develop SVD have a poor prognosis.
Aims and methods: The aim of this study was to assess the clinical risk factors for early SVD in aortic bioprostheses. From 1999 until 2014 the patients after cardiac surgery were prospectively followed up. The inclusion criterion was the patients who underwent aortic bioprostheses without in-hospital mortality. In the follow-up the patients were seen after discharge, third and twelfth months. During each visit an echocardiogram was performed. SVD was defined as stenosis type if the progression of mean aortic transprosthetic gradient double from baseline with thickening of leaflet. The incompetence type SVD was diagnosed when aortic regurgitation was either moderate or severe.
Results: 257 patients were discharged after the surgery. Median follow-up was 3,8 years, 96.1% follow-up was completed. Mitroflow was the most frequent biosprosthesis model (61%) followed by Carpentier-Edwards (18%). Mean transprosthetic gradient was higher in bioprostheses with prosthesis-patient mismatch (PPM) than those without PPM (16±6 mmHg vs. 13±5 mmHg, P<0.001) at baseline and these differences persisted at the first year after valve replacement. During the follow-up the diagnosis of SVD was carried out in 21 patients at mean 3.9±2.3 years. SVD as stenosis was observed in 16 cases and regurgitation in 5 cases. On univariable analysis, SVD was associated with diabetes (57% vs. 31% P=0.01). At 3 and 5 years after valve replacement freedom from SVD was 95% and 79% in diabetic patients, significantly lower than in non-diabetic patients (97% and 95%, respectively) (Log-Rank, P=0.005). Free from SVD in patients with PPM was 92% and 81% significantly lower than patients without PPM (99% and 95%) (Log-Rank, P=0.001) at 3 and 5 years. Clinical risk factors to develop SVD in multivariable analysis revealed that diabetes and PPM were independent predictors of SVD. The combination of both predictors for SVD shows that in diabetic patients with PPM, survival freedom from SVD was 81% at 5 years.
Conclusions: In the present study, diabetic patients and PPM in aortic bioprostheses are strong predictors of SVD. When both clinical predictors are combined, the free-SVD survival rate in this group decreases progressively when compared with the combination of other predictors.

ROBOTIC SURGERY

P6493 | BENCH
Minimally invazive transcatheter ventricular restoration (TCVR)

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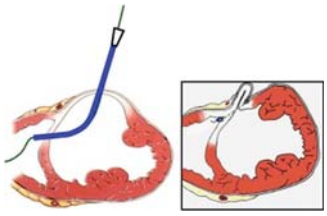
Background: Post myocardial infarction left ventricle (LV) remodeling is the key proces in worsening the outcome of the patients with ischemic heart disease. This single center study is the first report of transcatheter technique of LV volume reduction (TCVR) for ischemic cardiomyopathy.
Patients and methods: 10 patients (Ø age 63,5 years; 7 M/3W; Ø BSA 1,93); all with LV apical-septal aneurysm, were indicated for TCVR procedure. Hybrid approach is performed in catheterization lab/hybrid room under fluoroscopy. Revivent anchor plication concept is based on surgical introduction of external anchor placed through left mini-thoracotomy and internal anchor introduced by puncture technique from right internal vein. The primary endpoint of the Revivent study was safety and total reduction of LVESVI.
Results: In 10 patients we carried-out TCVR fully hybrid way. Average time of the procedure was 226 minutes. The procedure was done in all patients successfully and an average 3 anchors per patient were placed. In one month the total reduction of LVESVI was 39% (baseline LVESVI 126 ml/m^2, one month LVESVI 78 ml/m^2). LV EF increase from
Ø 32% at a baseline to 41%. NYHA at baseline 2,5 droped to 1,5 at one month, 6 minutes walking test increased from baseline 382m to 449 m. Only one patient got significant TIA immediatelly after the procedure with fast recovery.



Conclusion: 1.our single center results confirmed transcatheter TCVR "exclusion" of LV aneurysm safe and effective; 2. learning curve is reasonable short; 3.the real clinical benefit needs to be confirmed by larger studies.

AORTA, PERIPHERAL ARTERIAL AND VENOUS SURGERY

P6494 | BEDSIDE

Bypass surgery versus endovascular therapy in chronic hemodialysis patients with critical limb ischemia due to infra-inguinal disease

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Background: Lower limb revascularization with surgical or percutaneous procedure has been widely performed to treat critical limb ischemia (CLI). However, it remains controversial which procedure should be optimized. On the other hand, CLI is frequently seen in hemodialysis (HD) patients, who are consistently at a highest cardiovascular risk. We investigated long-term clinical outcome after bypass surgery or endovascular therapy (EVT) in HD patients with CLI due to infra-inguinal disease.
Methods: We enrolled a total of 566 consecutive HD patients electively undergoing infra-inguinal revascularization. Of them, 234 patients underwent bypass surgery and 332 patients underwent EVT. They were followed up to 10 years. Amputation-free survival (AFS), defined as freedom from major amputation or all-cause death, was primarily evaluated. Incidence of any revascularization was also analyzed. To reduce the selection bias between the procedures, propensity score with all baseline characteristics was incorporated into Cox proportional hazards model as a covariate.
Results: Tissue loss was seen in 69.4% of patients, and 42.6% of them had infra-popliteal disease. During follow-up period, 61 major amputation (10.6%) and 171 death (30.2%) occurred. Propensity score-adjusted AFS at 10-year was comparable [47.2% in bypass group vs. 35.7% in EVT group, adjusted hazard ratio (HR) 1.14, 95% confidence interval (CI) 0.83–1.58, p=0.41]. However, on a landmark analysis, the bypass group had poorer AFS during 1 year compared to the EVT group (adjusted HR 1.53, 95% CI 1.03–2.28, p=0.037), and inversely tended to have better prognosis after 1 year (adjusted HR 0.60, 95% CI 0.33–1.04, p=0.068). Also, only declined body mass index (adjusted HR 0.94, 95% CI 0.90–0.98, p=0.0064) and elevated C-reactive-protein (adjusted HR 1.05, 95% CI 1.02–1.07, p=0.0007) were identified as independent predictors for lower rates of AFS. Similarly, adjusted survival rates were also comparable between two groups for amputation (78.9% vs. 81.3%, adjusted HR 1.38, 95% CI 0.76–2.53, p=0.29) and for all-cause mortality (52.6% vs. 41.5%, adjusted HR 1.06, 95% CI 0.74–1.51, p=0.74), respectively. Freedom from any revascularization was consistently higher in the bypass group than in the EVT group (78.5% vs. 48.2%, adjusted HR, 0.42, 95% CI 0.27–0.65, p<0.0001).
Conclusion: Although bypass surgery had lower rates for revascularization compared to EVT, rates of AFS were comparable between two procedure groups in HD patients. Pre-procedural comorbid conditions should be more cared in this high-risk population.

P6495 | BEDSIDE

Assessment of aortic dissection risk in Marfan syndrome patients by analysis of aortic viscoelastic properties

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Background: Marfan syndrome is an autosomal dominant genetic disorder characterized by an abnormal fibrillin-1 (a structural protein of connective tissue) synthesis. Aortic root dilation and dissection are the main problems affecting patients prognosis in these patients. Their pharmacological prophylaxis with losartan or with a beta-blocker counteracts the aortic root dilation, but a close follow-up is required to assess therapeutic response rate and to identify non-responders. Unfortunately genotype-phenotype studies do not allow to determine the exact risk profile in these patients and there is no reliable method to accurately predict their risk of aortic dissection.
Purpose: Aim of this study was to evaluate non-invasive markers for identification of Marfan patients at higher risk of aortic complications.
Methods: We studied 187 Marfan patients (identified according to 2010 Revised Ghent Criteria and positive genetic analysis), age 32.3±16.5 yrs (mean±SD). 52 patients (27.8%) had undergone surgical ascending aorta replacement (David or Bentall procedure). Central pressure curves were recorded by PulsePen tonometer, and the aortic viscoelastic aortic properties were studied by determination of carotid-femoral pulse wave velocity (PWV).
Results: With reference to the age related distribution of PWV values in a normal population, defined according to Arterial-Stiffness-Collaboration, PWV mean values in Marfan patients corresponded to 60th percentile in non-operated patients and to the 67th percentile in those operated. Adult Marfan patients (n=146) generally displayed a low blood pressure, because of the pharmacological prophylaxis, and were compared with a population of 189 adult healthy subjects (81 males), matched by age (38±13 vs 38±16 yrs.), heart rate (64±9 bpm vs 64±11 bpm) and blood pressure (mean BP = 78±9 mmHg vs 79±4 mmHg) values. Average PWV value was higher than in healthy controls (PWV = 7.0±1.7) both in not operated (PWV = 7.6±1.6; p=0.0003) and in operated (PWV = 9.5±3.2; p<0.0001) Marfan patients. Among non operated patients, PWV was significantly correlated to aortic root diameters (Aortic annulus: R^2=0.14; Valsalva sinuses: R^2=0.22; Sinotubular junction: R^2=0.28).
Conclusions: A significant reduction of the distensibility of the aorta was found in Marfan syndrome. Further analyses are needed to assess the prognostic significance of PWV changes seen in these in these patients.

P6496 | SPOTLIGHT

Demonstration of the mechanisms of aortic regurgitation in type a aortic dissection by real time 3D transesophageal echocardiography

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Objective: The aim of this study was to explore incremental value of real-time 3D transesophageal echocardiography (RT-3D-TEE) in demonstrating the anatomic mechanisms of aortic regurgitation (AR) in type A aortic dissection involving aortic root so as to assist the surgeon in selecting a personalized and reasonable aortic root surgical strategies.
Methods: Non-continuous 54 patients with type A aortic dissection involving aortic root (normal aortic valve number and quality) who underwent aortic root surgeries were included, intra-operative RT-3D-EE was performed before thoracotomy using an iE33 system, to reconstruct the three-dimensional morphology of aortic root structures and analyze the anatomical mechanism of AR, and the results of RT-3D-TEE were compared with the operative findings.
Results: (1) RT-3D-TEE showed three types of the anatomical mechanism of AR in patients with type A aortic dissection (normal aortic valve number and quality): incomplete cusps closure or short coaptation length of cusp due to relevant valsalva sinus dilation or dissection (type I); aortic leaflet prolapse due to cusp commissural fusion tethering in the intimal flap (type II); diastolic intimal flap prolapse through the aortic valve orifice resulting in incomplete aortic valve closure (type III). (2) The RT-3D-TEE demonstration results of functional anatomic mechanism of AR have a good consistency to those of operative findings (Kappa=0.867). (3) The Youden index of RT-3D-TEE on type I, II and III were 0.93, 0.86 and 0.73 respectively, the misdiagnosis rate were 0, 8.8% and 2% respectively; and the missed diagnosis rate were 6.7%, 5% and 25% respectively.(4) Surgical strategies for aortic root predicted by RT-3D-TEE have a good consistency to operative surgical treatment selections (Kappa=0.919).
Conclusions: RT-3D-TEE could be used to visually and accurately demonstrate the anatomic mechanism of AR in patients with type A dissection, providing necessary and objective imaging support for surgeons to select a personalized aortic root surgical strategies, especially a valve-sparing aortic root replacement.

P6497 | BEDSIDE

Aortic insufficiency indicated higher risk for progressive ascending aorta dilatation and adverse aortic events in bicuspid aortic valve disease after isolated aortic valve replacement

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Purpose: Aberrant flow pattern in the context of congenital fragility bestows bicuspid aortic valve disease (BAVD) with propensity towards ascending aorta dilatation, aneurysm and dissection. Whether isolated aortic valve replacement (AVR), the routine practice to remedy valve dysfunction, can prevent further dilatation in ascending aorta remains controversial. The present study compared long term adverse aortic events after AVR among BAVD patients with stenosis or insufficiency valve dysfunction, and intended to illuminate on the rationale for preventive aortic interventions.
Methods: BAVD patients who underwent isolated AVR procedure in our facility from June 2006 to January 2009 were retrospectively included. All patients were followed up annually by transthoracic echocardiography, and adverse aortic events defined as the occurrence of aortic dissection/rupture, aortic related death or the need for ascending aortic surgery were duly recorded.
Results: Among 196 BAVD patients included in the present study, 84 had an aortic insufficiency phenotype (BAV-AI group), and 112 were aortic stenosis (BAV-AS group). BAV-AI group demonstrated younger age [(46±13) vs. (56±14) years, p<0.001], male preference (79.8% vs. 67.0%, p=0.047), and wider aortic root diameter [(38.1±4.6) vs. (34.0±3.9) mm, p<0.001]. The median follow-up was 72 (66–78) months, and isolated AVR could prevent further dilatation in aortic root [(35.8±4.7) vs. (36.0±4.9) mm, p=0.121] but not in ascending aorta [(39.9±4.6) vs. (41.8±5.7) mm, p<0.001]. Annual rate of dilatation in ascending aorta was 0.29 (0.19–0.79) mm in BAV-AI and 0.18 (0.10–0.29) mm in BAV-AS groups (p<0.001). Multivariate linear regression analysis identified aortic insufficiency (standard-

ized β=0.317, p<0.001) and ascending aorta diameter (standardized β=0.271, p<0.001) as major factors associated with annual ascending aortic dilatation rate in BAVD patients after AVR. The incidence of adverse aortic events was significantly higher in BAV-AI group (15.5% vs. 4.5%, p=0.008). Cox regression analysis further revealed aortic insufficiency (HR=3.723, p=0.019) and preoperative ascending aortic diameter over 45mm (HR=16.840, p<0.001) as independent risk factors for adverse aortic events.
Conclusions: BAVD patients with aortic insufficiency demonstrated higher risk for accelerated ascending aorta dilatation and adverse aortic events after AVR. Preventive aortic intervention along with AVR procedure might be warranted among BAVR patients with ascending aorta diameter over 45mm, especially those with aortic insufficiency valve dysfunction.

P6498 | BEDSIDE
Bicuspid aortopathy: does it really exist? An histological study

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Background: Bicuspid aortic valve (BAV) is frequently associated with ascending aortic aneurysms (AA), which has been linked to intrinsic aortic wall fragility ("bicuspid aortopathy"). However, the mechanisms leading to development or progression of aortic disease are poorly understood. Our aim was to analyze media structure in AA of patients with and without BAV to further define the features of bicuspid aortopathy.
Methods: 134 consecutive patients (75% males, mean age 63) undergoing elective surgical repair of an AA were included and classified according to valve morphology (54 patients had BAV). All clinical variables, including aortic dimensions, pattern of dilatation and valve function were prospectively collected. Samples of ascending aortic wall were obtained during surgery and processed for light microscopy. A specialized pathologist evaluated each of the sections. Total thickness of the media, depth of penetration of vasa vasorum within the media and degenerative changes were analyzed (fibrosis, elastic fibers fragmentation, cystic medial necrosis and calcification).
Results: BAV patients were significantly younger (p<0.001) than those having a tricuspid valve (TAV) and presented with less comorbidity. Maximum aortic diameters at the time of surgery were significantly larger in patients with TAV (56 mm vs 52.7 mm, p=0.004), but we found no differences regarding the pattern of dilatation. In patients with BAV the most frequent valve lesion was stenosis (41%), whereas valve regurgitation (61%) was the most common valve dysfunction in patients with TAV (p=0.002). Media thickness was not significantly different in both groups. Patients with TAV showed a more prominent vasa vasorum network, characterized by a significantly deeper penetration in the media layer (516 micron vs 356 micron, p<0.001). These differences persisted after correcting for total media thickness. No differences were found in the presence or severity of cystic medial necrosis or calcification. However, fibrosis was more extensive and the proportion of patients showing elastic fibers fragmentation was higher among those having a TAV (p=0.039 and p=0.042, respectively).
Conclusion: There were no major differences regarding aortic media structure in these two groups of patients. Some degenerative changes (i.e fibrosis and elastic fibers fragmentation) were even more marked in TAV patients. These patients also had more prominent pattern of vascularization of the media layer. Our data do not support a different surgical attitude in patients with AA and a BAV

P6499 | BEDSIDE
Thrombogenic state after vascular surgery and perioperative cardiovascular events

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Background: Cardiovascular events (CVE) are the most limiting prognostic factor after vascular surgery. The underlying mechanism is thrombosis in patients with high atherosclerotic burden.
Purpose: To identify baseline coagulation markers related to CVE and to analyze the behavior of those markers after surgery.
Methods: Thrombin generation, assessed as endogenous thrombin potential (ETP) and ETP ratio (with-to-without thrombomodulin), and platelet aggregation in response to arachidonic acid (Aggr) were evaluated before and after surgery, for 183 patients under aspirin use. Patients were monitored for CVE detection:acute coronary syndromes, isolated troponin elevation, stroke, reoperation due to thrombosis and cardiac death. Our ethics committee approved the study and patients provided informed consent.
Results: The only baseline coagulation marker independently related to CVE was Aggr, so that patients in the 4th quartile had a 2.42 fold increased risk (p=0.034). After exclusion of patients without post-operative test and 53 who received hemoderivatives, we analyzed the behavior of ETP, ETP-ratio and Aggr for 110 patients. There was a marked increase in ETP: 648 NM*min ±457 X 887±494; p<0.001, ETP-ratio 0.43±0.25 X 0.61±0.28; p<0.001, and a significant decrease in Aggr: 5.34Ω ± 5.69 X 3.38Ω ± 5.30 (p<0.001) and in platelet count*1000:229±76 X 194±73; p<0.001. We calculated the individual variable differences (Δ) after and before surgery, and then we compared those means between patients with and without CVE. There was no difference in ΔETP (p=0.87), Δ ETP-ratio (p=0.61) or Δplatelet count (p=0.57), but patients with CVE had a greater ΔAggr (–4.27 X– 1.37; p=0.04).
Conclusion: There is a pro-thrombotic state triggered by the surgical stress. The apparent contradiction of increase in thrombin generation and decrease in Aggr suggests platelet consumption, which is greater when CVE occurs. Aspirin responsiveness before surgery is more important than net thrombin generation for the occurrence of perioperative CVE.

P6500 | BENCH
Screening for abdominal aortic aneurysm during echocardiographic examination in high risk patients

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Background: The aneurysm of the abdominal aorta (AAA) is one of major devastating cardiovascular pathologies. Its screening in the general population is costly and unrealistic, but examination of the abdominal aorta appears reasonable in high risk cardiological population.
Patients and methods: As the abdominal aorta is easily accessible to standard transthoracic echocardiographic equipment, we tested this hypothesis in 692 consecutively referred patients, 465 (67.19%) men and 227 women (32.80%) by imaging the abdominal aorta at the end of the cardiac examination.
The acquisition of the dynamic images was carried out in the transverse plan by a probe 3 S phased array sectoral with electronic sweeping at variable frequency of 1.8–3.8MHZ at a dorsal patient in decubitus.
Results: The native infra renal segment most often involved in AAA was visualized in 674 out of 692 patients what corresponds to a feasibility of 97.4%. It takes only a reasonable time of the maximum 5 minutes and does not generate any additional cost.
An AAA was detected among 31 patients (4.6%). the ratio of men to women was 7.11:1 Risk factors associated with AAA were to current and former smoking and age.
We reported some echocardiography specific factors, such as left ventricular hypertrophy or dilation and poor left ventricular ejection.In This study makes it possible to propose a surgical act among 06 patients (0.9% of the population studied) after the discovery of an aneurysm diameter more than 55mm.
Conclusion: Prevalence of dilative alterations of the abdominal aorta is high in cardio logical patients. Visualization during trans thoracic echocardiography of the most important infra renal segment is nearly always feasible (97.4%).Since detection of life-threatening but asymptomatic AAA may save lives by offering safe elective surgical treatment or stenting, opportunistic examination of the abdominal aorta during routine trans thoracic echocardiography, which involves little time and no additional cost, would appear to be highly effective and should be included in routine examinations, at least in patients over 60 years of age.

P6501 | BENCH
Role of matrix metalloproteinase single nucleotide polymorphisms in thoracic aortic aneurysm development

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Objectives: Thoracic aortic aneurysm (TAA) is a dangerous disorder with very strong genetic component, while all involved genes are not known yet. Matrix metalloproteinases plays crucial role in TAA development. Therefore, we investigated whether polymorphisms in MMP genes were associated with TAA.
Methods: The genotypes of MMP1,MMP2,MMP9, MMP13 genes were determined for 287 patients with TAA (mean age 55.4±10.3, m:f ratio 2.8:1, maximum aortic diameter 54.2±11.1 mm) and 227 controls (mean age 56.5±10.3, m:f ratio 2.4:1, maximum aortic diameter 34.4±3.7mm) using real time PCR. The associations of genotypes with TAA were assessed using logistic regression models adjusted for sex, age and hypertension.
Results: The polymorphism -8202 A/G (rs11697325) of MMP9 was strongly associated with TAA. Carriers of rs11697325 AA genotype were at increased risk for TAA, compared with noncarriers: the odds ratio (OR) was 2.7 (95% Confidence Interval (CI) 1.2–6.1). Maximal aortic diameter was significantly higher in carriers with AA variant (58,2±16.4 mm) comparing with AG (49.8±11.7 mm) and GG (48.8±8.1 mm) genotype (p<0.05). There were no any association of MMP1,MMP2,MMP9, MMP13 genes polymorphisms with TAA.

Association of MMP polymorphism with TAA

Genotype	Case	Control	OR	95%CI	P-Value
AA	31	40	2.7	1.2–6.1	P=0.01
AG	201	174	0.92	0.6–1.4	P=0.7
GG	55	43	Ref		

Conclusion: Among all studied MMP genes polymorphisms rs11697325 MMP9 gene variants only had strong association with TAA. Persons with AA variant of rs11697325 are predisposed for greatest dilatation. Investigation of TAA associated SNPs might improve risk assessment in this group and are believed to help in appropriate and timely selection patients for surgical treatment.
Acknowledgement/Funding: Financing of the Russian government

P6502 | BEDSIDE

Influence of the false lumen status on acute type A aortic dissection without urgent surgical repair

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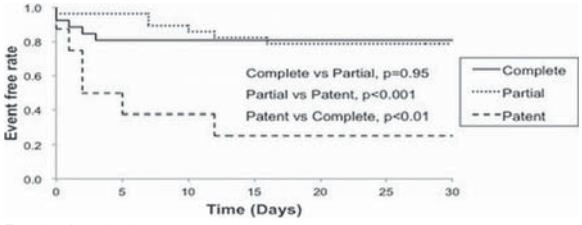
Background: Recently much attention has been focused on partial thrombosis of the false lumen in acute aortic dissection. However, the issue about partial thrombosis of the false lumen has not been clearly elucidated especially in type A aortic dissection.
Purpose: The purpose of this study was to evaluate the influence of status of the false lumen including partial thrombosis in patients with acute type A aortic dissection received initial medical treatment.
Methods: Sixty-two patients (29 males, mean age 73±13 years) with acute type A aortic dissection received initial medical treatment at 4 hospitals were enrolled. Patients were divided into three groups according to the status of the false lumen on enhanced computed tomography image (complete thrombosis, n=26; partial thrombosis, n=28; patent, n=8). Furthermore, patients with partial thrombosis were divided into two groups; thrombus dominant partial thrombosis if more than 50% of the false lumen was thrombosed (n=18), and flow dominant partial thrombosis as for the rest (n=10).
Results: In-hospital mortality rate was significantly higher in patients with patent false lumen (75% in patent, 25% in partial and 19% in complete) (vs partial, $p<0.01$, vs complete, $p<0.01$, respectively). In patients with partial thrombosis, flow dominant partial thrombosis had significantly higher in-hospital mortality rate than thrombous dominant partial thrombosis (60% in flow dominant, 5.6% in thrombus dominant; $p<0.01$).



Freedom from death

Conclusion: The patients with partial thrombosis and complete thrombosis of the false lumen might have better in-hospital outcomes compared with patent false lumen in acute type A aortic dissection without urgent surgical repair. Furthermore in partial thrombosis, the proportion of thrombus seems to influence short-term mortality.

P6503 | BEDSIDE

Carbon dioxide-aided angiography decreases contrast volume and prevents kidney injury in peripheral vascular interventions

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Background: Chronic kidney disease is a common comorbidity in patients with peripheral artery disease. In this population, the use of iodinated contrast media (ICM) bears an enhanced risk of contrast-induced nephropathy (CIN), a condition associated with significant morbidity and mortality. Lowering ICM volume is an effective strategy to prevent CIN.
Objective: We investigated the safety and efficacy of carbon dioxide gas (CO2) as a supplemental alternative contrast agent to decrease contrast volume during fluoroscopy-guided peripheral vascular procedures in routine daily practice.
Materials and methods: We compared ICM volume, irradiation time, technical success, and kidney function in 191 consecutive peripheral interventions of the lower extremity (n=63 iliac, n=83 femoral, n=24 popliteal, n=36 below-the-knee) in patients with Fontain IIb-IV that were performed with ICM alone (n=154) or with the aided or exclusive use of CO2 (n=37).
Results: In 154 cases we used only ICM, in 33 both ICM and CO2, and in 4 case CO2 exclusively. The technical success rate (overall average 97%), total irradiation (23±16 min), and intervention time (80±37 min) were not significantly different between the ICM and CO2 groups and no severe procedure-related complications were noted. The average contrast volume was significantly lower In the CO2 groups [34±41 ml (IIb: 49±53 ml, III&IV: 24±23 ml)] as compared to the ICM group [112±76 ml (Fontain IIb: 125±79 ml; III&IV: 95±65 ml), $p<0.0001$ vs CO2 each]. Although creatinine and eGFR were significantly lower in the CO2 groups at baseline (CO2: 2.1±1.3 mg/dl and 22±34 ml/min, ICM: 1.1±0.6 mg/dl and 76±28 ml/min, $p<0.0001$ each), the rate of CIN was significantly lower in CO2 (5%) as compared to ICM (19%, p=0.04).
Conclusion: Our analysis underscores that CO2 is an alternative contrast agent that can be applied safely, efficiently, and routinely to reduce contrast volume and prevent CIN during peripheral interventions even in patients with disease of the popliteal artery and below-the-knee and critical limb ischemia.

P6504 | BEDSIDE

Increased pulse wave velocity indicates presence of coronary artery disease in patients with abdominal aortic aneurysms

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Pulse wave velocity (PWV) is a valid, clinically feasible, measure of arterial stiffening and a strong predictor of future cardiovascular events and all-cause mortality in patients with CAD. The aim of the present study was to assess aortic elastic properties in patients with abdominal aortic aneurysms (AAA) with and without coexisting coronary artery disease (CAD)
Methods: We enrolled 95 patients with AAA eligible for interventional repair (European Society for Vascular Surgery Guidelines) and 73 patients with CAD. A group of 29 healthy subjects served as controls (HC). PWV was measured in all participants using Complior method. The presence of CAD was documented by at least one coronary stenosis>70% at coronary angiography.
Results: Patients with AAA and HC did not differ in anthropometrical characteristics, lipid profile and blood pressure levels ($p>0.05$). PWV was found considerably higher in AAA group compared to HC group (11.92±2.69m/s vs 7.63±2.38m/s, $p<0.001$). Importantly, among patients with AAA, those patients with concomitant history of CAD (n=41) had greater PWV than their non-CAD counterparts (n=54) (13.4±2.91m/s vs. 11.7±2.35m/s, p=0.03). Univariate analysis revealed significant correlations of PWV with systolic blood pressure (b regression coefficient=0.428, p=0.012), diastolic blood pressure (b=0.393, p=0.024). the presence of CAD (b=0.551, p=0.001). By multivariate analysis, a PWV>12m/sec had an odds ratio for the presence of CAD of 1.8 (95% CI: 1.1–2.0, p=0.03) in a model including age, sex and traditional atherosclerotic risk factors. The sensitivity and specificity of PWV>12 m/sec for CAD in patients with AAA was 88% and 81% respectively.
Conclusion: PWV is higher in patients abdominal aortic aneurysms compared to healthy controls. Increasing PWV values are a valid marker of concomitant CAD in patients with abdominal aortic aneurysms.

P6505 | BEDSIDE

Impact of one-stage systematic endovascular treatment for multilevel (femoropopliteal and below the knee) lesions in patients with critical limb ischemia

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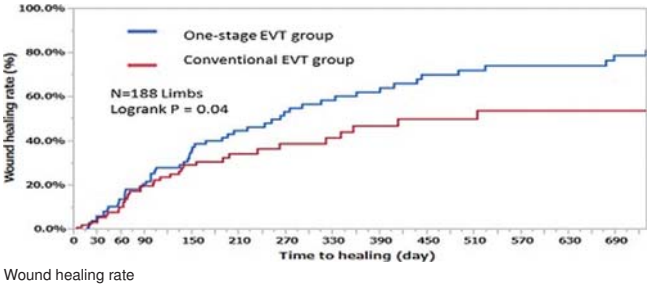
Background: The purpose of this study is to investigate whether one-stage endovascular treatment (EVT): systematic interventions in multilevel (femoropopliteal: FP and below-the knee: BTK lesions) vessels, is effective to achieve wound healing in patients with critical limb ischemia (CLI).
Methods: We retrospectively analyzed 188 consecutive limbs of patients with Rutherford category 5 (168 patients, male 56%; mean age 73±10 years) who underwent EVT in our institute between April 2007 to September 2014. All the limbs were with multilevel overlapped (FP and BTK) lesions. We divided them into two groups; one-stage EVT group (90 limbs; EVT of both FP and BTK at one time) and conventional EVT group (98 limbs; EVT in FP alone). Outcome measures were complete wound healing, amputation-free survival (AFS) and major adverse limb event (MALE) and perioperative complications including distal embolism, pseudo aneurism, blood transfusion and undergoing hemodialysis.
Results: Mean follow up period was 23±18 months. Wound healing rate at 1 year was significantly higher in one-stage EVT group than in conventional EVT group (47.8% vs. 32.7%, p=0.03). Freedom from MALE was tended to be higher in one-stage EVT group (51.0% vs. 37.8%, p=0.06) whereas there was no significant difference in AFS (49.0% vs. 52.2%, p=0.65) and perioperative complications (11.1% vs. 8.2% p=0.49). At 3,6 months and 1.5 years after initial EVT, there was significant difference in healing rate between two groups (17.3%, 38.0% and 74.4% vs. 17.3%, 27.4% and 54.1%, p=0.04). After multivariate analysis, one-stage EVT group was an independent predictor of wound healing.



Wound healing rate

Conclusions: One-stage systematic EVT for FP and BTK lesions may be effective to achieve wound healings in CLI patients without increase of complications.

P6506 | BEDSIDE
Central blood pressure correlates with size of abdominal aortic aneurysm

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Introduction: Central blood pressure reflects arterial stiffness and vascular resistance better then brachial artery measurement. There are data demonstrating that parameters of central blood pressure predict progression of abdominal aortic aneurysm (AAA). However, the relationship between the size of AAA and indices of central blood pressure has not been studied.
Aim of the study: To evaluate a correlation between the maximum aortic diameter and parameters of central and peripheral blood pressure.
Methods: We studied 57 patients (18 woman, 39 man; mean age: 73±8), diagnosed with AAA. Parameters of central blood pressure were determined non-invasively by applanation tonometry (SphygmoCor). Size and morphology of AAA were evaluated with ultrasound.
Results: The AAA diameter ranged from 30 to 55 mm (median: 45 mm). The analysis showed no correlation between the AAA diameter and age, height or weight, but confirmed a negative correlation with parameters of central blood pressure, while there was no significant correlation with brachial measurements.

Table 1. Correlation between central, peripheral blood pressure parameters and the maximum aortic diameter

Blood pressure parameter		r	P value
Central	C_SP (systolic pressure)	–0.275	<0.05
	C_P1 (first systolic peak pressure)	–0.266	<0.05
	C_P2 (second systolic peak pressure)	–0.275	<0.05
Peripheral	P_SP (systolic pressure)	–0.256	NS
	P_P1 (first systolic peak pressure)	–0.254	NS
	P_P2 (second systolic peak pressure)	–0.255	NS

Conclusions: Our data show that the size of AAA may affect parameters of central blood pressure probably by modification of the backward (reflected) wave.

CIRCULATORY ASSIST AND OTHER

P6507 | BEDSIDE
Acute proteolysis of Von Willebrand factor at initiation of continuous-flow left ventricular assist devices

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Background: A high rate of surgical bleedings is observed after implantation of continuous-flow Left Ventricular Assist Devices (CF-LVAD). Several studies have reported that CF-LVAD therapy induce a constant degradation of von Willebrand factor (VWF) high molecular weight multimers (HMWM), essential for haemostasis. Although HMWM loss has been reported within days after LVAD implantation, the precise time course of VWF degradation is still unknown. Moreover, the mechanism underlying HMWM loss is still debated since both mechanical demolition and shear-induced proteolysis have been reported.
Aims: To investigate the time course of VWF degradation at initiation of CF-LVAD therapy and its underlying mechanims.
Methods: A time-course of VWF degradation was assessed in-vitro using a HeartMate-II® (HM-II) mock circulatory system (MCS) and after HM-II implantation in patients in-vivo (n=8). In-vitro, HM-II MCS was perfused with anticoagulated human blood from healthy donors at 9000 rpm (n=10), as in HM-patients, and at 3000, 6000, and 12000 rpm (n=3). Three more runs were performed at 9000 rpm with EDTA, an unspecific inhibitor of enzymatic proteolysis. Samples were collected, both in-vitro and in-vivo, before (T0) and after initiation of HM-II® support (T5, T30 and T180 minutes) for VWF antigen, propeptide (VWFpp), VWF proteolytic fragments, VWF multimeric analysis, and PFA-Closure time ADP (PFA-CADP).
Results: VWF degradation in-vitro was dependent from HM-II speed (12000>9000>6000 rpm) and almost fully inhibited by EDTA at 9000 rpm. At similar LVAD speed (9000 rpm), VWF degradation was more pronounced in-vitro ($p<0.0001$) than in-vivo ($p<0.01$). PFA-CADP was significantly increased 5 min after initiation of LVAD support in-vivo (p=0.01). An acute increase of VWFpp, already significant at 5 min (p=0.01), was observed in-vivo indicating an acute liberation of VWF by vascular endothelium. A time-dependent increase in VWF proteolytic fragments was observed in HM-II patients.
Conclusion: VWF degradation occurs within 5 minutes after CF-LVAD implantation.in accordance with the high bleeding rate reported after this surgery. Shear-induced proteolysis seems the main contributor of HMWM loss while mechanical demolition of VWF seems accessory.

P6508 | BEDSIDE
Structural and functional echocardiographic responses to left ventricular assist device implantation: focus on the right ventricle

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Background: There are limited prospective, serial echocardiographic data on the structural and functional changes of cardiac chambers in response to continuous-flow left ventricular assist device (LVAD) implantation. Data on right ventricular (RV) recovery are particularly limited.
Methods: We conducted an interim analysis of serial echocardiograms performed before (within 7 days) and 30 and 90 days after LVAD implantation as part of an ongoing prospective study. In addition to standard parameters, we obtained RV mechanics with speckle tracking.
Results: Among the first 22 patients, 20 (91%) survived to 90 days; all survivors (age 53±14 years; 8 women; 8 white, 12 black; 11 HeartMate II, 9 HeartWare; 11 bridge-to-transplant, 9 destination therapy) completed the protocol. Overall, LV and left atrial size decreased significantly by 30 days without change in LV ejection fraction (Table 1). Right-sided pressures and pulmonary vascular resistance consistently decreased over time. Despite a small decrease in RV systolic size, conventional functional RV parameters yielded conflicting results: one-dimensional measures (TAPSE, RV S') suggested substantial RV function worsening whereas fractional area change and myocardial performance index suggested improvement. However, global longitudinal strain and strain rate suggested no actual change in RV function.
Conclusions: Despite a decrease in right-sided pressures after LVAD implantation, minimal short-term changes in RV size and mechanics suggest no immediate improvement in RV function. If further confirmed, these findings may have clinical implications for LVAD candidates with poor baseline RV function.
Acknowledgement/Funding: American Heart Association

P6509 | BEDSIDE
Management of oesophageal fistulae after transcatheter or intraoperative radiofrequency ablation for atrial fibrillation - a single center experience over 15 years

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Background: Oesophageal fistula represents a rare, under-reported, and typically fatal complication after radiofrequency ablation (RA) for atrial fibrillation (AF). However, no consensus regarding the optimal management strategy for these high-risk patients currently exists. Three different types of fistulae have been described in the literature: (1) oesophago-atrial fistulae (OAF), (2) oesophago-pericardial fistulae (OPF) and (3) oesophago-mediastinal fistulae (OMF).
Purpose: To analyse the outcome of surgical and interventional management in patients with oesophageal fistulae following RA therapy over a period of 15 years as a single centre experience.
Methods: Between 10/1999 and 10/2014, 11 patients (median age 65.31; IQR 56.4–69.0) were treated at our institution due to oesophageal fistulation into the atrium (N=6), the pericardium (N=3) or mediastinum (N=2) following transcatheter (N=8) or intraoperative (N=3) RA for AF. Median time-to-fistula after RA therapy was 23 days (IQR 17.0–24.5). On admission clinical symptoms comprised new onset fever (N=4), elevated c-reactive protein or leucocytes (N=5), dyspnea (N=4), transitory ischaemic attack (N=2) or stroke (N=3), and chest, back or abdominal pain in 3, 2 and 1 cases, respectively. Open surgery for oesophageal resection with or without left atrial reconstruction was performed in 9 pts

Abstract P6508 – Table 1. Echocardiographic responses

Parameter	Baseline	30 days	90 days	P value	Parameter	Baseline	30 days	90 days	P value
LV end-diastolic volume index, cm^3/m^2	159±35	108±55***	101±34***	<0.001	RV myocardial performance index	0.71±0.38	0.57±29	0.42±0.21*	0.062
LV ejection fraction, %	16±7	16±13	18±13	0.59	RV global longitudinal strain, %	–8.0±2.8%	–6.8±3.0%	–7.5±2.8%	0.13
Left atrial volume index, cm^3/m^2	74±19	43±21***	40±12***	<0.001	RV global longitudinal strain rate systolic, 1/s	–0.57±0.16	–0.52±0.25	–0.48±0.17	0.48
RV end-diastolic area (indexed), cm^2/m^2	16±6	14±5	14±4	0.14	Pulmonary artery systolic pressure, mmHg	57±16	39±14***	32±7***	<0.001
RV end-systolic area (indexed), cm^2/m^2	13±6	11±5	10±4**	0.044	Pulmonary artery mean pressure, mmHg	42±11	34±7**	28±7***	0.009
RV fractional area change, %	22±10	26±10	30±10**	0.021	Pulmonary vascular resistance, Wood units	4.4±1.5	3.6±1.3**	3.1±0.8***	0.007
Tricuspid annular plane systolic excursion, cm	1.7±0.6	1.2±0.3*	1.1±0.3**	0.013	Mitral regurgitation (semiquantitative 0–5)	3.4±1.5	1.5±1.6***	1.4±1.6***	<0.001
RV TDI S', cm	10±4	6±2***	7±2***	0.001	Tricuspid regurgitation (semiquantitative 0–5)	2.8±1.5	2.4±1.7	2.0±1.6	0.17

*P<0.05; **P<0.01; ***P<0.001 (vs. baseline, Bonferroni adjustment). LV, left ventricle; RV, right ventricular; TDI, tissue Doppler imaging.

suffering from mediastinitis due to OAF (N=7) or OMF (N=2)–incl. a single patient with previous oesophageal stenting who had developed massive mediastinal infection post-interventionally and required stent removal. The 3 remaining OPF pts–without signs of acute mediastinitis–were treated by pericardial drainage and oesophageal stenting.
Results: The respective in-hospital and 1-year mortality rates were 0 and 18.2% (N=2). After a median follow-up (100% complete) of 34.0 months (IQR 8.9–118.7), 8 patients (72.8%) were still alive. Postoperative complications comprised post-cardiotomy low cardiac output syndrome (N=1), new stroke (N=2), respiratory insufficiency (N=4) requiring percutaneous tracheostomy (N=3) and re-thoracotomy for haemorrhage (N=1) or right pneumoectomy (N=1). No relevant complications were noted in the 3 OPF pts treated by oesophageal stenting.
Conclusions: High-risk patients suffering from oesophageal fistulation into the atrium, pericardium or mediastinum after transcatheter or intraoperative RA may be successfully treated by open surgery or oesophageal stenting. However, we feel that oesophageal stenting should be avoided in patients with clinical signs of acute mediastinits (OAF and OMF) to avoid stent infection with adverse outcome.

P6510 | BEDSIDE
The utility of CHA2DS2-Vasc and HAS-BLED scores as predictor of thromboembolic and bleeding risk after left ventricular assist device implantation

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Purpose: CHA2DS2-VASc score predicts thromboembolic (TE) event risk and HAS-BLED score predicts major bleeding risk in patients on anticoagulation with atrial fibrillation. We aimed to evaluate if these scoring systems would be predictive of TE and major bleeding complications following continuous-flow left ventricular assist device (CF-LVAD) implantation.
Methods: Baseline CHA2DS2-VASc and HAS-BLED scores were retrospectively determined for patients with CF-LVADs. We identified 145 patients with a HeartMate II (n=31), Heartware (n=113) and ReliantHeart (n=1) LVAD implanted in a single center between 12/2010 and 12/2014. After device implantation, all patients were on warfarin (goal INR 2–3) as well as 300 mg of aspirin daily.
Results: Mean age was 50.7±11.2 years, 85.5% were male and 53.1% had ischemic cardiomyopathy. Median length of support was 316 days (range 31–1060) with 22 TE (15.2%) and 32 major bleeding (22.1%) events. The mean (±SD) CHA2DS2- VASc score was 2.3±1.4 and 2.5±1.2 (p=0.2) in patients with and without TE event, respectively. The mean (±SD) HAS-BLED score was 1.8±0.8 and 1.42±0.6 (p=0.004) in patients with and without major bleeding, respectively.
Conclusion: Baseline high HAS-BLED score was predictive of major bleeding events following CF-LVAD implantation, while baseline CHA2DS2- VASc score was not predictive of TE events.

P6511 | BEDSIDE
Comparison of radiation exposure between vascular approach sites in diagnostic coronary angiography and interventional procedures in a contemporary time period analysis

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Purpose: Recently, more interests are focused on radiation exposure during catheterization. From many observational studies, transradial approach has been suspected as a culprit of higher radiation exposure to patients and operators. However, recent several meta-analysis and studies which evaluated large patient population by only experienced operators revealed that transradial approach might be same with transfemoral approach in terms of radiation exposure. We evaluated the radiation exposure between transradial and transfemoral approach during catheterization in a contemporary time period.
Methods: Between February 2014 to July 2014, 544 consecutive diagnostic coronary angiography and percutaneous coronary intervention (PCI) by experience operators was evaluated in a single catheterization laboratory. We compared the dose area product (DAP) and air kerma (AK) between transradial and transfemoral approach. Right heart catheterization, coronary spasm provocation test, peripheral or aorta procedure, and device procedures were excluded in this study.
Results: Among them, 337 cases (61.9%) were diagnostic coronary angiography and the other 207 cases (28.1%) were PCI cases. Overall transradial approach was done in 383 (70.4%) cases [281 (83.4%) cases in diagnostic angiography and 102 (49.3%) cases in PCI, respectively]. DAP and AK were significantly lower in transradial group compared to transfemoral group (45,498.2±45,329.3 vs. 73,737.5±59,135.1 mGycm^2 and 798.5±938.9 vs. 1,272.0±1,099.3 mGycm^2, respectively). However, DAP and AK per number of runs did not differ between the two groups (3,116.9±1,465.4 vs. 3,294.7±1,877.2 mGycm^2 and 51.6±27.8 vs. 53.9±28.7 mGycm^2, respectively). Vascular access site was not associated with radiation exposure dose, considering urgency and diagnosis at the time of procedure, body surface area, age, sex, and accessary procedures such as intravascular ultrasound examination, fractional flow reserve, optical coherence tomography, and intra-aortic balloon counterpulsation.
Conclusions: This study showed that transradial approach was not associated with a higher radiation exposure to patients as well as operators compared to transfemoral approach in a contemporary time period analysis in patients who underwent cardiac catheterization by experienced operators.

P6512 | BEDSIDE
Cardiac resynchronization therapy can be a rescue therapy for inotrope-dependent patients with advanced heart failure?

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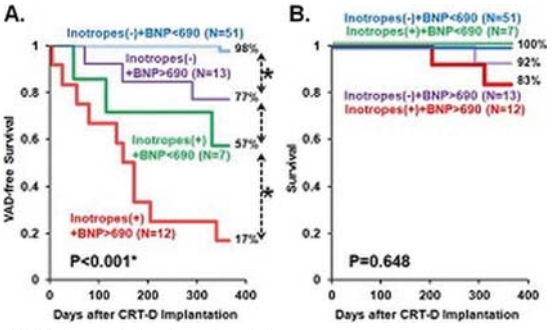
Background: Although the "off-label usage" of cardiac resynchronization therapy with defibrillator (CRT-D) has spread recently in advanced heart failure (HF) patients in the real-world practice, its clinical effect remained uncertain.
Methods: A total of 84 in-hospital <65-year old patients with advanced HF undergoing CRT-D were enrolled, and the predictors of cardiac death <1 year were examined.
Results: Seventeen patients (20%) had been dependent on inotropes at the time of CRT-D implantation, and 17 suffered cardiac death within a year. Both inotrope dependence and elevated plasma levels of B-type natriuretic peptide (BNP) (>690 pg/mL) at the time of CRT-D implantation were independent predictors of cardiac death within a year by Cox regression analyses ($p<0.05$ for both). These 2 parameters could significantly stratify 1-year ventricular assist device (VAD)-free survival: inotrope-free low (1) or high BNP (2), or inotrope-dependent low (3) or high BNP groups (4) (98, 77, 57, and 17%, respectively, $p<0.001$) (Fig A). In contrast, there were no significant differences in actual 1-year survival among the four groups (Fig B). Logistic regression analyses demonstrated that baseline left bundle branch block and left atrial diameter <47 mm were significant predictors of a good response to CRT-D defined as the improvement of LV ejection fraction >10% during six months ($p<0.05$ for both).



1Y VAD-free survival and actual survival

Conclusion: CRT-D may not rescue inotrope-dependent patients with advanced HF. LVAD treatment should be considered instead of CRT-D in such too sick patients.

P6513 | BEDSIDE
Right ventricular function improves through pump speed optimization in patients on long-term left ventricular assist devices

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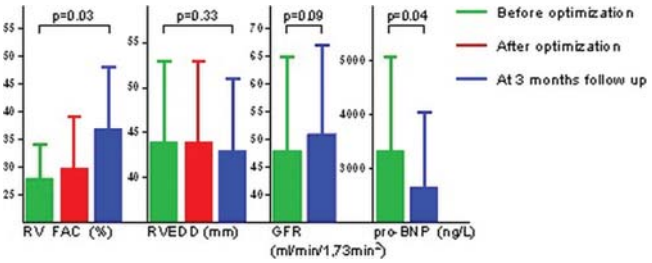
Background: Optimal interaction between left ventricular assist device (LVAD) and right ventricular (RV) function is paramount for survival in patients receiving mechanical assistance as destination therapy (DT). Assessment of adequate LVAD pump speed is recommended before hospital discharge. However, the role of systematic re-assessment of optimal speed setting in ambulatory patients at long-term follow-up is unclear.
Purpose: The aim of the current study was to assess whether echocardiographically guided pump speed optimization is associated with improved clinical and echocardiographic performance at 3 months follow-up.
Methods: Ambulatory HeartWare DT-LVAD patients underwent speed optimization at least 6 months after implantation. Biventricular performance was echocardiographically assessed for incremental speed settings with steps of 100 rotations per minute to determine optimal hemodynamics. Evaluation at 3 months follow-up included laboratory and echocardiographic measurements.
Results: Assessment of optimal pump speed was performed in 14 patients (58±13 years; 11 males; 19 [IQR 10–32] months on LVAD support). In 7 patients (50%) pump speed was adjusted (increase 171±111RPM; $p<0.01$). Three months after optimization RV fractional area change (RV FAC) improved (28±6 to 37±11%) without RV dilatation (RVEDD 44±9 to 43±8 mm). Furthermore, pro-brain natriuretic peptide level (pro-BNP) had decreased (3349±1732 to 2658±1386 ng/L), while glomerular filtration rate (GFR) tended to improve (48±17 to 51±16 ml/min/1.73m^2) (figure 1).



Effect of LVAD pump speed optimization.

Conclusion: Systematic re-assessment of LVAD speed setting reveals the need for optimization in a substantial proportion of patients on long-term support, resulting in enhancement of RV function, a decline in pro-BNP, and a tendency towards improved GFR.

P6514 | BENCH
A novel right heart assist device- the perkat (percutoneous catheter pump technology) sytem

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Background: Acute right heart dysfunction is a life-threatening condition with a poor prognosis and occurs in the setting of right ventricular infarction, severe pulmonary embolism, post cardiac transplant, and post left ventricular assist device. Temporary mechanical right ventricular support could be a reasonable adjunctive treatment option.
Purpose: Our intention was to develop a novel percutaneously implantable and pulsatile working device for patients with severe right heart failure.
Methods: The PERKAT (PERkutane KATheterpumptechnologie-percutaneous pump technology) device consists of a self-expandable nitinol cage which is covered with layers of membranes. The outer membrane consists of over hundred foil valves. On the proximal side there is a flexible outlet trunk with a pigtail shaped ending. The whole system is folded into an 18 French sheet and is completely percutaneously implantable in seldinger technique and should be placed in the inferior vena cava, with the flexible outlet trunk bypassing right atrium and right ventricle while the pigtail end sitting in the pulmonary trunk. After nitinol cage deployment a IABP balloon has to be inserted into the cage and connected with a IABP console. After starting the IABP support blood runs into the nitinol cage during balloon deflation through the foil valve concept of the membranes. During balloon inflation blood is guided through the flexible trunk and leaves the device through valves at the pigtail ending.
Results: In an in-vitro setting with a 40 ccl IABP balloon the device was evaluated with increasing pump cycles of 80, 90, 100, and 110/min. In this series, PERKAT generated a flow of 2.5, 2.8, 3.0, and 3.1 l/min, respectively. In-vivo evaluation in a sheep model of acute right heart failure was performed to investigate the implantation procedure and hemodynamic effect. Implantation was feasible with excellent function and right ventricular support resulting in a 60% increase of cardiac output from 1.3 l/min (native measurement in cardiogenic shock) to 2.1 l/min (with PERKAT support). The device was easy to remove into the sheet without difficulties
Conclusion: The novel PERKAT device offers a circulatory support of more than 3 l/min in an in vitro setting. First in-vivo experiments in sheeps demonstrated feasibility and hemodynamic effects of the device. Current studies are investigating the hemodynamic effect of the device in an animal model of right heart failure. Based on the first results we believe that the system is a hopefully approach and could be used in clinical settings for patients who need right ventricular support in near future.
Acknowledgement/Funding: Grant from the Bundesministerium für Bildung und Forschung (BMBF)

RESTENOSIS

P6515 | BEDSIDE
Efficacy of drug eluting balloons for patients with in-stent restenosis: a meta-analysis of 8 randomized controlled trails

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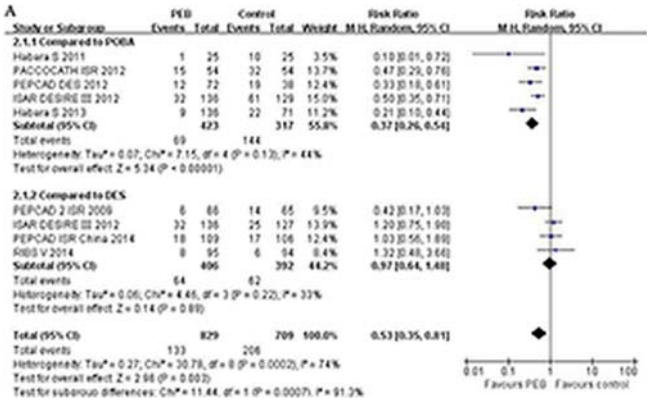
Background: The optimal treatment for in-stent restenosis (ISR) of both bare-metal stent (BMS) and drug eluting stent (DES) is currently unclear.
Objective: The aim of this meta-analysis was to assess the role of drug eluting balloon (DEB) as an optimal treatment for ISR.
Methods: We searched PubMed, MEDLINE, EMBASE, BIOS and Web of Science from 2005 through July 2014. Eight Random controlled trials, enrolling 1413 patients, were included in the meta-analysis. Main endpoints of interests were late lumen loss (LLL), minimal lumen diameter (MLD), binary in-segment restenosis (BR), diameter stenosis (DS), major adverse cardiac events (MACE), target lesion revascularization (TLR), death cases, myocardial infarction (MI), stent thrombosis (ST).
Results: Compared with POBA, DEB treatment significantly reduced the risk of MACE[RR 0.37, p<0.01], decreased the incidence of death [RR 0.44, p=0.04], TLR[RR 0.27, p<0.01], and associated with better outcomes of LLL [–0.50 (–0.65, –0.35)mm, p<0.01], MLD[MD 0.53 (0.44,0.63), p<0.01], DS[–17.06 (–20.49, –13.63), p<0.01]. However, the differences were not significant between DEB treatment and DES treatment in all primary and secondary endpoints.



Forest plots of risk ratios of MACE

Conclusions: Drug-eluting balloon is an optimal treatment in treating ISR when compared with POBA. However, it has similar effects with drug-eluting stent.

P6516 | BEDSIDE
Treatment of drug-eluting stents in-stent restenosis with paclitaxel-coated balloon angioplasty: insights from the French real-world prospective GARO registry

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Background: Data about paclitaxel-eluting balloon (PCB) angioplasty to treat drug-eluting stents (DES) in-stent restenosis (ISR) were mainly collected in selected patient populations in the setting of randomized trials. The main goal of this prospective registry was to confirm the positive findings of these studies in an unselected population in clinical practice.
Methods: Consecutive patients with DES-ISR treated by PCB angioplasty were recruited in this prospective real-world registry. The primary endpoint was clinically driven target-lesion revascularization (TLR) at 9 months. Secondary endpoints included acute technical success, in-hospital outcomes, 9-month major adverse cardiac events (MACE) a composite of death, myocardial infarction (MI) and TLR and the occurrence of target vessel revascularization.
Results: A total of 206 patients (67.7±10.2 years, 80.6% male, 41.3% diabetics) with 210 lesions were recruited. Unstable coronary artery disease was present in 55.3% of patients. The time from DES implantation to DES-ISR was 3.0±2.4 years. Quantitative analyses revealed that patterns of treated DES-ISR were focal in 55.7% and diffuse in 44.3%. The reference diameter was 2.76±0.64 mm. The 9-month follow-up rate was 90.8% (187/206). At 9 months, the TLR rate was 7.0% (13/187) whereas the rates for MACE, MI and cardiac death were 10.7% (20/187), 4.8% 9/187) and 2.1% (4/187) respectively. Results were consistent in patients with paclitaxel and non-paclitaxel-eluting stents (PES) ISR.
Conclusion: This large prospective registry demonstrated acceptable rates of TLR and MACE at 9 months after treatment of DES-ISR by PCB angioplasty. PCB angioplasty was equally effective in patients with PES-ISR and non PES-ISR.
Acknowledgement/Funding: Research funding from B.Braun for data acquisition and analysis

P6517 | BEDSIDE
Results of percutaneous coronary intervention of stent restenosis lesions with sequent please paclitaxel eluting balloon catheter at a very long-term follow-up

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Introduction: Drug eluting balloons currently constitute one of the therapeutic

tools used in percutaneous coronary intervention (PCI) of in-stent restenosis lesions. Nowadays, their results at a very long-term follow up are unclear.
Purpose: The main objective of this study was to evaluate the efficacy and safety of second-generation Sequent Please® paclitaxel eluting balloon (PEB) over in-stent restenosis at 6 years.
Methods: We prospectively included 121 consecutive patients (67±13 years, 79.3% male) with 121 restenotic lesions treated with PEB between March 2009 and March 2014. We evaluated the presence of major cardiac events (MACE) after a prolonged clinical follow-up (median 43 months): death, nonfatal myocardial infarction, target lesion revascularization (TLR) and thrombosis.
Results: 47.1% of patients had stable coronary artery disease and 52.9% acute coronary syndromes (47.9% Non-STEMI and 5% STEMI). 53.7% of patients were diabetic. 10.7% of lesions were bifurcations. 36.4% were focal restenosis (type IA or IC of Mehran classification) and 63.6% were diffuse restenosis (type II or IV). 31.4% were drug-eluting stent (DES) restenosis and 68.6% bare metal stent (BMS) restenosis. Predilatation at high atmospheres was performed in 93.4% of patients with a balloon/stent diameter ratio of 1–1.5. PEB inflation, at a mean pressure of 18.2±1.6 atm, had a duration of at least 45 seconds. There were no significant differences regarding baseline characteristics of these two groups neither in the MACE rate after a long-term follow-up (p=0.6). During follow-up, 8.3% of patients experienced adverse events: 7 patients died (2 cardiovascular and 5 non-cardiovascular deaths), TLR rate was 5% and there was one case of non-fatal myocardial infarction (0.8%). No cases of thrombosis were observed, immediately after the procedure nor during follow-up. 24.8% of patients had an angiographic follow-up.
Conclusions: Despite the presence of both clinical (53.7% diabetic patients) and angiographic (diffuse restenosis 63.6%) unfavorable risk factors, treatment with Sequent Please® PEB over BMS or DES in-stent restenotic lesions, provide a very good results at a very long-term follow up.

P6518 | BENCH
Efficacy of a novel paclitaxel-eluting balloon in reducing in-stent restenosis in a porcine model

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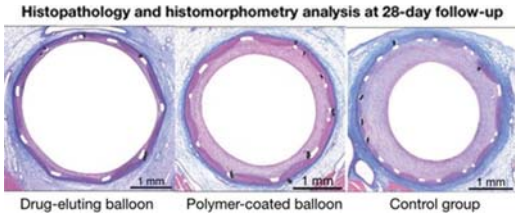
Background: Drug eluting balloon (DEB) is an attractive alternative to drug-eluting stents because they provide short duration of drug exposure, while potentially inhibiting in-stent restenosis.
Purpose: The purpose of this study was to evaluate the effectiveness of a novel paclitaxel-eluting balloon (PEB) in reducing in-stent restenosis in the porcine model.
Methods: We implanted 18 metallic stents in 7 domestic swines, inserting 1 stent per major coronary artery. Stent postdialatation was performed with the paclitaxel-eluting balloon (n=6), polymer-coating balloon (n=6) and control balloon (n=6). Microscopic evaluation of stented coronary arteries was done at 28±2 days post treatment. The restenosis rate and the vascular healing parameters (edothelialization rate, neointima fibrin and vascular injury) were analyzed.
Results: The restenosis rate of PEB group was significant lower compared with the polymer-coating balloon group and control group (19.3%±7.8% vs. 29.4%±13.7% vs. 37.8%±18.1%) by QCA. The vascular injury and inflammation scores were very low and similar among three groups. The marked increase in neointima fibrin (1.7±0.6 vs. 0.4±0.3 vs. 0.3±0.3) and lower endothelial rate (3.3±0.6 vs. 4.0±0 vs. 4.0±0.0) in the PEB group compared to the polymer and control groups indicated the effective drug deposition. DEB treatment also produced generally mild to moderate hypocellularity in both the neointima (1.7±0.5 vs. 0.1±0.3 vs. 0.1±0.3) and in the media (2.0±0.7 vs. 0.0 vs. 0.0), which suggested the efficacy of drug transfer.



Histopathological analysis

Conclusion: In this preclinical trial, treatment of stented coronary artery with PEB resulted in a significant reduction of stenosis rate. The marked increase of neointima fibrin and moderate hypocellularity in the PEB group indicated a drug deposition response.
Acknowledgement/Funding: This work was supported by National Natural Science Foundation of China (No. 81370323),the National Basic Research Program of China (No. 2011CB503905)

P6519 | BEDSIDE
The incidence and risk factors of late catch up phenomenon after second generation des deployment

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Background: The previous studies showed clinical restenosis within 1 year after PCI had been remarkably reduced with the appearance of second generation drug-eluting stents (DES). However, the late catch up (LCU) phenomenon remains one of the issues even in the DES era. The aim of this study is to investigate the incidence and risk factors of LCU after second generation DES deployment.
Methods: We performed PCI for de novo 2456 lesions in 1955 patients that were treated with second generation DES (zotarolimus-eluting stent: ZES, everolimus-eluting stent: EES, and biolimus-eluting stent: BES) in a single center from April 2009 to December 2012. Of that, 1752 lesions (71.3%) were clinically followed up more than 1 year and performed 6–12 month follow up angiography. We divided into LCU group and non-LCU group and assessed the incidence, outcomes, and predictive factors of the LCU phenomenon, defined as secondary revascularization 1 year after index stenting.
Results: The mean clinical follow up period was 745±265 days. Of all lesions, the LCU was found in the 98 lesions (3.9%). There were no significant differences in terms of patient background and lesion characteristics except HD, DM, and calcified lesion. (HD: 15.2% vs 3.5%; $p<0.0001$ DM: 57.6% vs 41.3%; p=0.002 calcified lesion: 24.5% vs 16.3%; p=0.04) Moreover, hinge motion, stent fracture (SF), and tortuosity were higher in the LCU group. (hinge motion: 9.9% vs 2.9%; p=0.01, SF:8.8% vs 1.2%; p=0.0003, tortuosity:8.5% vs 1.7%; p=0.004) QCA analysis showed there was significant decrease in minimal lumen diameter (MLD) at follow up in the LCU group. (2.30±0.56 mm vs 1.76±0.71 mm; $p<0.0001$) After multivariate analysis, HD (OR: 5.19 95% CI: 2.05–12.5, p=0.0008), SF (OR: 5.20 95% CI: 1.06–23.6, p=0.04), tortuosity (OR: 4.29 95% CI: 1.23–13.1, p=0.02), and MLD (OR: 2.39 95% CI: 1.33–4.47, p=0.003) are the independent predictors of LCU.
Conclusion: The LCU phenomenon after second generation DES deployment occurs in 3.9% and the predictive factors are HD, SF, tortuosity, and MLD. Of that, SF is the highest risk for LCU phenomenon.

P6520 | BENCH
Incidence and predictors of late catch-up phenomenon after second generation drug-eluting stent implantation

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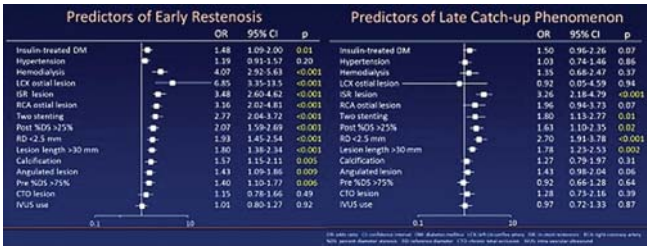
Purpose: To evaluate the incidence and predictors of late catch-up phenomenon after second-generation drug-eluting stent (DES) implantation.
Methods: The study population consisted of 6866 lesions after second-generation DES implantation from 2010 to 2013: 3918 XIENCE and 1018 PROMUS everolimus-eluting stents and 1930 NOBORI biolimus-eluting stents. The mid- and late-term follow-up angiography was scheduled 8 and 20 months. The population in which late-term follow-up angiography was performed without in-stent restenosis (ISR) and target lesion revascularization (TLR) at mid-term follow-up was 4046 lesions. ISR was defined as more than 50% restenosis. Late catch-up phenomenon was defined as ISR without ISR within 1 year after index stent implantation. The follow-up duration was 2 years.
Results: The early (midterm) restenosis rate was 7.4% (401/5455) and the late catch-up phenomenon rate was 5.1% (205/4046) of the lesions. A univariate analysis revealed that the predictors of early restenosis or late catch-up phenomenon ($p<0.10$) were insulin-treated diabetes mellitus, hypertension, hemodialysis, percent diameter stenosis before (>75%) or after (>25%) stent implantation, reference diameter <2.5 mm, lesion length >30 mm, ostial lesion in the left circumflex artery or in the right coronary artery, ISR lesion, calcified lesion, angulated lesion, chronic total occlusion lesion, two-stenting strategy, and intra-vascular ultrasound use. A multivariable regression analysis of the predictors of early restenosis and late catch-up phenomenon are shown in the table.



Predictors of early or late restenosis

Conclusion: The predictors of late catch-up phenomenon after second-generation DES implantation could be different from those of early restenosis.

P6521 | BEDSIDE

Three-year clinical outcomes after treatment of drug-eluting Stent restenosis with paclitaxel-eluting balloon vs. everolimus-eluting stent

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Background: Drug-eluting stent (DES) implantation is a very effective treatment of bare-metal stent restenosis (BMS-ISR). The optimal treatment for DES-ISR remains undefined. There are promising but limited clinical follow-up data concerning drug eluting balloons (DEB) in the treatment of DES-ISR. This study compared three year clinical outcomes after use of drug-eluting balloon (DEB) to second generation evirolimus-eluting stent (EES) for treatment of DES-ISR.
Methods: This observational study included 86 patients with 86 DES-ISR. 40 patients were treated by repeat PCI using an EES. 46 patients were treated by repeat PCI using a DEB. Follow-up periods were 36 months. The primary endpoint of the study was survival free of major adverse cardiac events (MACE) at three year follow-up. Secondary endpoints were survival free of need for revascularization of the target lesion and definite stent thrombosis (ST).
Results: Baseline clinical parameters were comparable between the two groups. The two groups were comparable with regards to lesion length, reference vessel diameter, and minimal lesion diameter. There were no differences between the two groups with regards to restenosis length, length of the priovisously implanted restenotic stents, length of study device (EES 20.5±12.9 mm, DEB 21.2±5.6 mm, p=0.745), stent diameter. Clinical follow-up during the total follow-up period was obtained in 99% of patients. Freedom from major adverse cardiac events at three year follow-up were 42.5% and 32.6% (p=0.3779) for the EES and DEB groups, respectively. Target lesion revascularization rates, rates of myocardial infarction and death for the EES and DEB group at three year follow-up were 25% versus 13%, p=0.1758, 7.5% versus 8.6%, p=1.0000, and 15% versus 17.3%, p=1.0000, respectively. Definite ST occurred in none of the patients of the DEB group and in one patient of the EES group (1 day after the index procedure) (0% vs. 2.5%, respectively, p=0.4651).

Clinical outcomes at three years

Variable	Everolimus-eluting stent (N=40)	Drug-eluting balloon (N=46)	P-value
Major adverse cardiac events	17 (42.5%)	15 (32.6%)	0.3779
Death	6 (15%)	8 (17.3%)	1.0000
Cardiac death	2 (5%)	2 (4.3%)	1.0000
Non cardiac death	4 (10%)	6 (13%)	0.7452
Myocardial infarction	3 (7.5%)	4 (8.6%)	1.0000
Target lesion revascularization	10 (25%)	6 (13%)	0.1758
Target vessel revascularization	11 (27.5%)	7 (15.2%)	0.1912
Definite stent thrombosis	1 (2.5%)	0 (0%)	0.4651
Early stent thrombosis	1 (2.5%)	0 (0%)	0.4651
Late stent thrombosis	0	0	1.0000
Very late stent thrombosis	0	0	1.0000

Conclusion: Efficacy of DEB for treatment of DES ISR is comparable to second generation EES at three year follow-up. Although use of a DES for treatment of DES ISR is a common treatment strategy, the use of a DEB should be considered in the treatment of DES ISR.

P6522 | BEDSIDE

Incidence and distribution of thin high signals detected by optical coherence tomography in patients treated with paclitaxel-coated balloon

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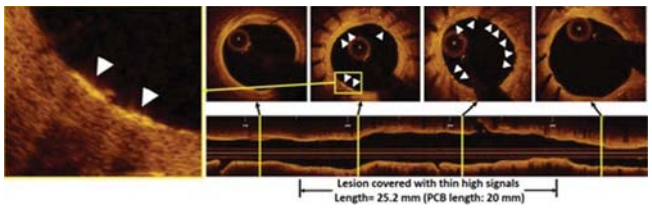
Introduction: The effectiveness of paclitaxel-coated balloon (PCB) catheter in patients with in-stent restenosis has been established. In addition, a recent report has demonstrated that frequency-domain optical coherence tomography (FDOCT) presents thin high signals on in-stent restenotic tissue after PCB angioplasty.
Purpose: We aimed to investigate the incidence and distribution of thin high signals after PCB angioplasty for in-stent restenosis.
Methods: FDOCT images were obtained after PCB angioplasty from 14 lesions in 13 patients with in-stent restenosis, electively treated by single PCB catheter. For these lesions, the extent of thin high signals was assessed by the agreement of two observers who were blinded to the PCB length. For evaluating the distribution of thin high signals, the sum of the arc was visually estimated at the frame showing minimal lumen area of each lesion.



Results: The representative case is shown in the figure below. Thin high signals were detected in all 14 lesions. The length of thin high signals showed agreement with PCB length (19.4±6.4 mm vs. 18.4±4.4 mm, p=0.56), although the correlation was poor (R=0.29; p=0.32). The sum of the arc with thin high signals was different depending on the lesion; maximum: 165 degrees, minimum: 30 degrees, mean ± standard deviation: 71.8±39.1 degrees.
Conclusions: This study demonstrated that the thin high signals observed by FDOCT are indicative of paclitaxel coverage on in-stent restenotic tissue. Distribution of drug following PCB angioplasty may be different depending on the lesions treated. Further investigations may be warranted to explore whether the distribution of paclitaxel impacts on clinical outcomes after PCB angioplasty.

P6523 | BEDSIDE

Estimation value of prediction plasma osteopontin levels in patients undergoing percutaneous coronary intervention

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Coronary stents are commonly used for treatment of coronary artery disease nowadays. However there are promising improvements in stent technology, new problems have been encountered with their increasing use. main problem is the inability to predict patients who will develop stent restenosis. Osteopontin (OPN), a calcium-binding, phosphorylated glycoprotein and a macrophage chemotactic protein, is originally identified as a mediator associated with bone remodeling, chronic inflammatory and autoimmune diseases and subsequently demonstrated to play an important role in cardiovascular disease development. Clinically, a significant association between plasma OPN levels and atherosclerotic plaque formation has been demonstrated, independent of traditional risk factors. The aim of our study is to evaluate predictive value of serum osteopontin levels for stent restenosis.
Our study group consists of the 91 patients with previous stent implantation history and has an indication for coronary angiography, 60 of them are in free of restenosis group and 31 of them are in restenosis group and 60 patients with normal coronary angiogram for control group. In study group mean age was 60.8±9.7 years, and 83 (54.9%) of patients were male, mean time passed to control coronary angiography was 36.7±35.1 months. Serum OPN levels were measured by elısa method.
We found statistically significant difference of OPN levels between groups (p=0.001). The difference is statistically significant between restenosis group and control group (p=0.002). The difference between restenosis group and free of restenosis group is also statistically significant (p=0.011) but there is no significant difference between control group and free of restenosis group (p=0.312). In comparison with the presence of coronary artery disease and osteopontin levels, osteopontin levels are significantly higher in patients with coronary artery disease (p=0.008). In multiple regression analysis with every 100 pg/ml increase in osteopontin level was found to be associated with 2.9-fold increase in development of restenosis.
In conclusion, OPN levels can be used as a marker of stent restenois but further studies with large patient populations are required to examine predict if value of OPN and factors that affect OPN levels.

P6524 | BEDSIDE

Long-term results of treatment of in-stent restenosis in aortocoronary saphenous vein grafts with paclitaxel-eluting balloon and paclitaxel eluting stent

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Background: Although percutaneous coronary intervention (PCI) for native vessel stenoses and in stent restenosis (ISR) have been established and enhanced with drug-eluting stents, conduit lesion interventions have been more controversial. The procedural characteristics and long-term outcomes of patients with SVG-ISR have not been reported.
This study compared 12 months clinical outcome after use of paclitaxel-eluting balloon (PEB) to first generation paclitaxel-eluting stents (PES) for the treatment of SVG-ISR.
Methods: This was a retrospective single center study which included 41 consecutive patients with 41 SVG-ISR treated with either PES or PEB. 31 patients were treated by repeat PCI using a PEB. 10 patients were treated by repeat PCI using a PES. All procedures were technically successful. The primary endpoint of the study was survival free of major adverse cardiac events (MACE) defined as death from any cause, MI or need for target lesion revascularization (TLR) at 12 months follow-up. Secondary endpoints were survival free of need for TLR and definite stent thrombosis (ST). Need for TLR was determined based on significant narrowing of the lumen within the stent or the lesion including 5-mm distal or proximal to the stent (>50% angiographic diameter stenosis) in the presence of symptoms or objective signs of ischemia.
Results: Baseline clinical and angiographic parameters were comparable between the two groups. Clinical follow-up during the total follow-up period was obtained in all of patients. Freedom from major adverse cardiac events at long term follow-up were 20% and 6.4% (p=0.2454) for the PES and DEB groups, respectively. Target lesion revascularization rates, rates of myocardial infarction

and death for the PES and DEB group at one year follow-up were 10% versus 6.4%, p=1.0000, 10% versus 3.2%, p=1.0000, and 10% versus 0%, p=0.2439, respectively. There was no definite ST observed in both groups at 12 months.

Clinical event rates at 12 months follow

Variable	Paclitaxel-eluting stent (N=10)	Drug-eluting balloon (N=31)	P-value
Major adverse cardiac events	2 (20%)	2 (6.4%)	0.2454
Death	1 (10%)	0 (0%)	0.2439
Cardiac death	0 (0%)	0 (0%)	1.0000
Non cardiac death	1 (10%)	0 (0%)	0.2439
Nonfatal myocardial infarction	1 (10%)	1 (3.2%)	1.0000
Target lesion revascularization	1 (10%)	2 (6.4%)	1.0000
Target vessel revascularization	1 (10%)	2 (6.4%)	1.0000
Definite stent thrombosis	0 (0%)	0 (0%)	1.0000
Early stent thrombosis	0 (0%)	0 (0%)	1.0000
Late stent thrombosis	0 (0%)	0 (0%)	1.0000

Conclusion: Event rates between PEB and PES were comparable after treatments of SVG-ISR at 12 months follow up.

P6525 | BEDSIDE
Percutaneous coronary intervention for restenosis with stent fracture after drug-eluting stent implantation for de novo vs. in-stent restenosis lesions

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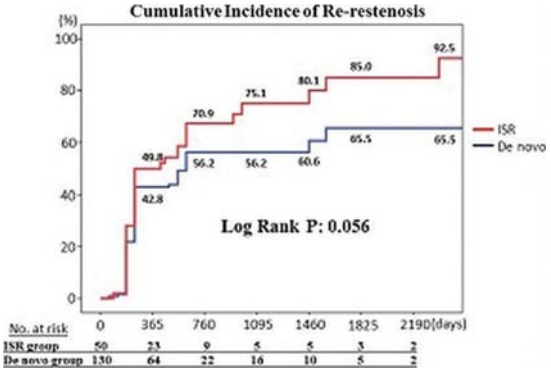
Background: Stent fracture (SF) is related to restenosis after drug-eluting stent (DES) implantation. As percutaneous coronary intervention (PCI) cases for complex lesions increased, those for restenosis with SF also increased; however, their results remain unclear.
Purpose: To compare the results of PCI for restenosis with SF after DES implantation between de novo and in-stent restenosis (ISR) lesions.
Methods: From November 2002 to December 2013, 10437 patients with 17798 lesions underwent DES implantation successfully. Of these, 14412 lesions were angiographically followed up after 6 to 8 months (midterm f/u) and 10999 lesions were followed up 12 months after midterm f/u. If myocardial ischemia was suspected, coronary angiography was performed at any time. Restenosis with SF was defined as a restenosis lesion within 5 mm from a SF site. SF occurred in 602 (4.2%) of the 14412 lesions, and restenosis with SF occurred in 214 lesions, in which PCI was performed on 199 lesions. The 199 lesions consist of 146 de novo lesions and 53 ISR lesions at the time before DES implantation causing restenosis with SF.
Results: As shown in the figure, the cumulative incidence of re-restenosis in ISR lesions increased over a long period of time and was much higher than that in de novo lesions.



Conclusions: The results of PCI for restenosis with SF after DES implantation in ISR lesions were more undesirable. DES implantation for ISR lesions with possibility of SF requires reconsideration.

P6526 | BEDSIDE
Clinical outcome after successful implantation of drug eluting and bare metal stents in large coronary arteries

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Objective: Randomized trials have demonstrated that drug-eluting stents (DES) reduce the risk of target vessel revascularization (TVR) compared to bare-metal stents (BMS). This benefit is less pronounced as artery diameter increases. Whether DES is superior to BMS for larger coronary arteries in the setting of routine clinical practice is unknown. This study sought to evaluate the safety and effectiveness of DES compared to BMS for patients with large coronary vessels.
Methods: From April 2007 to October 2012, 408 consecutive patients undergoing de novo lesion PCI with reference vessel diameter greater than or equal to 3.5 mm were prospectively enrolled into this study. All enrolled patients were divided into DES group (n=308) and BMS group (n=100). We obtained 24-month clinical outcome including death, myocardial infarction (MI), thrombosis, target lesion revascularization (TLR), target vessel revascularization (TVR), and major adverse cardiac events (the composite of death, MI, and TVR). We used Cox's proportional-hazards models to assess relative risks of all the outcome measures after propensity match.
Results: After propensity match, 100 DES-treated patients were matched to 100 BMS-treated patients. The patients treated with BMS were associated with higher risk of TLR (HR=2.24, 95% CI: 1.41–3.57, P=0.0007), TVR (HR=1.80, 95% CI: 1.21–2.68, P=0.004) and MACE (HR=1.475, 95% CI: 1.05–2.07, P=0.024). All ARC definition stent thrombosis at 24-month were comparable in the two groups.
Conclusion: In patients requiring stenting of large coronary arteries use of DES was associated with significant reductions in the risks of TLR, TVR and MACE at long-term follow-up.

P6527 | BEDSIDE
Morphological and circulatory markers of the in-stent restenosis: matching and relevance

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Aim: Evaluation of the correlation between morphological markers assayed in tissue pattern of in-stent restenosis (ISR) and circulatory markers in patients with ISR.
Material and methods: Using the techniques of confocal and immunofluorescence microscopy the expression and quantity of extracellular RNA (eRNA), reactive oxygen species (ROS), IL-1β, TNF-α, MMP-2, TIMMP-2, fibrilar collagen type I and its markers of synthesis (PICP) and degradation (CITP) have been determined in tissue pattern of ISR and normal coronary artery (control) taken from 19 died patients. In 73 patients with ISR the serum levels of 36 markers of systemic inflammation, oxidative stress as well as RNA-ase, MMP-2 and CITP have been measured and compared with control markers referred to 27 healthy persons.
Results: The ISR evolution is associated with eRNA expression raising in stented coronary artery wall. Its quantity increased proportionally to ISR degree achieving in muscular media of moderate-severe restenosis a 3–4 times increment compared to control. Likewise the ROS, IL-1β and TNF-α expression increased correlatively to ISR degree. More than that, between these markers and eRNA has been established a robust positive correlation. Extracellular matrix reorganization is a hallmark sign of ISR exhibited mostly by excessive fibrilar collagen type I degradation, CITP being elevated up to 5 times in media of severe ISR, and denaturized collagen I molecules accumulated in neointima. On the other hand, PICP has fallen of 4-fold. MMP-2 expression markedly (in a range of 3–5 times) elevated in RIS while TIMMP-2 in a similar ratio decreased, suggesting thus a real cause of boosted collagen degradation.
Remarkably, close changes have been found in the blood. The used multi-marker panel showed a notable activation of inflammation and oxidative stress in patient with ISR. Most relevant predictive values belong to such markers as IL-6, TNF-α, resistine, hereguline-1β, total antioxidant activity, malonic dialdehyde and advanced oxidized protein products. The blood RNA-ase is significantly decreased in a proportion with proinflammatory markers rise. The circulating levels of CITP and MMP-2 have been found increased in ISR by 72% and 61% respectively vs control marker.
Conclusions: 1. The conspicuous matching between morphological and circulatory markers offer a strong support concerning the role of inflammation and oxidative stress in ISR pathogenesis, and eRNA appears as a putative triggering factor. 2. Assaying of the underlined circulatory specific markers can be an important and reliable step in ISR diagnosis and prognosis.

P6528 | BEDSIDE
The level of plasma myeloperoxidase predicts rate of drug-eluting stent restenosis

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Background: Restenosis is one of the main problems after percutaneous coronary intervention (PCI) even with drug-eluting stents (DES) implantation. Few data on the role of neutrophil activation in developing restenosis after DES implantation is available.
Purpose: To evaluate the prognostic value of the level of myeloperoxidase (MPO) in predicting the development of restenosis after PCI with DES implantation
Methods: The study included 55 patients (41 males) aged from 57 to 71 years (mean age 62 years), with coronary artery disease, who undergoing coronary angiography after PCI with DES implantation. The MPO level in all the patients had been measured before the procedure.
Results: According to the results of the coronary angiography 13 patients had stent restenosis. In 42 patients restenosis was not identified. Patients in these

groups did not differ in age, sex, relationship smokers and nonsmokers, the presence of hyperlipidemia. Mean MPO level in group with restenosis was 122,9 pmol/l (78,5–238,5 pmol/l), and in the group without restenosis 87 pmol/l (75,4–135 pmol/l). By the level of MPO patients were divided into two groups: those with MPO levels below the median (<99,0 pmol/l, n=31) and above the median (>99,0 pmol/l, n=24). In the group with MPO below the median of distribution restenosis rate was lower (4 patients, 14%) than in the group with MPO levels above the median of the distribution (9 patients, 60%), $p<0.05$.
Conclusion: In the patients undergoing PCI with DES implantation and with higher levels of plasma MPO the occurrence of restenosis was more frequent than in the patients with lower levels of MPO, which allows to suggest a link between increased activity of MPO and restenosis.

P6529 | BEDSIDE
Incidence of in-stent restenosis over 13 years - a study based on a national registry

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Background: In-stent restenosis (ISR) is one drawback of coronary angioplasty with stent implantation.
Purpose: We investigated the incidence of ISR, its clinical presentation and treatment from a national registry.
Methods: From all patients (pts) undergoing percutaneous coronary intervention (PCI) from 2002 to 2014, we selected those who had previous history of PCI (n=15326). ISR was defined as diameter stenosis ≥50% in stent segment, being selected the interventions in which, at least, 1 IRS lesion was treated (n=3069). They were divided in 3 temporal groups: 2002–2003 (group 1, n=179, 5.8%) – bare metal stent era; 2004–2008 (group 2, n=816, 26.6%) – 1st generation stent era; 2009–2014 (group 3, n=2074, 67.6%) – 2nd generation stent era. For each group we compared clinical features and treatment.
Results: Over time, it has been observed a reduction in IRS incidence (24.8 vs 23.5 vs 18.6%;p for trend <0.001). Pts from group 3 were older (p=0.01), had higher prevalence of hypertension (63.7 vs 75.6 vs 78.4%;p<0.001), dyslipidemia (61.5 vs 68.5 vs 73.9%;p<0.001) and diabetes (31.3 vs 33.5 vs 38.5%;p=0.012). They also had more frequently history of previous myocardial infarction (p<0.001). Although admissions were more frequently due to stable angina (41% of total) or post non-ST segment myocardial infarction (16.3% of total); it was noticed, over time, an increase in admissions due to ST segment elevation myocardial infarction (1.1 vs 7.4 vs 11.4%;p<0.001) and unstable angina (1.1 vs 1.8 vs 3.7%;p<0.001). Most of pts presented with good systolic ventricular function, but an increase of pts with moderated (2.6 vs 9.0 vs 11.2%;p<0.001) and severe (1.3 vs 1.4 vs 4.7%;p<0.001) systolic dysfunction was observed. From 3069 PCI performed, a total of 3461 IRS lesions were treated. It was observed, at most, 3 IRS lesions for PCI. Over time, the most frequent presentation was 1 lesion for PCI (88.4% of total), being noticed a decreasing in number of multiple IRS lesions (15.1 vs 11.3 vs 9.6%;p=0.035). Incidence of ISR has increased in left descendant coronary artery (34.5 vs 39.8 vs 42.4%;p<0.001) and treatment was more frequently performed in more complex lesions (p<0.001). It was noticed a reduction in treatment with stent (72.7 vs 74.4 vs 52.8%;p<0.001) and an increasing use of only PCI balloon (39.3 vs 57.8 vs 45.8%;p=0.002) and trombectomy (0.0 vs 2.2 vs 8.2%;p<0.001).
Conclusion: In spite of increasing in risk profile of pts over time, it was observed a reduction of incidence of ISR and multiple ISR lesions. It also was observed an increasing number of interventions avoiding second stent implantation.

P6530 | BEDSIDE
Bifurcation angle between left main trunk and left anterior descending artery is independently related to restenosis after stent implantation for proximal left anterior descending artery disease

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Background: Restenosis after percutaneous coronary intervention (PCI) for proximal left anterior descending (LAD) artery disease is still a significant clinical problem. Although many risk factors for restenosis after PCI have been identified so far, coronary anatomical characteristics for restenosis have not been fully studied.
Purpose: The aim of this study is to investigate the relationship between LAD bifurcation angle and restenosis after PCI for proximal LAD artery disease.
Methods: We analyzed the data of consecutive 177 patients undergoing PCI for diseased proximal LAD artery, followed by coronary angiography (CAG) from 2008 to 2013. The bifurcation angles between left main trunk and LAD artery (LMT-LAD angles) were measured using left or right anterior oblique (LAO or RAO) caudal view in CAG.
Results: Stent restenoses were found in 33 out of 177 patients. 12 patients had an in-stent restenosis and 21 patients had an in-segment restenosis. The mean LMT-LAD angle was measured as 34.1°±18.5° among all the patients. The average LMT-LAD angle measured in patients with no-restenosis and in-stent restenosis was 32.0°±18.1° and 52.2°±14.5°, respectively, in LAO caudal view with significant difference between these two groups (P<0.001). We also observed that the average LMT-LAD angle in patients with no-restenosis and in-segment restenosis was 17.5°±10.1° and 27.3°±14.3°, respectively, in RAO caudal view (P<0.001). Multivariate analysis showed that indicators for in-stent restenosis were final minimum lesion diameter, lesion length and LMT-LAD angle (OR, 0.12; P=0.036, OR, 10.13; P=0.016 and OR, 7.63; P=0.035, respectively) and indicators for in-segment restenosis were LMT-LAD angle and distance between the ostial LAD artery and proximal edge of stent (OR, 3.83; P=0.024 and OR, 6.37; P=0.006, respectively).
Conclusion: This study suggests that larger LMT-LAD angle is associated with restenosis after stent implantation for proximal LAD artery disease.

P6531 | BEDSIDE
Difference of the development of restenosis with respect to time for various drug-eluting stents

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Background: The temporal pattern of restenosis development in patients implanted DES has not been clearly defined.
Purpose: This study aims to compare the efficacy of sirolimus-eluting stents (SES), paclitaxel-eluting stents (PES), zotarolimus-eluting stents (ZES), and everolimus eluting stents (EES) via sequential angiographic follow-up.
Methods: Patients who underwent elective percutaneous coronary intervention (PCI) with drug-eluting stents (DES) were selected. Patients were randomized to receive SES, PES, ZES, or EES. Enrollment continued until 30 patients were assigned to each group. Follow-up angiography was performed at 12 and 24 months after PCI. We analyzed late loss (LL) and defined 2 time periods: “early” (within first year of follow-up) and “late” (after the first year)
Results: In all groups, mean minimal lumen diameter decreased slightly during the 2-year period after the procedure. Compared with the SES and the EES group, the PES and the ZES groups showed significantly greater early LL. However, the SES group showed significantly greater late LL compared with the other DES (Table 1).

Table 1. Base-line characteristics of the patients and late loss

	SES	PES	ZES	EES
Mean (±SD) age, yr	66.7±11.3	66.2±9.2	68.2±10.6	67.6±9.0
Sex, M	23	25	24	25
Diabetes mellitus, n	9	12	7	12
Hypertension	17	19	18	13
Hyperlipidemia	14	13	17	16
Artery affected, n				
Left anterion descending coronary	16	14	13	12
Circumflex coronary	4	9	6	10
Right coronary	10	7	11	8
Late Loss (LL)				
Total LL	0.231±0.209	0.326±0.334	0.505±0.486	0.181±0.138
Ealy LL	0.124±0.122	0.302±0.324	0.491±0.371	0.166±0.128
Late LL	0.107±0.089	0.024±0.045	0.014±0.033	0.015±0.039

Conclusion: Serial angiographic analysis revealed differences in the rate of restenosis development over time for various DES. Of the studied DES, EES showed the best results in both early and late LL.

P6532 | BEDSIDE
The optimal strategy for in-stent restenosis at the right coronary artery ostial lesion after stent implantation

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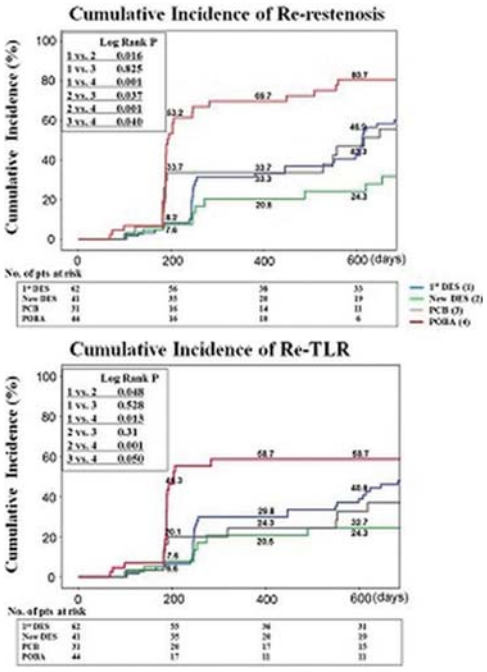
Background: Drug-eluting stent (DES) has markedly reduced the incidence of in-stent restenosis (ISR); however, the incidence of ISR at the right coronary artery (RCA) ostial lesion is still high. Thus, we investigated the optimal percutaneous coronary intervention (PCI) strategy for ISR by comparing the results of PCI with plain old balloon angioplasty (POBA), paclitaxel-coated balloon (PCB), 1st generation DES (sirolimus-eluting stent, paclitaxel-eluting stent) and new generation DES (everolimus-eluting stent, biolimus-eluting stent) for ISR at the RCA ostial lesion.
Methods: From March 1998 to January 2014, 205 ISR lesions at the RCA ostium were treated by PCI. Follow up coronary angiography (CAG) was scheduled at 6 to 8 months (midterm f/u) and at 20months (late f/u), especially for chronic total occlusion lesions, three months follow up CAG was performed. If myocardial ischemia was suspected, CAG was performed at any time. Of these, 44 lesions were treated with POBA, 33lesions with PCB, 62 lesions with 1st generation DES and 41 lesions with new generation DES. In this study, an ostial lesion was defined as a lesion within 5 mm from the ostium.
Results: The data are shown in the figure. The cumulative incidence of re-restenosis and re-TLR were significantly higher after POBA than other strategies at late f/u. After new generation DES implantation, the cumulative incidence of restenosis rate was significantly lower than other strategies and the cumulative incidence of re-TLR was significantly lower than other strategies except for PCB at late f/u.



Conclusions: New generation DES could be a preferable treatment modality for ISR at the RCA ostial lesion.

P6533 | BEDSIDE
Is bare-metal stent sill useful for improving outcomes of percutaneous coronary intervention? From the FU-Registry

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Background: It is not clear the role bare-metal stent (BMS) plays in the field of percutaneous coronary intervention (PCI) in the current drug-eluting stent (DES) era.
Purpose: To identify whether the clinical and angiographic outcomes of BMS implantation are equivalent to those of DES in large vessels.
Methods: Among 2197 patients (2653 lesions) in the FU-Registry, a follow-up coronary angiogram was available for 859 patients (1032 lesions) of which 344 patients (405 lesions) were treated with BMS and 515 patients (627 lesions) with DES. In those patients, the cut-off value of lesion reference (LR) regarding restenosis after PCI calculated using relative cumulative frequency distribution was 3.08mm in BMS and 2.72mm in DES. The clinical and angiographic outcomes with LR larger than 3.08 was compared between the BMS and the DES groups.
Results: Baseline patient characteristics were similar between the two groups except the lower incidence of prior PCI in the BMS group. Mean LR and lesion length in BMS and DES were 3.5±0.3 mm vs. 3.3±0.3 mm (P<0.001) and 14.2±6.2 mm vs. 19.1±12.6 mm (P<0.001), respectively.
At 9 months follow-up, death or myocardial infarction occurred 2.9% in the BMS group and 0% in the DES group (P=0.09). The incidence of definite stent thrombosis was similar between the two groups (0.9% in BMS, 0% in DES; P=0.31). The restenosis rate was also similar between the two groups (16.7% in BMS, 13.9% in DES; P=0.49).
After multiple logistic regression analysis, BMS was not related to any incidences of in-stent restenosis nor death/myocardial infarction.
Conclusion: BMS is useful in patients with large vessels, especially in patients with a high risk of bleeding to avoid long term dual anti-platelet therapy.

P6534 | BEDSIDE
Two-year restenosis rate and its predictors after femoropopliteal drug-eluting stenting

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Background: Restenosis rate and associated factors after paclitaxel-coated nitinol drug-eluting stent (DES) implantation in femoropopliteal (FP) lesions remain to be elucidated in real-world practice. The objective of this study was to investigate 2-year clinical outcomes after intravascular ultrasound (IVUS)-guided DES implantation.
Methods: Between July 2012 and March 2013, FP lesions in 114 limbs from 95 patients (72±8 years; 26% female) were treated with DES implantation under IVUS guidance. Outcome measure were primary patency and freedom from target lesion revascularization (TLR) analyzed by Kaplan-Meier estimation. Restenosis (>50% diameter stenosis or duplex ultrasound PSVR >2.5) was assessed at 24 months, and its independent predictors by Cox proportional hazards model.
Results: Sixty-five % [62] had diabetes mellitus (DM) and 29% [28] were on regular dialysis. Critical limb ischemia (CLI) was present in 33% [31] of the limbs; 18% [21] of lesions were in-stent restenosis and 63% [72] were TASC II C/D, with mean length of 184±106 mm. Restenosis was observed in 38 limbs at mean follow-up of 549±201 days. Primary patency was 75% and 55%, while freedom from TLR was 86% and 66% at 1 and 2 years, respectively. In Cox regression analysis, minimum stent area (MSA) <12.5 mm^2 [HR, 5.20; P<0.001] and female gender [HR, 2.75; P=0.006] were independently associated with restenosis.

Variables	Univarate analysis				Multivarate analysis		
	Overall	Restenosis (+)	Restenosis (-)	p value	Hazard Ratio	95% CI	p value
MSA <12.5 (mm^2)	15 (13)	12 (32)	3 (4)	<0.001	**5.20**	**2.18-12.4**	**<0.001**
Female	39 (26)	16 (42)	14 (18)	0.002	**2.75**	**1.33-5.66**	**0.006**
DM	70 (61)	24 (63)	46 (61)	0.72	1.09	0.53-2.22	0.82
HD	34 (30)	10 (26)	24 (32)	0.69	0.72	0.30-1.71	0.46
CLI	37 (32)	12 (32)	25 (33)	0.55	1.16	0.55-2.46	0.69
Lesion length >150 (mm)	69 (61)	28 (74)	41 (54)	0.043	1.58	0.74-3.37	0.24
Poor BK run-off	8 (7)	2 (5)	6 (8)	0.72	1.28	0.28-5.73	0.75

CI, confidence interval

Predictors associated with restenosis

Conclusions: MSA <12.5 mm^2 and female gender were restenosis predictors after DES implantation in FP lesions.

P6535 | BEDSIDE
In-stent neoatherosclerosis can be a possible mechanism of the impaired flow after re-percutaneous coronary intervention for the in-stent restenosis

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Background: Although in-stent restenosis generally have stable process with an early peak in neointimal proliferation, impaired coronary flow [TIMI 0, 1, 2] is sometimes experienced after re-percutaneous coronary intervention (re-PCI) for the in-stent restenotic sites (ISRs), and its etiology is not clear. On one hand, in-stent neoatherosclerosis (ISNA) have been reported by pathological findings or optical coherence tomographic (OCT) studies, which has been reported as a cause of late stent complications.
Purpose: The aim of this study was to investigate the incidence of impaired flow after re-PCI for ISRs and to evaluate the relationship between impaired flow after re-PCI and in-stent neoatherosclerosis.
Methods: From April 2004 to August 2014, we had performed PCI to consecutive 1751 ISRs. ISRs were defined more than 75% diameter stenosis with ischemia. Post re-PCI coronary flow was angiographically evaluated in retrospective manner. Impaired coronary flow was judged by two skilled interventionists. 233 ISRs were examined by OCT during re-PCI to ISRs.
Results: Impaired flow after re-PCI to ISRs had developed in 48 ISRs (2.7%). ISNA defined by OCT was found in 26 lesions (11.2%) with ISRs during re-PCI to ISRs. Incidence of the impaired flow occurred significantly higher in patients with ISNA [ISRs with ISNA vs. ISRs without ISNA, 13.0% vs. 1.4%, P<0.01]. The ISRs with ISNA was revealed regardless of the type of stent [BMS vs. DES, 11.1% vs. 11.2%, n.s.] with longer duration from initial PCI to re-PCI [71.7±53.4 vs. 39.4±43.7, P<0.01]. In multivariate analysis, the impaired flow had significantly correlated to ISRs with ISNA [odds ratio:8.20, 95% confidence interval:1.29 to 52.2, P<0.05].
Conclusions: Impaired flow was seen in 2.7% of the lesions after PCI to ISRs. Impaired flow occurred significantly higher in the lesions with in-stent neoatherosclerosis.

PROGNOSIS I

P6536 | BEDSIDE
Usefulness of geriatric nutritional risk index for assessing the nutritional status and its prognostic impact in elderly patients with acute heart failure

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Background: Malnutrition was reported to be an important determinant of worse clinical outcomes in elderly patients with heart failure (HF). However, the appropriate tools for evaluating the nutritional status in HF patients remain unclear. Recent studies showed that geriatric nutritional risk index (GNRI) was a useful tool for assessing the nutritional status in elderly patients.
Purpose: To evaluate the prognostic significance of GNRI in HF.
Methods: We examined 477 consecutive patients with acute HF (AHF) in our prospective registry. Those with under 65 years of age, acute coronary syndrome and without accessible GNRI data on admission were excluded. Finally, 364 patients were obtained and divided into two groups according to the GNRI; lower

GNRI group (<106, by ROC cut-off) and higher GNRI group (≥106). Adverse events were defined as worsening HF and death.
Results: During a mean period of 218 days, adverse events occurred in 96 patients (26%). Lower GNRI group had higher age (P<0.01), lower systolic blood pressure (SBP) (P=0.01), and higher plasma brain natriuretic peptide (BNP) level (P<0.01) than higher GNRI group. There were no significant differences in terms of sex, serum creatinine, sodium levels, and left ventricular ejection fraction (LVEF) between two groups. The incidence of adverse events was significantly higher in lower GNRI group than higher GNRI group (Figure). In multivariate analysis, lower GNRI was an independent determinant of adverse events (HR 0.97, 95% CI 0.94–0.99, P=0.005) among variables including age, SBP, BNP level, and LVEF.

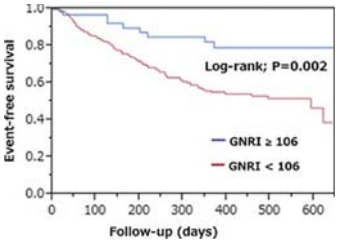

Figure 1

Conclusions: Lower GNRI was independently associated with worse clinical outcomes in elderly patients with AHF, and GNRI may be a useful tool for evaluation of nutritional status and identifying high-risk patients.

P6537 | BEDSIDE
The prognostic value of the transtubular potassium gradient in patients with acute decompensated heart failure

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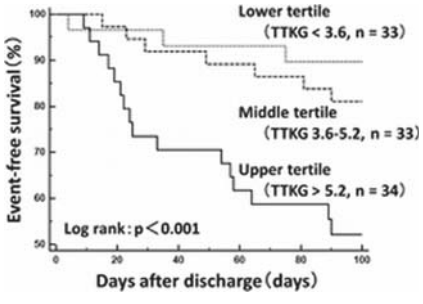
Background: The renin-angiotensin-aldosterone system (RAAS) is involved in the pathophysiology of acute decompensated heart failure (ADHF). The transtubular potassium gradient (TTKG) has been reported to reflect renal aldosterone bioactivity, and may be a more sensitive indicator of RAAS activity than plasma aldosterone concentration.
Purpose: To investigate the prognostic value of TTKG in patients with ADHF.
Methods: We analysed 100 ADHF patients and 30 control subjects. Prior ADHF hospitalisations within the last 12 months were identified in each patient. We measured morning TTKG values at discharge in ADHF patients, as well as the following possible prognostic factors of chronic heart failure: plasma brain natriuretic peptide, serum sodium, creatinine, urea nitrogen concentration, and left ventricular ejection fraction (LVEF) using echocardiography. TTKG was also measured in the control subjects. The clinical outcomes were 100-day cardiac mortality and ADHF readmissions. Cox regression analyses were used to determine the independent predictors of the outcomes. ADHF patients were divided into tertiles based on TTKG values, and the cumulative survival estimates of each group were calculated using the Kaplan-Meier method.
Results: TTKG was significantly higher in ADHF patients than in control subjects (4.8±1.9 vs 3.6±1.3; p<0.001). The results identified TTKG (hazard ratio: 1.37; 95% confidence interval: 1.16–1.62; p<0.001), LVEF, and prior ADHF hospitalisations to be independent predictors of the outcomes. Kaplan-Meier analysis confirmed a stepwise decrease in event-free survival as TTKG values increased (Figure).



Conclusion: Our findings showed that TTKG at discharge is a novel prognostic marker in ADHF patients, and may be a useful guide in their clinical management.

P6538 | BEDSIDE
Left ventricular global longitudinal displacement assessed by tissue Doppler imaging is the strongest echocardiographic predictor of all-cause mortality in patients with heart failure

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Introduction: Tissue tracking (TT), obtained by tissue Doppler imaging (TDI), can be utilized to assess the mitral annular longitudinal displacement (LD) during systole.
Purpose: In this study, we wanted to investigate the prognostic value of LD in a large cohort of Heart failure patients and compare LD to the conventional and novel echocardiographic measurements.
Methods: Transthoracic echocardiographic examinations of 1061 patients were retrieved from our hospital heart failure clinic's database. The exams were performed from 2005 to 2013. The echocardiographic images were subsequently analyzed obtaining data by conventional echocardiographic measurements, myocardial strain and TDI from the parasternal and apical projections. Global LD was calculated as a mean from the three apical projections with sampling at six mitral annular sites in total.
Results: During a median follow-up of 40 months 177 (16.7%) patients died. Mean global LD in this group was 5.01±2.41 cm. A remaining 884 (83.3%) of patients were alive at follow-up with a mean global LD of 6.70±2.53 cm. The risk of dying increased with decreasing tertile of LD, being approximately 5 times higher for patients in the lowest tertile compared to the highest tertile (1. tertile vs. 3. tertile: HR: 4.78, 95% CI: 3.04–7.54, p-value<0.001) (see figure).
Many of the conventional echocardiographic parameters presented as predictors of mortality (LVEF, LVMI, LAVI, E, E/e', deceleration time and TAPSE). In addition, the speckle tracking parameter global longitudinal strain (GLS) was also a significant predictor of outcome. Both GLS and global LD remained as the only independent echocardiographic predictors of mortality in the cox proportional-hazards models after adjusting for age, gender, BMI, total cholesterol, heart rate, atrial fibrillation, non-independent diabetes mellitus and conventional echocardiographic parameters (GLS: p-value=0.014; LD: p-value=0.014). However, in direct comparison global LD had the highest c-statistics (c-stat=0.70) for predicting mortality of all echocardiographic parameters and it was significantly higher than the c-statistics obtained by the LVEF (0.70 vs. 0.66, p-value=0.019). In contrast, GLS did not contribute with a significantly higher c-statistics than LVEF (0.67 vs. 0.66, p-value=0.21).
Conclusion: In patients with severe heart failure, global LD is an independent predictor of all-cause mortality. Furthermore, global LD proved to be a superior prognosticator when compared to conventional echocardiographic parameters and GLS.

P6539 | BEDSIDE
Recent trends in the prevalence, management and clinical outcomes of patients with symptomatic chronic heart failure in Japan - A report from the CHART studies

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Background: The number of patients with chronic heart failure (CHF) is increasing worldwide.
Purpose: To examine the recent trends in the prevalence, management and clinical outcomes of CHF patients.
Methods: Using the databases of the Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART)-1 (2000–2005, N=1,278) and the CHART-2 (2006–present, N=10,219) Studies, we prospectively examined a total of 4,679 consecutive patients with symptomatic CHF.
Results: Between the CHART-1 and the CHART-2, there was no difference in age (69 vs. 70 y.o.), the prevalence of male sex (64 vs. 66%) or systolic/diastolic blood pressure (126/71 vs. 125/72mmHg). From the CHART-1 to the CHART-2, uses of beta-blockers (29 vs. 51%), RAS inhibitors (69 vs. 73%) and aldosterone antagonists (19 vs. 27%) were significantly increased, whereas those of loop diuretics (77 vs. 56%) and digitalis (49 vs. 25%) were decreased (all P<0.01). The prevalence of ischemic CHF was markedly increased from 27% (CHART-1) to 47% (CHART-2), which was mainly attributable to the increase in ischemic CHF with

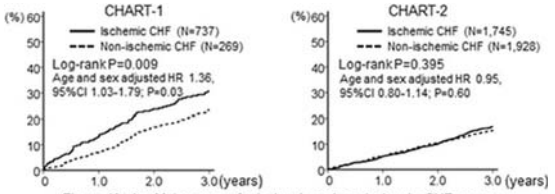

Figure. Kaplan-Meier curves for ischemic and non-ischemic CHF groups in the CHART-1 and CHART-2 Studies

left ventricular ejection fraction >40% (from 17 to 38%). In contrast, the prevalence of dilated cardiomyopathy was decreased from 26% to 14%. The 3-year mortality rate was significantly improved from 24% to 14% (P<0.01), where the difference in the mortality rate between ischemic and non-ischemic CHF noted in the CHART-1 (29 vs. 22%, P<0.01) disappeared in the CHART-2 (15 vs. 14%, P=0.40) (Figure).
Conclusions: These results indicate that the prevalence of ischemic CHF, especially that of preserved LVEF, has markedly increased in Japan and that the prognosis of CHF patients has been improved along with implementation of evidence-based medications, particularly in those with ischemic CHF.
Acknowledgement/Funding: Grants-in-Aid from a Research Grant from the Ministry of Health, Labour, and Welfare

P6540 | BEDSIDE
Quantification of fibrosis in left ventricular endomyocardial biopsy can be a valuable tool to estimate prognosis and individualize therapy in heart failure patients

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Introduction: Endomyocardial biopsy (EMB) contributes important information to the diagnosis and etiology of cardiomyopathies. Myocardial fibrosis, defined by a substantial increase in the collagen volume fraction (CVF) of myocardium, has been shown to be one common histopathological feature in idiopathic dilated cardiomyopathy (DCM), which leads to diastolic dysfunction and possibly worsens systolic function. However, large, longitudinal studies investigating the correlation between histopathological characteristics of EMB and clinical course and prognosis of patients with DCM are still missing.
Purpose: In this study we investigated the prognostic value of fibrosis as a common histopathological finding in a large DCM cohort with a follow up period of up to 10 years.
Methods: We included a total number of 643 patients who had undergone left ventricular EMB (LV-EMB) due to suspected DCM. Using automated image processing and analysis softwares, we developed algorithms based on Bayesian classification to automatically evaluate high-resolution automated scans of LV-EMB for fibrosis. Univariate as well as multivariate analyses between histopathological and clinical findings of these patients have been carried out.
Results: Using machine learning techniques, we established an automated method for quantification of fibrosis in patients' LV-EMBs. Classification of myocardial fibrosis based on Trichrome (Tri) and Elastic van Gieson's stainings (EVG) showed very good agreement. We could also show that LV-EMB is a safe procedure with a total complication rate of 2.3 in 100 patients in our center with no case of death. Further data analyses showed that the extent of fibrosis significantly correlates with cardiac biomarkers such as hsTnT (p=0.01) and NT-proBNP (p=0.048) as well as with cardiac imaging such as LV-EF (p=0.02), LV-ESD (p=0.01), LV-EDD (p=0.01), LV-ESV index (p=0.02), and LV-EDV index (p=0.02) measured with cardiac MRI. Kaplan Meier survival curves showed that percentage extent of fibrosis was a significant predictor of all-cause mortality (p=0.02) and cardiovascular mortality, heart transplantation or cardiopulmonary resuscitation (p<0.001).
Conclusions: Our results suggest that EMB is a reliable and precise tool to characterize DCM tissue properties. Further analyses show promising correlations between extent of LV-fibrosis and clinical variables in DCM and strengthen the role of LV-EMB in evaluation of clinical course and outcome of patients with this type of cardiomyopathy.

P6541 | BEDSIDE
A useful risk assessment tool of malnutrition and its prognostic impact in patients with acute heart failure

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Background: Malnutrition is a potential predictor of poor clinical outcomes in heart failure (HF), however, there exist few assessment tools.
Purpose: We aim to investigate the prognostic impact and the validity of malnutrition assessed by controlling nutritional status score (CONUT).
Methods: 477 consecutive patients with acute HF (AHF) in our prospective registry were examined. Those with in-hospital death and without accessible CONUT at discharge were excluded. Finally 390 patients with median follow-up of 354 (IQR 118–491) days and 17 events (all-cause death) were analyzed.
Results: The median of CONUT was 3 (IQR 2–4). The event risk increased in accordance with the score stratum (Figure). After adjustment for potential confounders, including age, gender, hemoglobin, renal function, serum sodium and BNP, the hazard ratio for malnutrition assessed with CONUT was 1.45 (95% CI 1.15–1.83). The addition of CONUT to an established prediction model of short-term death in HF increased the C-statistics from 0.68 to 0.74 (P=0.008). Net reclassification improvement afforded by CONUT was 6% for events, 67% for non-events and 73% for overall (P=0.003). We further evaluated the validity of CONUT for nutritional risk assessment and compared the C-statistics of various nutritional indexes; CONUT 0.77 (P=0.02), body mass index (P=0.22), nutritional risk index (P=0.57), serum albumin (P=0.14), total cholesterol (P=0.57), and neutrophil to lymphocyte ratio (reference).

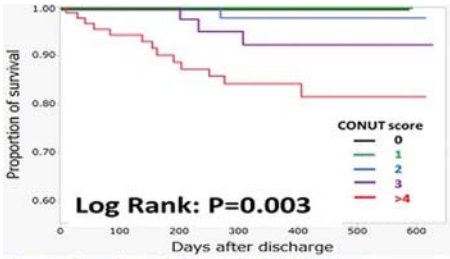

Figure: Kaplan-Meier survival curves for the each CONUT score stratum.

Conclusions: Malnutrition assessed with CONUT was an independent determinant of post-discharge death in AHF patients. Simple addition to the existing prognostic model significantly improved the predictive accuracy. CONUT might be the best nutritional assessment tool for the risk stratification in HF.

P6542 | BEDSIDE
Association of compromised right ventricular function with reduced exercise tolerance predicts survival in patients with chronic heart failure

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Background: Although right ventricular (RV) ejection fraction (EF) is an important determinant of effort tolerance, little is known about the role of RV function and exercise performance in outcome prediction of patients with chronic heart failure (HF).
Aim: We sought to evaluate the impact of RV function and 6-minute walking test (6-MWT) in risk stratification of patients with chronic stable HF.
Methods and results: 628 ambulatory patients (mean age: 70±12 yrs; 32% female) with chronic HF and left ventricular (LV) dysfunction underwent a complete echocardiographic examination. RV systolic function was evaluated by M-mode echocardiography using tricuspid annular plane systolic excursion (TAPSE). Effort tolerance by 6-MWT and B-type natriuretic peptide (BNP) plasma levels were evaluated at the time of the index echocardiogram. The end-point was all cause-mortality. LV ejection fraction (EF) was 42±8%. During the follow-up (31±19 months, median: 32 months), there were 83 deaths. Univariate predictors of overall survival included TAPSE (p<0.0001), BNP (p<0.0001), 6-minute walking distance (p<0.0001), aetiology (p<0.0001), age (p<0.0001), LV EF (p=0.0003), mitral regurgitation (p=0.0007), mitral E wave deceleration time (p=0.0083), diabetes (p=0.014) and LV end-diastolic volume (p=0.022). In a multivariate proportional hazards survival model, TAPSE (HR 0.86, 95% CI 0.81–0.91, p<0.0001) and 6-minute walking distance (HR 1.00, 95% CI 0.99–1.00, p=0.0002) were selected as the most powerful independent predictors of overall survival followed by aetiology (p=0.0023), BNP (p=0.024) and gender (p=0.024). Receiver operating curve analyses showed that TAPSE ≥18 mm and 6-minute walking distance ≥324 m were the best cut-off values for outcome prediction. At Kaplan-Maier survival analyses, patients with TAPSE <18 mm and 6-minute walking distance <324 m had the worst survival at 60 months (48%), while survival was 71% in patients with TAPSE <18 mm and 6-minute walking distance ≥324 m, 78% in patients with TAPSE ≥18 mm and 6-minute walking distance <324 m and 92% in those with TAPSE ≥18 mm and 6-minute walking distance ≥324 m (log rank 75.6, p<0.0001).
Conclusion: The results of this study show that the association of a compromised RV function as assessed by TAPSE with reduced exercise tolerance has a negative impact on survival of patients with chronic stable HF.

P6543 | BEDSIDE
Advanced age affects outcomes with LVAD support

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Background: Age affects available options to treat advanced heart failure. Advanced age is a known risk-factor for transplantation leading to few transplants being performed in patients ≥70 years old. Less is known regarding the risk of advanced age for LVAD support, although reports suggest increasing risk with increasing age.
Purpose: We sought to evaluate age ≥70 as a risk factor for death or readmission in our population of continuous-flow LVAD (cf-LVAD) patients.

Methods: We retrospectively identified all patients who underwent cf-LVAD placement and survived to discharge at our centre between 2007 and 2013 (n=114). Analysis was performed on demographic, clinical, and procedural data. Multivariable analysis was used to assess for predictors of mortality. The primary outcomes of interest were time to mortality and first hospitalization after LVAD.
Results: Age ≥70 was associated with increased mortality and time to readmission (figure 1). Using Cox analysis, after controlling for age, gender, and race, baseline creatinine ≥1.5 was the only independent predictor of mortality (HR 1.9 [CI 1.1–3.3], p=0.028). No significant predictors for readmission were identified.

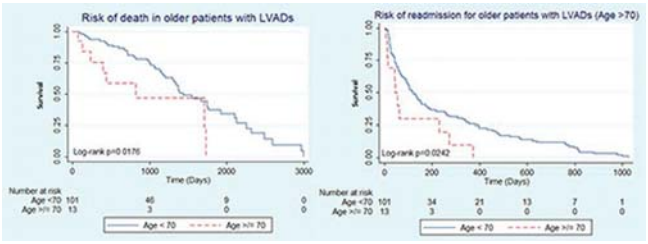

Figure 1

Conclusions: Our data support the notion of advanced age as a risk for death with LVAD support, even with a highly selected population felt to be at acceptable risk. Similar to previous analyses, the cause of death in the advanced age group is not well established and may reflect co-morbidities associated as much as LVAD problems or renal dysfunction. Unique in our analysis is demonstration of higher readmission rates in the advanced age group, suggesting higher morbidity in this cohort. LVAD support should be considered cautiously with advanced age, and renal insufficiency may be a marker of increased mortality in this cohort.

P6544 | BEDSIDE
Prognostic impacts of new onset atrial fibrillation in patients with chronic heart failure: an interim analysis of the CHART-2 study

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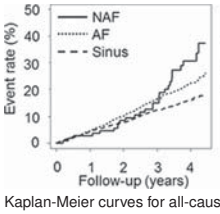
Background: The clinical significance of new onset atrial fibrillation (NAF) in patients with chronic heart failure (CHF) remains unclear.
Purpose: To elucidate the prognostic impacts of NAF in CHF patients.
Methods: Using our database of the Chronic Heart Failure Analysis and Registry-2 (CHART-2) study (N=10,219), we prospectively enrolled 4,811 consecutive CHF patients in Stage C/D. Among them, 1,859 had a prior or present history of atrial fibrillation (AF) at the time of registration. Among the remaining 2,953 patients, 106 developed NAF during the follow-up of 3.2 years, while 2,847 maintained sinus rhythm (SR). We compared clinical characteristics, treatments and long-term prognosis among the NAF, AF and SR groups.
Results: Patient characteristics in the NAF group were mostly intermediate between those in the AF and SR groups. In the AF, NAF and SR groups, mean age was 71.0, 68.3 and 67.7 yrs. (P<0.001), and eGFR was 58.9, 59.3 and 61.9 ml/min/1.73m^2 (P<0.001), respectively. In contrast, BNP levels were equally elevated in the NAF and AF groups and were higher compared with the SR group (152, 158 and 74.5 pg/ml, P<0.001). LVEF levels (56.8, 55.2 and 56.5%, P=0.591) and use of β-blockers (50.7, 50.9 and 48.0%, P=0.186) and renin-angiotensin system inhibitors (71.6, 70.8 and 73.0%, P=0.521) were comparable among the 3 groups. During the follow-up, there were 732 deaths. Compared with the SR group, both NAF and AF groups had poor prognosis (Figure). The multivariate Cox regression analysis revealed that the NAF group, but not the AF group, had worse prognosis than the SR group (adjusted hazard ratio (HR) 1.03, P=0.775 for AF and adjusted HR 1.72, P=0.003 for NAF).



	HR (95%CI)	P value
NAF	1.83 (1.25-2.69)	0.002
AF	1.38 (1.19-1.60)	<0.001

Kaplan-Meier curves for all-cause death

Conclusions: NAF is an independent prognostic factor in CHF patients.
Acknowledgement/Funding: the Grants-in Aid from the Ministry of Health, Labour, and Welfare and the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

P6545 | BENCH
Determinants and prognostic significance of delirium in patients with acute heart failure

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Background: Delirium is a common and serious, but potentially preventable syndrome in critically ill condition, such as acute heart failure (AHF). It is important to identify patients at risk for delirium who may benefit from earlier preventive strategies. However, determinants of delirium and its prognostic significance in AHF patients remain unknown.
Methods: We examined 477 consecutive AHF patients who admitted to our institution between January 2013 and December 2014 from prospective registry. Patients with acute coronary syndrome were excluded. Finally, 454 patients were included in this study. Delirium was diagnosed based on the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).
Results: Delirium was observed in 111 patients (24%) during hospitalization. Patients with delirium were older (80 vs. 74 years, P<0.01) and had higher prevalence of cerebrovascular disease (CVD) (38% vs. 20%, P<0.01) and malignant disease (21% vs. 13%, P=0.02), higher serum glucose (167 vs. 140 mg/dl, P=0.01) and CRP (2.3 vs. 1.4 mg/dL, P=0.02) levels, lower serum albumin (3.6 vs. 3.8 g/dL, P<0.01) and free T3 (2.1 vs. 2.4 pg/ml, P=0.03) levels on admission than those without. Patients with delirium had longer hospital stay (23 vs. 20 days, P=0.03), higher utilization of nursing care after discharge (59% vs. 25%, P<0.01) and higher rate of 90-day adverse events defined as composite of all cause death and worsening heart failure (23% vs. 8%, P<0.01) than those without. In multivariate logistic regression analysis, the development of delirium (OR 3.30, 95% CI 1.78–6.10, P<0.01), as well as lower systolic blood pressure (<135mmHg) (OR 2.28, 95% CI 1.19–4.52, P=0.01) and NYHA functional class IV (OR 2.14, 95% CI 1.14–4.08, P=0.02), was an independent determinant for 90-day adverse events. Furthermore, multivariate logistic regression analysis indicated that higher age (>80 years) (OR 2.69, 95% CI 1.66–4.41, P<0.01), history of CVD (OR 2.59, 95% CI 1.55–4.35, P<0.01) and hypoalbuminemia (serum albumin <3.5mg/dL) (OR 1.99, 95% CI 1.15–3.44, P=0.01) were independent determinants for the development of delirium.
Conclusions: AHF patients with development of delirium have unfavorable outcomes, particularly higher adverse events, longer hospitalizations, and a greater degree of dependence on nursing care after discharge. These findings suggest that early recognition and prevention of delirium may be important to improve clinical outcomes in AHF patients.

P6546 | BEDSIDE
Mortality after hospitalization for heart failure: a Slovenian national database analysis 2004 to 2012

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Background: Heart failure (HF) mortality is decreasing in Western Europe and USA while information about trends in Central and Eastern Europe is limited.
Purpose: To investigate mortality after hospitalization for HF in Slovenia.
Methods: Slovenian national hospital discharge registry was used to identify patients with HF hospitalized between 2004 and 2012. In subjects without HF hospitalization during 2004 to 2008, HF related admission in period 2008 to 2012 was considered as first HF hospitalization. Survival status was retrieved from Central population registry; database was censored on December 31, 2013. We calculated annual mortality rates per 100,000 person. Kaplan-Meier curves and Cox models of proportional hazards were used for survival analysis.
Results: Overall, 157,695 hospitalizations in 80,180 subjects (76±12 years, 52% women, 5±3 comorbidities) were identified. After hospitalization with HF, non-significant decrease in standardized mortality rate per 100,000 inhabitants at 30 days (152 to 150, p=0.41) and at 1 year (297 to 284, p=0.27) was recorded. Proportion of hospitalized patients who died at 30 days and 1 year increased or remained stable, respectively (Figure). For those first hospitalized with HF, mortality rate reductions at 30 days (80 to 67, p=0.017) and 1 year (128 to 105, p=0.011) were significant. In Cox models of proportional hazard, increased mortality at 1 year or at the end of follow-up was independently predicted by male sex, age, chronic obstructive pulmonary disease, ischaemic heart disease, and cancer (p<0.001 for all).

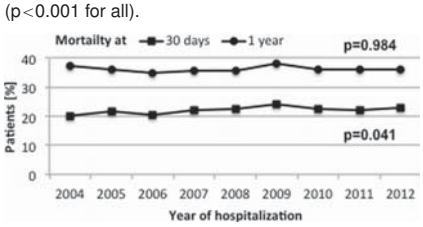

Figure. Mortality after HF discharge.

Conclusions: Mortality rate after discharge with HF remains high, with little change in proportion of deceased patients at 30 days and 1 year. Age, male sex, and comorbidity increase risk of death in an independent fashion.

P6547 | BEDSIDE

Apolipoprotein J but not high-density lipoprotein is an independent predictor of mortality in patients with advanced heart failure

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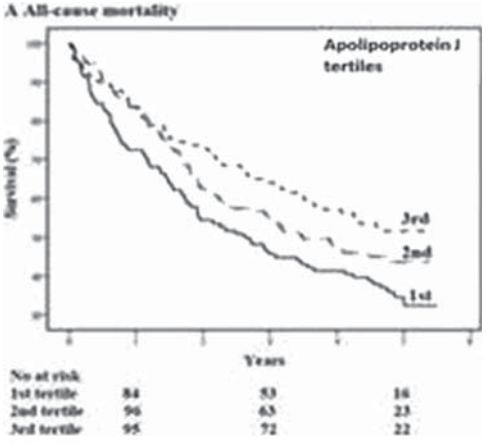
Background: Apoptosis, inflammation and atherogenesis are implicated in the multifactorial pathophysiology of heart failure (HF). The multifunctional glycoprotein apolipoprotein J, also known as clusterin, is associated with high-density lipoprotein (HDL) and exerts multiple anti-apoptotic, anti-atherogenic, cell-protective and anti-inflammatory properties.
Purpose: To assess the predictive value of apolipoprotein J and HDL in advanced HF patients.
Methods: Apolipoprotein J plasma levels and HDL serum levels were determined in 346 patients with advanced systolic HF (median 75 years, 66% male).
Results: During a median follow-up of 4.9 years (IQR: 4.6–5.2), 55.9% of patients died. Apolipoprotein J (median 277 ug/ml (IQR: 216–344 ug/ml) was a significant inverse predictor of all-cause mortality with a hazard ratio (HR) per 1-standard deviation (SD) of 0.79 (95% confidence interval (CI): 0.69–0.92, P=0.002). This association remained significant after multivariable adjustment for demographics, clinical predictive variables and N-terminal pro-B-type natriuretic Peptide (HR per 1-SD 0.84, 95% CI: 0.72–0.98, P=0.03). The predictive value of apolipoprotein J did not significantly differ between patients with ischemic and non-ischemic HF (P=0.401). In contrast, HDL did not predict mortality (p=0.842). Interestingly, apolipoprotein J levels were significantly higher in patients on statin (HMG-CoA-reductase Inhibitor) therapy ((300ug/ml (245- 355ug/ml) versus 275ug/ml (209–331 ug/ml), P=0.033) potentially reflecting a further pleiotropic effect of statins.



Kaplan-Meier curves

Conclusion: Circulating apolipoprotein J with its cytoprotective and anti-inflammatory effects is an independent inverse predictor of mortality in advanced HF patients. Our data indicate an implication of apolipoprotein J in HF progression.

PROGNOSIS II

P6548 | BEDSIDE

Pericardial effusion is a marker of increased mortality in thalassemia major patients

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Introduction: In different types of not-hematological diseases the presence of a small pericardial effusion (PE) was associated with worse survival even after adjustment for patient characteristics, suggesting that it is a marker of underlying disease. In thalassemia major (TM) pericardial effusion was shown to be one of the manifestations of heart disease but its potential prognostic importance has never been investigated in the modern era. Cardiovascular Magnetic Resonance (CMR) by cine SSFP sequences was demonstrated to be extremely sensitive to even a small amount of PE.
Purpose: This is the first prospective study evaluating if the presence of pericardial effusion is associated with increased mortality in TM.
Methods: 1259 patients (648 females, 31.02±8.64 years) enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) were prospectively followed from their first CMR scan. CMR was used to quantify myocardial iron (MIO) overload by a multislice multiecho T2* approach and to assess biventricular function parameters and to detect PE by cine SSFP sequences.
Results: PE was present in 25 (2.0%) patients. Patients with and without PE were comparable for age and ratio of men/women. At the baseline, the percentage of patients with MIO (global heart T2*<20 ms) was comparable between patients with and without PE (12.0% vs 28.7%; P=0.074) and left ventricular and right ventricular ejection fractions were not significantly different between the two groups.
Mean follow-up (FU) time was 44.55±20.35 months and there were 15 deaths.
Mortality was greater for patients with PE compared to those without an effusion (8.0% vs 1.1%, P=0.034).
PE was a significant predictive factor for death (hazard ratio-HR=12.64, 95% CI: 2.78–57.42, P=0.001). PE remained a significant prognosticator for death also in a multivariate model including MIO (PE: HR=17.36, 95% CI: 3.65–82.62, P<0.0001 and global heart T2*<20 ms: HR=3.07, 95% CI: 1.07–8.75, P=0.036).
Conclusions: PE is quite rare in TM patients and it is not related to MIO. An important role in the development of PE could be played by the 'iron-induced' pericardial siderosis but, due to the limitations of the current non-invasive CMR techniques, we were not able to address this issue.
PE was found to be a strong predictor for death, independently by the presence of MIO. The non-invasive diagnosis of pericardial effusion is important for a more complete definition of the cardiac involvement of TM patients. The increased risk of death associated with PE may be used along with other clinical characteristics when estimating a patient's prognosis and monitoring.

P6549 | BEDSIDE

Outcomes in patients with probable cardiac sarcoidosis in comparison with definite cardiac sarcoidosis

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Background: Although early diagnosis of cardiac sarcoidosis (CS) is important to initiate steroid treatment before pathological lesions are irreversible, it is difficult to confirm the diagnosis even in patients who have signs compatible with CS. In a clinical setting, patients with probable CS who satisfied only clinical cardiac findings for CS are not uncommon. However, patients with probable CS are not treated with steroids because their prognosis is unknown.
Aim: We aimed to compare outcomes in patients with probable CS to those in patients with definite CS treated with steroids.
Methods: The study population consisted of 101 consecutive patients who satisfied clinical cardiac findings for CS. Patients with definite CS were defined as having histological or clinical confirmation of CS according to the Japanese Ministry of Health and Welfare guidelines revised by Japanese Society of Sarcoidosis and Other Granulomatous Disorders, and were treated with steroids. Patients with probable CS were defined as having only the CS diagnostic guidelines' clinical cardiac findings but not definite CS because of no histological confirmation or extracardiac sarcoidosis, and were not treated with steroids. The endpoint was major adverse cardiac events (MACE), including cardiac death, ventricular fibrillation, sustained ventricular tachycardia, or hospitalization due to heart failure.
Results: Forty-seven patients had definite CS and the other 54 had probable CS. Except for serum angiotensin-converting enzyme levels and left ventricular dysfunction, clinical characteristics were similar between the two groups. Over a median follow-up of 15 months (range, 1–149 months), MACE occurred more frequently in patients with probable CS than in those with definite CS (74% vs. 53%, p=0.029). Kaplan-Meier analysis showed that the event-free survival rate was worse in patients with probable CS than in those with definite CS (log-rank test, p=0.006). Cox proportional hazard analysis showed that MACE were independently associated with probable CS, New York Heart Association functional class III or IV, and history of sustained ventricular tachycardia or ventricular fibrillation.
Conclusion: Outcomes are worse in patients with probable CS than in those with definite CS treated with steroids. Our finding suggest that the initiation of steroid treatment can be considered for patients who satisfy only clinical cardiac findings for CS. Further investigation is needed to assess therapeutic strategies for patients with probable CS and to determine how the diagnostic approach is modified.

P6550 | BEDSIDE

Prevalence and impact of coronary artery disease in patients with takotsubo cardiomyopathy

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Background: Takotsubo Cardiomyopathy (TTC) is suggested to occur in the absence of coronary artery disease (CAD). However recent studies show, that CAD may be present in patients with TTC. Therefore, the role of CAD in TTC has been underappreciated, and data on the prevalence and its impact on prognosis are still limited.

Purpose: We sought to investigate the prevalence of CAD and its impact on prognosis in patients with TTC.
Methods: 1639 patients with TTC were enrolled in our study. Out of these 1517 patients with complete information on the coronary artery status were included in the final analysis.
Results: Coexistent obstructive CAD was present in 15.3% (n=233) of all TTC patients. Out of these, 21.9% were diagnosed with multi-vessel disease (MVD; n=51) while 78.1% (n=182) presented with only single-vessel disease (SVD). 65.2% (n=152) of the patients had mid-grade stenosis of 50–69% and 34.8% high-grade stenosis of ≥70% (n=81). The mortality (13.3% vs. 7.8%, p=0.004) and MACCE rate (20.0% vs. 13.6%, p=0.003) of TTC patients with CAD was substantially higher than in patients without significant stenosis after 5 years of follow up. Patients with TTC and MVD had even higher mortality (25.5% vs. 10.4%, p=0.001) and MACCE rates (33.3% vs. 17.0%, p<0.001) compared to those with SVD. In an multivariate analysis, MVD emerged as an independent predictor of death and MACCE (HR 3.10, 95% CI 1.14–8.40, p=0.027; HR 2.80, 95% CI 1.17–6.67, p=0.021; respectively).
Conclusions: Our study highlights that the prevalence of CAD is higher than previously thought. Furthermore, co-existence of CAD might lead to a worse outcome including increased death and MACCE rates. MVD is probably associated with an unfavorable prognosis in patients with TTC.

P6551 | BENCH
YKL-40 In chronic heart failure: Analysis from the controlled rosuvastatin multinational trial in heart failure (CORONA)

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Background: The inflammatory biomarker YKL-40 is associated with the presence and severity of coronary artery disease and may predict adverse outcome. We hypothesized that circulating YKL-40 can give prognostic information in patients with ischemic heart failure (HF) and identify a subgroup of patients who may benefit from statin therapy.
Methods: The association between serum levels of YKL-40 and the primary end point (cardiovascular [CV] death, nonfatal myocardial infarction, nonfatal stroke), all-cause mortality, CV death, the composite of all-cause mortality/hospitalization for worsening of HF or the coronary end point was evaluated in 1344 patients aged >60 years with ischemic systolic HF in a subset of patients from the Controlled Rosuvastatin Multinational Trial in HF (CORONA) population (n=5011), randomly assigned to rosuvastatin 10 mg or placebo.
Results: Serum levels of YKL-40 were associated with outcome in univariate analysis, but added no predictive information after full multivariable adjustment including hs-CRP and NT-proBNP. Statin treatment moderately reduced YKL-40 levels, whereas an increase was observed with placebo (difference in change between the groups p=0.002). A significant interaction between baseline YKL-40 and rosuvastatin on the primary endpoint (p=0.008) and CV death (P=0.027) was observed. Thus, whereas rosuvastatin had no effect in those with intermediate or high YKL-40 levels, primary endpoint and CV death were significantly reduced by rosuvastatin in tertile 1 also after full adjustment (primary outcome, HR 0.50 [0.30–0.82] p=0.006; CV death, HR 0.54 [0.30–0.97] p=0.040).
Conclusions: Circulating levels of YKL-40 were of limited predictive value in patients with chronic ischemic systolic HF. However, a beneficial modification of outcome was observed with statin therapy in patients with low YKL-40 levels.

P6552 | BEDSIDE
Clinical utility of combined platelet count and neutrophil-to-lymphocyte ratio in predicting cardiovascular outcome in patients with chronic heart failure

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Background: Neurohormonal and inflammatory activation is thought to play a key role in the pathophysiology of Chronic Heart Failure (CHF) and inflammatory cytokines such as interleukin-6 (IL-6) have been associated with the disease progression, mediating adverse cardiac remodelling. Neutrophil-to-Lymphocyte ratio (NLR) and reactive thrombocytosis are cellular components of systemic inflammation that are regulated by cytokines especially IL-6. Here we investigated the prognostic impact of a combination of platelet count and NLR (collectively named the CPNR) in predicting cardiovascular outcome in CHF patients.
Methods: We reviewed 1557 CHF patients (mean age 76±11 y, 66% males) from the BIOSTAT-CHF Scotland cohort. Bloods were drawn and routine laboratory measurements including full blood count was performed at baseline from which NLR and platelet count was determined. Patients with both an elevated platelet count (>275) and an elevated NLR (>3) were allocated a score of 2, and patients showing one or neither were allocated a score of 1 or 0, respectively. Multivariate cox proportional hazard models were used to evaluate the prognostic impact of CPNR.
Results: Mortality rates (95% CI) were higher in CPNR 2 (CHF: 129, & CVD: 116 deaths per 1000 person years) as compared to CPNR 1 (CHF: 86, & CVD: 99 deaths per 1000 person years) and CPNR 0 (CHF: 28 & CVD: 42 deaths per 1000 person years) and a multivariate cox proportional hazard model showed that CPNR was a significant risk factor for cardiovascular outcome [CHF, HR=1.65 CI: 1.3–2.2; CVD, HR=1.5 CI: 1.2–1.9] and CHF hospitalization (HR=1.3 CI: 1.1–1.5).
Conclusion: An elevated CPNR is significantly associated with worse outcome in CHF patients. The CPNR is an inexpensive, easy to perform test and can be used in risk stratification of CHF patients.

P6553 | BEDSIDE
Incidence and predictors of new-onset heart failure in patients with atrial fibrillation: the fushimi af registry

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Background: Heart failure (HF) is the important comorbidity associated with atrial fibrillation (AF) and related to poor prognosis. Despite that pre-existent HF or organic heart disease is a strong predictor for development of HF, it is suggested that AF per se may precipitate HF. However, the incidence and predictors of new-onset HF in AF patients without prior HF or organic heart disease were not clearly understood.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients who visited the participating medical institutions in Japan. Follow-up data were available in 3,390 patients (the median follow-up periods, 777 days). At baseline, 2,070 patients had neither prior HF (history of HF hospitalization, HF symptoms, or left ventricular (LV) dysfunction (EF<40%)) nor any organic heart disease (valvular heart disease, cardiomyopathy, and previous myocardial infarction). We investigated the incidence and predictors of new-onset HF in these patients.
Results: During the follow-up period, 64 (3.1%) patients experienced hospitalization for HF (incidence rate of 1.4 per 100 person-years). The incidence of HF was much less than that in the patients with prior HF or heart disease (7.8 per 100 person-years; p<0.0001). Patients developing new-onset HF were older than those without HF development, and had more comorbidities including previous stroke, anemia, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and mild LV dysfunction (EF<60%). The prevalences of hypertension and coronary artery disease were comparable between the groups. In the univariate analysis, age, type of AF (permanent or persistent), previous stroke, anemia, CKD, COPD, prescription of loop diuretics, and mild LV dysfunction were associated with new-onset HF. Multivariate cox proportional hazard analysis showed that female gender (hazard ratio (HR) 2.1, 95% confidence interval (CI) 1.1–4.1), anemia (HR 3.1, 95% CI 1.5–6.1), COPD (HR 4.8, 95% CI 1.7–11.6), and mild LV dysfunction (HR 3.2, 95% CI 1.6–6.4) were independent predictors for new-onset HF. In the Kaplan-Meier analysis, new-onset HF was associated with higher mortality during the follow-up period (24.8% vs 11.7%; p=0.006).
Conclusion: Among AF patients, those without prior HF or organic heart disease are less likely to develop new-onset HF, and it was associated with poor prognosis. Female gender, anemia, COPD, and mild LV dysfunction were independent predictors for new-onset HF.
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P6554 | BEDSIDE
Additional prognostic impact of sequential organ failure assessment on 30-day mortality in acute heart failure

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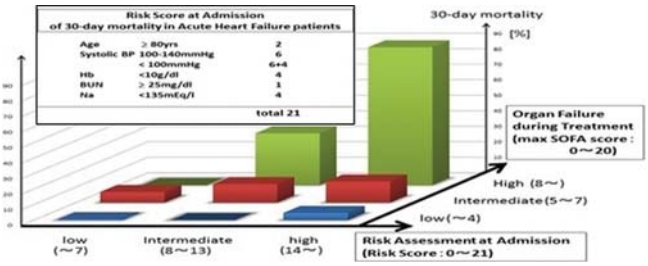
Background and purpose: Although several prognostic value factors for short-term mortality of patients with acute heart failure have been reported, their prognostic predictive abilities, mostly evaluated at admission, are not satisfactory. We examined whether sequential organ failure assessment (SOFA) score obtained during treatment had further impact in addition to traditional prognostic factors.
Methods: We investigated consecutive 432 acute heart failure patients hospitalized in cardiac care unit from January,2009 to December,2013 (mean age:75.9±15.2y.o., female:46.7%, mean LVEF:42.8±16.5%, ischemic etiology:30.8%). An endpoint was 30-day mortality. We made prognostic risk score of 30-day mortality from traditional risk factors at admission (age, systolic blood pressure, blood level of hemoglobin, blood urea nitrogen and sodium) and evaluated prognostic value of maximal SOFA score during treatment (with exception of neurological score) by multivariable logistic regression analysis.
Results: Thirty-day mortality was 6.3% (27 cases). In addition to risk score at admission (Table), maximal SOFA score after admission was identified as an independent prognostic factor of 30-day mortality (Odds Ratio [95% confidence interval]: 1.45 [1.27–1.70], 1.33 [1.10–1.60]; p-value: <0.0001, 0.0037, respectively), and showed more detailed risk stratification (Figure).
Conclusion: Sequential organ failure assessment during treatment might have remarkable impact on mortality in acute heart failure. We might be able to predict



30-day mortality of acute heart failure

short-term prognosis more accurately by addition of dynamic assessment after admission to initial assessment.

P6555 | BEDSIDE
Growth differentiation factor 15 (GDF-15) is a strong predictor of outcome in heart failure patients with anaemia-results from the RED-HF study

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Background: Growth differentiation factor 15 (GDF-15), a stress-responsive cardiokine, was recently identified as a hepcidin-suppression factor that is expressed at high levels in patients with ineffective erythropoiesis.
Purpose: We investigated the predictive value of circulating GDF-15, and interactions with darbepoetin alfa treatment, on clinical outcomes in patients with heart failure (HF) and anaemia.
Methods: Serum levels of GDF-15 were analysed by enzyme immunoassays in 1588 patients with HF, reduced ejection fraction, and mild to moderate anaemia, followed for median 28 months in the Reduction of Events by Darbepoetin alfa in Heart Failure (RED-HF) trial. Association between baseline and change in GDF-15 (≥15% increase, ≥15% decrease or no change) and the primary composite outcome of all-cause death and HF hospitalization was evaluated with in multivariable Cox proportional hazard models. Modifying effects and interaction with darbepoetin alfa (to achieve a hemoglobin target of 13 g/dL) on GDF-15 were also assessed.
Results: Lower GDF-15 levels were negatively correlated with higher haemoglobin levels (r=0.20, p<0.001) at baseline. In univariate analyses, the risk for the primary composite outcomes steadily increased with successive tertiles of baseline GDF-15 [2nd tertile HR 2.10 [1.72–2.57], 3rd tertile HR 4.05 [3.25–4.90] relative to the lowest tertile (p<0.001). The association was attenuated, but persisted after multivariable adjustment: tertile 3 HR 1.56 [1.23–1.98] p<0.001. No interaction between baseline GDF-15 levels and darbepoetin alfa treatment was observed with regard to the primary composite outcome, despite a relatively greater decrease in GDF-15 within the treatment group (p=0.032) than in non-treated patients (p=0.039). An increase in serum GDF-15 of >15% during 6 months follow-up was associated with a higher incidence of the primary outcome in univariate (HR 1.39 [1.15–1.69] p<0.002) and multivariable (HR 1.68 [1.38–2.06] p<0.001) analysis. No interaction between treatment and change in GDF-15 on outcome was observed.
Conclusions: In patients with HF, reduced ejection fraction, and anaemia, both higher serum levels GDF-15 and an increase during follow-up, were associated with adverse outcome. Baseline GDF-15 did not identify subgroups of patients who might benefit from correction of anaemia.

P6556 | SPOTLIGHT
Usefulness of child-turcotte-pugh score for predicting death in patients with acute decompensated heart failure

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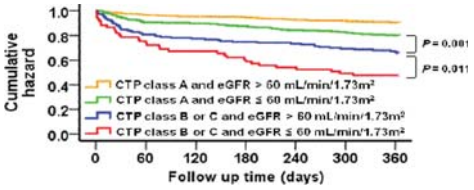
Purpose: Cholestasis has been recognized as a feature in patients with acute decompensated heart failure (ADHF). However, the development of cirrhosis secondary to HF was not evaluated. Our study aimed to evaluate the usefulness of Child-Turcotte-Pugh (CTP) scores for predicting death in patients with ADHF.
Methods: We consecutively studied 1102 patients hospitalized with ADHF. CTP scores were calculated to evaluate liver function on admission. Patients were divided into 2 groups according to CTP class A (n=895) and CTP class B or C (n=207).The endpoint was all-cause death.
Results: After 1-year follow up, 197 deaths were identified. Those who presented with CTP class B or C had greater 1-year mortality (39.6%) than patients with CTP class A (12.8%). Multivariable Cox regression analyses showed patients with CTP class B or C had a markedly increased risk of death in comparison to patients with CTP class A, with an adjusted hazard ratio of 2.0 (95% confidence interval, 1.5 to 2.8; P<0.001). After combining with renal function based on estimated glomerular filtration rate (eGFR) of either > or ≤60 mL/min/1.73m^2, the highest risk was observed when CTP class B or C and eGFR ≤60 mL/min/1.73m^2. When only one of their functions was abnormal, patients with CTP class B or C have more risk of death compared with patients with eGFR ≤60 mL/min/1.73m^2.



Kaplan-Meier curves for all-cause death

Conclusions: CTP scores significantly associated with death in patients with ADHF, and may be a stronger predictor for death than eGFR.
Acknowledgement/Funding: Key Projects in the National Science & Technology Pillar Program of the 12th Five-year Plan Period (No. 2011BAI11B02, project for heart failure), Bei

P6557 | BEDSIDE
Factors predicting mortality after transcatheter aortic valve implantation in patients with severe aortic stenosis with the corevalve prosthesis

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Background: Transcatheter aortic valve implantation (TAVI) has become the standard of care extreme surgical risk patients with symptomatic severe aortic stenosis and an alternative to open surgery in those deemed high risk. It is widely known the short and mid-term outcomes, however, is limited about long-term outcomes. The purpose of the present study was to analyze the survival and the factors predicting mortality after TAVI with the CoreValve prosthesis.
Methods: From April 2008 to December 2014, the CoreValve prosthesis (Medtronic, USA) was implanted in 441 patients with symptomatic severe aortic stenosis with deemed high risk.
Results: The mean age was 79.2±6.8 years. The logistic EuroSCORE and STS score were 17.6±11.9% and 7.4±5%, respectively. The implantation success rate was 98.7%. In-hospital mortality was 3.9%, and the combined endpoint of death, vascular complications, myocardial infarction or stroke had a rate of 13.9%. The late mortality (beyond 30 days) was 14.5%. Survival at 1, 2, 3, 4 y 5 years were 86.3%, 79.7%, 74.3% and 67.5% respectively, after a mean follow-up of 26±17 months. The NYHA functional class improved from 3.3±0.5 to 1.77±0.7 after a mean follow-up of 30.5±20 months.
The predictors of cumulative mortality were: Charlson index [HR 1.2 (95% CI 1.06–1.36), p=0.002], acute Kidney injury [HR 1.93 (95% CI 1.06–3.52), p=0.003], Stroke [HR 4.03 (95% CI 1.57–10.2), p=0.004] and vascular complications after TAVI [HR 9.26 (95% CI 3.56–24), p=0,001] and protective factors were a higher Karnofsky index [HR 0.979 (95% CI 0.965–0.992) p=0.002]
Conclusions: Survival during follow-up depends on the associated comorbidities and the complications of procedure.

PROGNOSIS III

P6558 | BEDSIDE
Prognostic impact of fat volume in men versus women with acute decompensated heart failure

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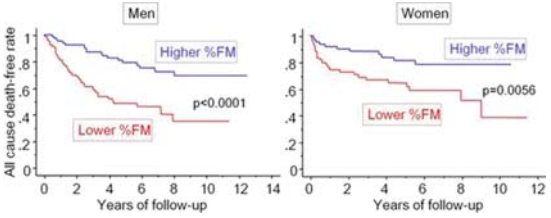
Background: Obesity paradox is well recognized in patients with heart failure, which is traditionally based on body mass index (BMI). Although fat distribution varies by gender, the prognostic impact of body composition (fat mass) has not been fully elucidated in patients admitted with acute decompensated heart failure (ADHF), relating to gender.
Methods and results: We studied 301 patients admitted with ADHF (men, n=170 and women, n=131) and discharged with survival. Fat mass (kg) is calculated by the following estimated formula: body weight (kg) – (7.38+0.02908×urinary creatinine[mg/day]). We used percentage of fat mass (%FM) normalized by their body weight. During a follow-up period of 4.2±3.2 yrs, 95 patients died. At multivariate Cox analysis, %FM but not BMI was significantly associated with the mortality independently of age, systolic blood pressure, estimated glomerular filtration rate and serum sodium level in not only men but also women. Patients with lower %FM (below the median value) had a higher risk of mortality than those with

higher %FM in men (%FM<15.2%: adjusted hazard ratio:2.1 95% CI [1.2–3.8], 49% vs 22%, p<0.0001) and women (%FM<20.8%: adjusted hazard ratio:2.4 95% CI [1.1–5.2], 36% vs 17%, p=0.0056).



Conclusion: Lower percent body fat was associated with the long-term poor outcome in both gender with ADHF, which suggested that adipose tissue is cardioprotective in the context of ADHF.

P6559 | BEDSIDE
Worsening heart failure in acute decompensated heart failure admissions: In-hospital and post discharge impact on prognosis

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Worsening heart failure (WHF) identifies patient subset with poor prognosis in acute decompensated heart failure (ADHF) admissions. However, its real impact on outcome is not fully understood.

Aims: To assess prevalence and impact of WHF on hospital, post discharge and 180-day prognosis in patients (P) admitted for NYHA class III/IV ADHF.

Methods: A total of 693 consecutive P admitted for ADHF between March 2011 and December 2014 were analyzed. WHF was defined as worsening signs or symptoms of ADHF requiring rescue IV therapy. Demographic, clinical and biochemical data were compared. In-hospital, post discharge and 180-day outcomes were reported.

Results: WHF was present in 127 P (18.3%). Although both groups did not differ in terms of gender, comorbidities and previous treatment, WHF P were younger (65 vs 71 years old; p<0.001) and had more frequently clinical evidences of hypoperfusion (35 vs 7.8%; p<0.001) at admission. P with WHF had lower blood pressure (113/70 vs 137/79 mmHg; p<0.001), left ventricular ejection fraction (34±17 vs 41±16%; p<0.001), low T3 serum level (80 vs 69%; p=0.03), higher right ventricular systolic pressure (54±23 vs 46±15 mmHg; p<0.001) and Uraemia (66±38 vs 58±32 mg/dL; p=0.02), as more frequently hyponatraemia (61 vs 47%; p<0.01). and Cholestasis (91 vs 80%; p<0.01) at admission.

In-hospital mortality (27.6 vs 5.7%; p<0.001; OR 6.3; CI95% 3–10) and early readmission (45.8 vs 19.4%; p=0.01) were higher in WHF P, but follow-up mortality and readmission rates were similar at 180-d (p=NS).

Length of stay (LOS) was longer in WHF P (15 vs 7 days; p<0.001), as prolonged LOS (>7 days) (76 vs 34%; p<0.001). In-hospital complications were more frequently observed in P with WHF, including Diuretic resistance (24 vs 5%; p<0.001) and inotropic use (59 vs 14%; p<0.001).

Whereas the combination of low T3 levels, cholestasis and hyponatraemia at admission was highly prevalent in WHF P (38 vs 0%; OR 1.6; CI95% 1.3–1.9; p<0.001), hypoperfusion at admission (HR 3.4; CI95% 1.8–6; p<0.001) and worsening renal function (HR 2.5; CI95% 1.5–4; p=0.001) were identified as independent predictors of WHF development.

We found low T3 at admission (HR 4.6; CI95% 1.3–15; p=0.01), WHF (HR 3.7; CI95% 1.8–8; p<0.001) and Diuretic resistance (HR 3.6; CI95% 1.6–8; p=0.002) as independent predictors of in-hospital mortality.

Conclusions: WHF was prevalent in P admitted for ADHF. It was associated with more complications during hospitalization for ADHF, including in-hospital mortality and early readmission. WHF risk prediction at admission might aid in decision making in ADHF setting.

P6560 | BEDSIDE
Prognosis and predictive factors for normalization of left ventricular ejection fraction in dilated cardiomyopathy

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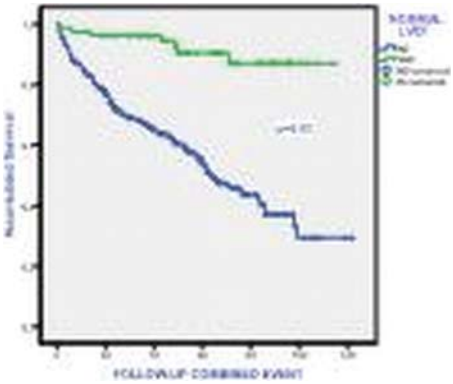
Introduction and purpose: Our aim is to know what factors are related to restoration of the left ventricular ejection fraction (LVEF) in order to early identify this subgroup of patients with a better prognosis.

Methods: A cohort of 387 consecutive outpatiens with dilated cardiomyopathy was analyzed. We considered that LVEF was normalized when it was over 55% at the end of follow-up

Results: Mean age 64.5±12.1 years, female gender 25.6%. Mean follow-up was 64.5±12.1 months. Normalization of the LVEF occurred in 20.9% (81 p) of patients.

Regarding long-term prognosis, overall mortality or heart transplantation (HTx) was 5.1% (4p) in patients with normalization of LVEF vs 30.1% (93p) in patients with impaired LVEF (p<0.001). Combined event (death, HTx or heart failure hospitalization) was 9.0% (7 p) in patients with normal LVEF vs 45% (139 p) in patients depressed LVEF.

Factors independently related to normalization of the LVEF were female gender (OR 2.22, 95% CI 1.15–4.35; p=0.018), New York Heart Association–Functional Class (NYHA-FC) at the end of the follow-up (OR 0.47, 95% CI 0.30–0.74; p=0.001), presence of atrial fibrillation (OR 0.53, 95% CI 0.28–0.99; p<0.05), number of coronary arteries with severe stenosis (OR 0.41, 95% CI 0.27–0.65; p<0.001), degree of mitral regurgitation at the end of the follow-up (OR 0.29, 95% CI 0.16–0.51; p<0.001) and time until first event –death, HTx or hospitalization for heart failure- (OR 1.02, 95% CI 1.01–1.03; p=0.020).



Conclusions: LVEF was normalized in a fifth of the population which had a significantly better prognosis.

The profile of the patient who normalized LVEF was a woman with mild NYHA-FC, without atrial fibrillation, absence of severe stenosis in coronary arteries, lack of significant mitral regurgitation and no early cardiac events.

P6561 | BEDSIDE
Age, clinical characteristics and outcomes for patients hospitalized with acute heart failure: insights from the Gulf aCute heArt failuRe rEgistry (Gulf CARE)

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Background: Acute Heart failure (HF) is a leading cause of hospitalization for adults and associated with worse outcomes worldwide.

Purpose: To evaluate age differences in clinical characteristics and outcomes among patients hospitalized with acute HF in the Middle East.

Methods: Data were collected from the Gulf aCute heArt failuRe rEgistr (Gulf CARE)which is a retrospective multicenter study from seven adjacent Gulf countries.Patients were divided into 3 groups: <65 years, 65–74 years and ≥75 years and their clinical characteristics and hospital outcomes were analyzed.Mortality and re-hospitalization rates were assessed at 3 and 12 month follow up.

Results: Among 5,005 consecutive acute HF patients. The overall mean age was 59±15 years, 60% were <65 years, 25% were 65–74 years and 15% were ≥75 years old. Increasing age was associated with higher rates of diastolic HF and Co-morbid chronic diseases.Among elderly, ischemic and hypertensive heart diseases were the most prevalent cause of acute HF (P<0.001).Elderly patients were more likely to have higher systolic blood pressure, higher troponin, first BNP or NT-Pro BNP, first mean urea and creatinine levels, and lower heart rate (P<0.001 for all).Moreover, they are more likely to have worse in-hospital course: Atrial fibrillation,stroke (P<0.04),major bleeding and systemic infection (P<0.05).The 3- and 12 months mortality and re-hospitalization rates were higher in elderly (P<0.001 for all) (Table 1). Old age was independent predictors for 3-month (age 65–74: OR 1.55; 95% CI 1.15–2.08, and age ≥75: OR 2.90; 95% CI 2.13–3.90) and 12-month mortalities (age 65–74: OR 1.68; 95% CI 1.39–2.04, and age ≥75: OR 3.03; 95% CI2.46–3.73).

Outcomes for acute HF patients

Variables (%)	<65 years	65–74 years	≥75 years	P-value
In-hospital mortality	183 (6.1)	78 (6.3)	52 (6.9)	0.8
3-month mortality	143 (5)	84 (7.4)	89 (13)	0.001
12-month mortality	360 (13)	233 (21)	220 (32)	0.001
3-month re-hospitalization	520 (20)	257 (22)	126 (27)	0.001
12-month re-hospitalization	615 (25)	337 (34)	123 (44)	0.001

Conclusions: Elderly patients hospitalized with acute HF had differential characteristics and unfavorable short- and long term outcomes. Evidently there is need for substantial research to improve outcome of acute HF among elderly patients.
Acknowledgement/Funding: Gulf CARE is an investigator-initiated study conducted under the auspices of the Gulf Heart Association and funded by Servier, Paris, France

P6562 | BEDSIDE
Troponin I by new ultrasensitive single molecule array technology: the determinants and prognostic role in chronic systolic heart failure

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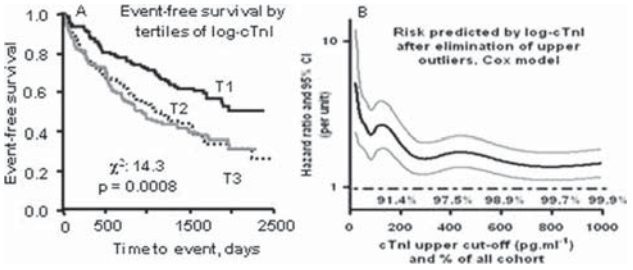
Introduction: Even small elevations of cardiac troponin I (cTnI) may have clinical significance.
Purpose: We examined determinants and prognostic value of cTnI measured by novel ultra-sensitive assay in a heart failure (HF) cohort.
Methods: Stable advanced HF patients referred for ICD/CRT or pre-transplant (Tx) work-up, underwent in-hospital assessment and were prospectively followed (combined endpoint of death/urgent Tx/LVAD). cTnI was measured by an automated digital immunoassay based on single molecule array (SIMOA) technology (LoD: 0.01 ng/L).
Results: 362 patients (84% males, NYHA 2.7±0.6, 54% coronary disease-CAD) were examined. cTnI was detected in 100% (median: 15.3 ng/L, IQR: 7.6–35.7, range: 0.4–1770, left-skewed distribution). Log-cTnI was significantly higher in males (+30%), diabetics (+24%), in patients with CAD (+24%), atrial fibrillation (+48%) and/or without ACEi/ARB therapy (+142%). Log cTnI correlated with age (r=0.17), LV mass (r=0.17), eGFR (r=–0.15), fasting glucose level (r=0.20) and HgbA1C (r=0.15). After 1086±724 days, 55% patients reached the endpoint. Log-cTnI was associated with worse outcome by K-M (figure A) and Cox analyses (HR 1.45, 1.2–1.8, p=0.0008). The association was considerably stronger in the lower range (<200 ng/L) of cTnI distribution (Figure B). In the untransformed data, cTnI was associated with outcome only after removal of 2.5% of outlying values (>400 ng/L) that likely reflect silent IM or myocarditis.



Conclusions: cTnI predicts long-term outcomes in stable HF patients, particularly in the low-range of values, most likely reflecting pathophysiological process distinct from high-range elevations. Low-range cTnI elevations are associated with aging, CAD, gender, diabetes, renal dysfunction, atrial fibrillation and lack of ACEi/ARB therapy.
Acknowledgement/Funding: Grants MSMT KONTAKTII-LH12052, IGA NT14050-3/2013 and NT14250-3/2013

P6563 | BEDSIDE
Different prognostic factors according to left ventricular systolic function in patients with acute myocardial infarction

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Background: Although there are many differences in baseline clinical characteristics according to left ventricular (LV) systolic function in patients with acute myocardial infarction (AMI), there has been lack of studies primarily focusing on the difference of prognostic factors in patients with AMI according to their LV systolic function.
Purpose: This study was performed to identify different prognostic factors in patients with AMI according to their baseline LV systolic function.
Methods: Total 12,988 patients with AMI were enrolled into a nationwide registry database study. Major adverse cardiovascular events (MACE) within 12 months of AMI including death, nonfatal MI and revascularization were assessed. Patients were stratified into 2 groups according to their LV ejection fraction (LVEF): LVEF <40% vs ≥40%, and prognostic factors for MACE were identified in each group.
Results: The 1,962 patients (15.1%) who had LVEF <40% were older and had more un-favorable cardiovascular risk factors than those with LVEF ≥40%. The rates of MACE in patients with LVEF <40% was higher than those with LVEF ≥40% (26.8% vs 11.4%, P<0.001). Independent predictors for 12-month MACE in patients with LVEF ≥40% were history of previous myocardial infarction, high Killip stage, three vessel disease, and lower renal function, which are already known risk factors. Otherwise, diabetes mellitus (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.12–2.11; P=0.008) and the nonuse of renninangiotensin system (RAS) blockers (HR, 0.67; 95% CI, 0.47–0.97; P=0.034)were independent risk factors for 12-month MACE in patients with LVEF <40%.
Conclusion: Prognostic factors determining 12-month MACE following AMI are different according to their LV systolic function. Management following AMI should be tailored according to LVEF.

P6564 | BENCH
Characteristics and outcome of patients admitted to hospital with heart failure according to the severity of peripheral oedema in the national (England & Wales) heart failure audit

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Introduction: The main presentations of heart failure requiring admission to hospital are breathlessness (pulmonary oedema) and peripheral oedema; many patients present with a mixed picture. Most studies of "acute" heart failure focus on breathlessness but peripheral oedema might be the more important presentation. We have here tested the hypothesis that severity of oedema is associated with length of hospital stay, mortality during index admission and after discharge.
Methods: Data was collected from April 2007 to March 2013 in more than 90% of hospitals in England & Wales for patients with a primary death or discharge diagnosis of heart failure. For this analysis, patients were grouped into "no", "mild", "moderate" and "severe" peripheral oedema. Patients' characteristics and mortality during the index hospital admission for up to three years after discharge were reported.
Results: Of 136,790 patients with a confirmed diagnosis of heart failure, peripheral oedema on admission was absent in 24%, mild in 25%, moderate in 32% and severe in 18%. Patients without oedema were younger (median age 77 years) as compared to mild, moderate and severe oedema (80, 80, and 79 years respectively (P- <0.001). Patients who had no oedema were more likely to have LVSD (66%) as compared to other groups (60%, 56% and 54% respectively) (P-<0.001) and had shorter length of stay during the index admission (6 (IQR 3–13) days compared to 7 (IQR 3–14), 9 (IQR 5–17) and 12 (6–21) days respectively) (P- <0.001). Index admission mortality was 7%, 8%, 10% and 16% (P-<0.001) respectively and at final censorship 39%, 46%, 52% and 59% (median follow-up 344 (IQR 94–766) days). The hazard ratio of death was 1.79 in patients with severe (P-<0.001), 1.49 with moderate (P-<0.001) and 1.23 (P-<0.001) with mild oedema when compared with those patients who did not have oedema.
Conclusion: Fewer patients with severe peripheral oedema had LVSD compared to those presenting with mild, moderate or no oedema. Mortality during index admission and after discharge increased with severity of peripheral oedema.

P6565 | BEDSIDE
Determinants of shock and mortality in Takotsubo cardiomyopathy: a cohort study

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Introduction: Takotsubo cardiomyopathy (TTC) is a form of catecholamine-induced myocardial inflammation. Once considered a rarity, TTC is now recognised as accounting for up to 10% of "heart attacks" in women, with associated in-hospital mortality of approximately 3%, largely through development of cardiogenic shock with preceding hypotension. We have shown that hypotension in TTC is multifactorial, encompassing vasodilatation as well as negative inotropy.1 We now sought to identify both clinical and physiological determinants of (1) shock, and (2) in-hospital death associated with shock among TTC patients.
Methods: We evaluated 208 consecutive TTC patients (94% female; median age of 67 years old). Of these, 29 (13.9%) developed shock while 9 subsequently died. Apart from demographics, we considered extent of endogenous catechol release, inflammatory activation (CRP, NT-proBNP) and haemodynamics as possible modulators of outcomes utilizing univariate followed by multivariate analyses.

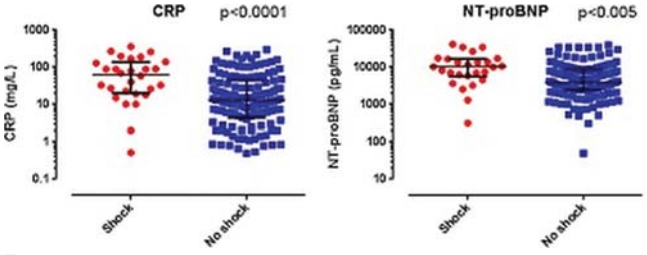

Figure 1

Results: (A) Determinants of shock: On univariate analyses, both CRP and NT-proBNP release were significantly higher in patients developed shock (Figure 1) with CRP remained a significant ($p<0.05$) multivariate correlate. (B) Determinants of mortality: Patients who died were significantly older than those who survived shock (76±14 vs 63±17, $p<0.05$) and were more likely to have received treatment with intravenous catechol (78% vs 45%, $p>0.05$): the latter was a multivariate determinant of mortality ($p<0.05$).
Conclusion: These data suggest that clinical measures of extensive inflammatory activation in TTC predicts shock, and emphasize that further administration of catechols in such patients may be counter-productive.

P6566 | BEDSIDE
Atrial fibrillation in acute heart failure: A secondary analysis of the ALARM-HF registry

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Background: Atrial fibrillation (AFib) has been associated with worse outcome in heart failure patients, but hitherto evidence remains inconclusive. We assessed the clinical characteristics and short-term outcome in AHF patients presented with AFib in a large cohort.
Methods: The Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) was conducted during 2006–2007 and included a total of 4953 patients hospitalized for AHF in 9 countries in Europe, Latin America and Australia. We compared clinical characteristics and in-hospital mortality between patients with AFib at presentation and those in sinus rhythm (SR).
Results: Baseline AFib was present in 2184 patients (44%), including 982 with paroxysmal AFib and 1044 with permanent AFib. Compared to patients in SR, those with AFib were significantly older, more frequently female and had more frequently NYHA class III or IV symptoms (all $p<0.001$) along with higher prevalence of non-cardiovascular comorbidities including lung disease, chronic renal disease, anemia and depression (all $p<0.001$; for anemia, $p=0.030$). In-hospital mortality was higher in AFib patients [crude HR: 0.79, 95% CI: (0.67, 0.95), Figure]. This difference was eliminated after adjustment for several baseline variables [adjusted HR: 0.87, 95% CI: (0.57, 1.32), Figure]. Similarly, subgroup analyses by baseline characteristics showed no significant differences in mortality after adjustment.

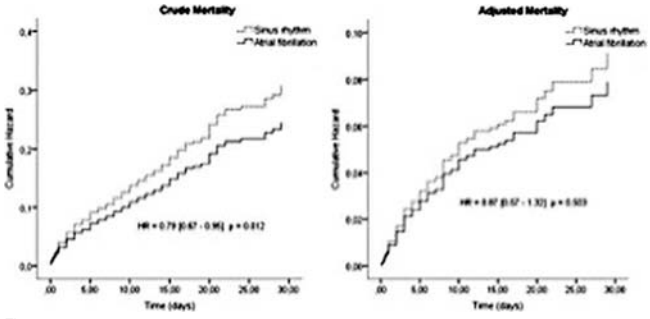

Figure 1

Conclusions: Hospitalized AHF patients with AFib at presentation represent a high-risk group with increased in-hospital mortality. This worse short-term outcome seems to be related to their constellation of risk factors and comorbidities and not to the arrhythmia itself.

P6567 | BEDSIDE
Echo and natriuretic peptide guided therapy in chronic systolic heart failure: a propensity score analysis from an observational study of 1,137 patients

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Background: Natriuretic peptides (NPs) and echo-Doppler are not only useful tools in acute heart failure (HF), their role may be also valuable in the management of stable patients during long-term follow-up, since they can actually contribute to a more complete understanding of the pathophysiology of the disease. Therefore, we believe that NPs and Doppler echocardiography, when utilized serially in an integrative and personalized manner, can be useful in monitoring ambulatory patients that are high risk for exacerbation with a significant benefit to the clinical outcome. The complimentarily of methodologies can overweight their intrinsic limitations, with crucial benefits for the patient.
Aim: The purpose of our study was to investigate the role of Doppler echocardiography and NPs assessment during follow-up visits in ambulatory patients with chronic HF.
Materials and methods: This was a multicenter, retrospective, observational study that involved 1,137 consecutive outpatients (total cohort) previously hospitalized for HF. Group A (Echo-NP-guided group) consisted of 570 patients (mean EF% 0.30±0.8), whose management was guided according to the presence of echo-Doppler signs of elevated left ventricular filling pressure and NPs serum levels; whereas group B (clinically-guided group) consisted of 567 pts (mean EF% 0.33±0.9), whose management was based on clinical judgment, and echocardiography was repeated only if symptoms changed. Propensity score matching was used to match pairs based on treatment strategy (matched cohort).
Results: The median follow-up duration was 40 months. During follow-up, after propensity matching, worsening of renal function ($\geq$0.3 mg/dL increase in serum creatinine) was observed in 12% of group A and in 23% of group B ($p=0.001$). The dose of loop diuretics did not change in Group A, while it increased by 13% in group B ($p<0.0001$). Survival analyses showed a lower incidence of death (HR 0.59, 95% CI: 0.37–0.95, $p=0.031$), and death or worsening renal function (HR 0.68, 95% CI 0.48–0.98, $p=0.036$) in group A compared to group B.
Conclusion: The results of this observational study suggest that patient's management can be effectively guided on the basis of Doppler echocardiography and NPs. The improvement in clinical outcome of stable patients with systolic HF who underwent follow-up evaluations that included echocardiography and assessment NPs can be attributed to prevention of clinically overt pulmonary congestion, refractoriness to loop diuretics and a better titration of cardiovascular drugs.

PROGNOSIS V

P6568 | BEDSIDE
Outcomes prediction in heart failure by measures of heart rate variability dynamics

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Purpose: Chronic Heart Failure (CHF) patients in New York Heart Association (NYHA) Class 1 or 2 for symptoms with a left ventricular ejection fraction of 35% or less and electrocardiogram evidence of asynchronous contraction of the heart may now receive treatment with Cardiac Resynchronisation Therapy (CRT) with a defibrillator (CRT-D) in order to improve quality of life, prognosis and symptoms. </SPAN>Until recently, only patients in NYHA Class 3 or 4 received this treatment. CRT-D has higher device-related morbidity than CRT alone, has a finite benefit scope with only a subset of patients truly yielding benefit, and is more costly. With the use of CRT-D set to increase, identification of patients with a low risk of sudden cardiac death (SCD) is important but remains a challenge. Heart rate variability (HRV) is an independent predictor of mortality in CHF patients. The authors investigated applying a novel mathematical algorithm to CHF patients whose long-term follow up data and HRV are known.
Methods: The R-R intervals extracted from 24 hour ambulatory ECGs recorded as part of the UK-HEART trial were reanalysed. For each subject the differential entropy H (calculated over 24 hour HRV sequences) and D coefficient (derived from the relationship between the short ($\alpha1$) and medium term ($\alpha2$) fractal dimensions determined by detrended fluctuation analysis) were recorded to investigate two novel metrics of HRV. The impact of H & D on survival was evaluated by fitting a Cox model. The data set comprised 397 CHF patients in NYHA Class 1 to 3 for symptoms.
Results: Both H and D have strong association with survival ($p<0.0001$). Spearman's test of rank correlation showed a significant negative correlation between the two quantities, suggesting they are measuring different aspects of HRV dynamics. The bootstrap estimate of the area under the receiver operating characteristic curve (a measure of discrimination accuracy) was 0.69. A prognostic index was derived which allowed patient stratification into high and low risk groups.
Conclusions: The parameters derived from differential entropy and fractal analysis of HRV are strongly associated with survival in CHF patients. Previously, only HRV characterised by variance and low frequency spectral power exhibited a weak association. This novel approach allows a low-risk subgroup of patients with CHF to be identified with high specificity, providing better predictions of death compared to currently available methods, allowing expensive and risk-inducing invasive device therapies to be targeted more appropriately.

P6569 | BENCH

Increase in ultra-sensitive troponin I is associated with poor prognosis in patients with acute heart failure

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Background: Novel ultra-sensitive assays for cardiac troponins (Tn) allow to reliably detect very low cardiac Tn concentrations in the blood reflective of minor myocardial damage. We evaluated whether such tests may provide practically useful information for the management of patients with acute heart failure (AHF).
Methods: For this study, we prospectively recruited patients hospitalized with AHF who on admission had cardiac TnI level assessed in our hospital laboratory below 3-times of the upper reference limit (URL, ie <0.21 ng/mL). Ultra-sensitive cardiac TnI (us-TnI) analysis was based on new diagnostic platform - immunoassay for plasma cardiac TnI by Single Molecule Counting technology (Singulex, Alameda, CA). The blood samples were taken on admission, after 24, 48 hours and on discharge. A significant rise in us-TnI was defined as at least one subsequent us-TnI value 20% greater than baseline.
Results: We analyzed 136 patients with AHF (age: 65±13 years, 78% men, 22% AHF de novo). The median us-TnI levels with the percentage above the usTnI URL (ie >10.19ng/mL) were: on admission: 13.13ng/mL (59%), 24-h: 13,16ng/mL (60%), 48-h: 13,27ng/mL (55%), on discharge: 11,02ng/mL (51%), respectively. Among 96 patients who presented on admission with negative TnI measured with standard methodology in our laboratory 42% had usTnI above URL. These patients had higher creatinine level, more often coronary artery disease, chronic kidney disease and diabetes mellitus ($p<0.01$ in all comparisons). During hospital stay, significant rise in us-TnI was detected in 40% of patients. These patients were older and had more often diabetes mellitus, atrial fibrillation ($p<0.05$ in all comparisons). During 1-year follow-up there were 36 (26%) cardiovascular deaths. Baseline level of usTnI did not predict survival (log-rank test p=0.7), however, 1 -year cardiovascular mortality was significantly higher in those who developed us-TnI rise (39% vs 16%, p=0.024). Interestingly, in the multivariable models us-TnI rise either at 24 or 48 hours (HR: 2.7 [1.1–6.8], p=0.04) and at 24 or 48 or on discharge (HR: 3.1 [1.0–9.5], p=0.05) were associated with higher mortality.
Conclusion: In AHF patients, assessment of cardiac troponin I with the ultrasensitive, provides important clinical message including prognostic information. This test may be a useful tool to identify high risk patients whom might be appropriate for more aggressive management.
Acknowledgement/Funding: This work has been supported by a grant from National Centre of Science (Poland) no NN 519 654340//6543/B/T02/2011/40

P6570 | BEDSIDE

Sleep-disordered breathing are associated with impaired cardiac sympathetic innervation and incrementally predict prognosis in heart failure patients

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Background: Unfavorable effects of sleep-disordered breathing (SDB) in heart failure (HF) are mainly mediated by impaired sympathetic activity. However, few data are available on SDB and cardiac adrenergic impairment evaluated at myocardial level.
Objectives: Aim of the present study was to assess the relationship between SDB, cardiac sympathetic innervation and prognosis in HF patients.
Methods: Ninety-four patients (66.1±9.8 years) with systolic HF (median left ventricular ejection fraction 32±7%) underwent nocturnal cardiorespiratory monitoring to assess presence and type of SDB by Apnea/Hypopnea Index (AHI), and 123I-MIBG myocardial scintigraphy to calculate heart-to-mediastinum (H/M) ratios and 123I-MIBG washout rate. Patients were prospectively followed for 29±18 months for the combined endpoint of cardiovascular death and HF hospitalization.
Results: Of 94 patients, 72 (77%) showed SDB and, compared to non-SDB, significantly reduced early (1.67±0.22 vs 1.77±0.13; p=0.019) and late H/M ratio (1.50±0.22 vs 1.61±0.23; p=0.038). At multiple linear regression analysis, early and late H/M remained independent predictors of AHI ($\beta=-0.749$; $p<0.001$; $\beta=-0.830$; p=0.001, respectively). Similarly, AHI was the only predictor of early ($\beta=-0.643$; $p<0.001$) and late ($\beta=-0.453$; $p<0.002$) H/M ratio. Patients with AHI above the median showed significantly higher event rates and worse survival compared to patients with AHI below the median (35% vs 9%, respectively; p=0.003). Similarly, patients with moderate-severe disorder showed significantly increased incidence of the combined endpoint and worse survival compared to patients with mild or no disorder (35% vs 11.7%; p=0.007). Adding SDB variables to the already known prognostic role of 123I-MIBG imaging, we observed an incremental prognostic discrimination with the worst survival in patients with both SDB and H/M impairment.
Conclusions: Patients with systolic HF and SDB show more impaired cardiac adrenergic innervation and more adverse prognosis compared to HF patients without SDB.

P6571 | BEDSIDE

Multi-parametric cardiac magnetic resonance for prediction of cardiac complications in thalassemia intermedia: a prospective multicenter study

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Background: Cardiovascular Magnetic Resonance (CMR) has an established role in managing and predicting prognosis of patients with Thalassemia Major (TM). Thalassemia Intermedia (TI) is a milder variant of beta-thalassemia showing a different clinical and prognostic profile; pulmonary hypertension (PH) is a more common complication in TI patients. We prospectively determined the predictive value of CMR parameters, including measurement of right ventricular mass, for cardiac complications in TI.
Methods: We considered 342 TI patients enrolled in the Myocardial Iron Overload in Thalassemia network; about half of them (178/302, 58.9%) were transfusion-dependent. Myocardial and liver iron overload were measured by T2* multiecho technique. Atrial dimensions, left and right ventricular mass and systolic function were quantified by cine images. Late gadolinium enhancement (LGE) images were acquired to detect myocardial fibrosis.
Results: Twenty-three patients were excluded because a cardiac complication was present at the time of first CMR, so we prospectively followed 319 patients.
All 319 patients were white, with a mean age at time of their first scan of 38.02±11.69 years and 165 (51.7%) of them were females.
Mean follow-up time was 52.24±24.87 months (median 54.64 months).
Cardiac events were recorded in 22 patients (6.9%): heart failure (HF) in 1 patient, arrhythmias in 12 patients, pulmonary hypertension (PH) in 7 patients and myocardial infarction (MI) in 2 patients.
Due to the low number of events, only arrhythmias, PH and cardiac complications globally considered were taken as cardiac outcomes for univariate and multivariate analysis.
In the multivariate analysis RV hypertrophy was the only independent predictive factor for arrhythmias (HR=33.83, 95% CI: 6.07–188.74, $P<0.0001$) and PH (HR=73.33, 95% CI: 10.00–537.57, $P<0.0001$). When cardiac complications were considered all together, RV hypertrophy (HR=24.12, 95% CI: 5.09–114.12, $P<0.0001$) and myocardial fibrosis by LGE (HR=6.59, 95% CI: 1.33–32.67, P=0.021) were independent prognostic factors in the multivariate analysis
Conclusions: For the first time we studied the prognostic value of right ventricular mass as part of multiparametric CMR imaging in a population of TI patients. RV hypertrophy identified patients at high risk for arrhythmias and PH. Both RV hypertrophy and fibrosis detected by LGE were independent predictive factor for cardiac complications. Measurement of RV mass should be part of the multiparametric CMR study of patient with thalassemia intermedia.

P6572 | BEDSIDE

Role of endogenous hydrogen sulfide synthesis enzymes gene variants in the 5-year prognosis of patients with ischemic cardiomyopathy related chronic heart failure in Chinese Han population

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Background: Endogenous hydrogen sulfide (H2S) was considered as the third gaseous transmitter and exert cardio-protective actions in ischemic cardiomyopathy (ICM) and chronic heart failure (CHF).
Purpose: To investigate the relationship between gene variants in endogenous H2S synthesis enzymes and the prognosis of ICM related CHF.
Methods: A total of 944 patients with CHF were genotyped for 7 gene variants involved in the endogenous synthesis of H2S, and the correlation between SNPs and the prognosis and severity of CHF was analyzed.
Results: During a median follow-up period of 65 months, 332 (35.17%) all-cause deaths occurred, including 123 (37.05%) patients experienced SCD, whereas 209 (62.95%) cases had NSCD (non-SCD). The C allele of rs2490281 on GOT-1 gene, which encodes the cytoplasmic cysteine aminotransferase (CAT), was associated with greater risk of all-cause death and NSCD after adjusting for other risk factors (HR 1.608, 95% CI 1.155–2.239, P=0.005; and HR 1.778,95% CI 1.181–2.676,P=0.006, respectively). In addition, multivariate regression analysis revealed that rs2490281 was also associated with increased risk of a lower LVEF (LVEF≤35%). (OR 1.783, 95% CI 1.099–2.890, P=0.019).

Figure 1

Conclusions: The rs2490281 in GOT-1 gene may serve as an independent predictor of all-cause death in ICM related CHF patients in Chinese Han population.

P6573 | BEDSIDE
The role of GDF-15, a marker of fibrosis, in cardiogenic shock

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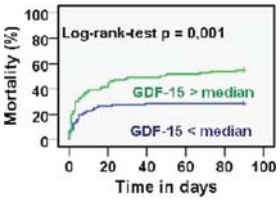
Purpose: To investigate circulating levels of Growth-differentiation factor 15 (GDF-15) in cardiogenic shock (CS) and their associations with etiology, markers of myocardial injury and all-cause mortality.
Methods: GDF-15, TnT and NT-proBNP was determined at baseline in 178 patients with CS of various etiologies in the prospective European multi-center CardShock study. Differences in GDF-15 levels between groups of CS etiology [acute coronary syndrome (ACS) (n=143) and non-ACS (n=35)] were assessed and the influence of GDF-15 on 90-day mortality.
Results: Mean age was 67 years, 26% were women and 42% of the patients died. Median levels of GDF-15 in the study population was 9577 pg/ml (interquartile range (IQR) 4502 - 19115), with no significant difference between ACS and non-ACS groups (9647 pg/ml [IQR 4497–18232] vs. 9171 pg/ml [IQR 4617–29825]; p=1.0). The correlation of GDF-15 with hsTnT (rs 0.137, p=0.07) or NT-proBNP (rs 0.37, p<0.001) was moderate at most.
Mortality at 90 days was higher in patients with GDF-15 levels above median (all 55% vs. 29%, p<0.001; ACS group 59% vs. 31%, p=0.001; non-ACS group 41% vs. 17%, p=0.11).
In univariate analysis GDF-15 above median was significantly associated with 90-day mortality (OR 3.0; 95% CI 1.6–5.7; p<0.001). On a multivariable analysis GDF-15 above median still seemed to be associated with a doubling of 90-day mortality risk (OR 2.4; 95% CI 0.9–6.3; p=0.07).



Conclusions: GDF-15 levels are markedly elevated on admission in CS of both ACS and non-ACS etiology. There is no relevant correlation between levels of GDF-15 and TnT, a measure of myocardial injury. GDF-15 levels above median are associated with increased mortality in CS, but the clinical utility of GDF-15 in this population with very high overall mortality remains to be determined.

P6574 | BEDSIDE
The use of different methods for the selection of patients with non-ischemic cardiomyopathy for cardiac resynchronization therapy

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Aim: The aim of the study was to use various methods of selection of patients for cardiac resynchronization therapy (CRT) and to evaluate prospects of method implementation in clinical practice to increase treatment efficacy.
Materials and methods: The study comprised a total of 180 patients aged 32 to 75 years (55±12 years) with dilated cardiomyopathy (DCM), NYHA functional class III heart failure, left ventricular (LV) ejection fraction (EF) of 30.1±3.8%, 6-min walk test distance of 290.5±64.3 m, end diastolic volume (EDV) of 220.7±50.9 mL, intraventricular and interventricular dyssynchrony of >120 ms. At the selection stage, patients were divided into three groups: group 1 (n=50) that received assessment of myocardial metabolism defect (MMD) by radionuclide methods, group 2 (n=70) that received assessment of tricuspid annular systolic velocity (TASV), and control group.
Results: One-year follow-up study showed that 141 patients (78.3%) clinically responded to CRT; 39 patients (21.7%) did not respond to CRT. Evaluation of the selection methods demonstrated that 6 (12%), 17 (24,3%), and 20 (33,3%) patients did not respond to CRT in group 1, 2, and 3, respectivley. Group 1 included 44 responders (88%) whose MMD was <15% prior to CRT; if initial MMD was >15%, patients did not respond to CRT. Group 2 included 53 responders (75,7%) whose TASV was >10 cm/s (12.5±2.1 cm/s) (p=0.0001).
Conclusions: (1) Preserved myocardial metabolism (LV MMD <15%) is a predictor of efficacious CRT in DCM patients. (2) Tricuspid annular systolic velocity is an independent predictor of response to CRT; TASV enables to identify CRT responders with sensitivity of 85% and specificity of 83% at the selection stage. (3) For selection of patients for CRT, the administration of all presented methods is rational in order to increase treatment efficacy.

P6575 | BEDSIDE
Prognostic predictors in a population-based cohort study of outpatients across different heart failure phenotypes

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Background: Although heart failure (HF) is a syndrome characterized by important variability in clinical findings and response to treatment, there is paucity of information on the different predictive factors and their prognostic impact across HF phenotypes.
Purpose: To evaluate and compare the predictive power of prognostic factors in a population-based cohort study of outpatients with different HF phenotypes (LVEF≤40% - HFrEF, LVEF 41–49% - HFbEF, LVEF ≥50% - HFpEF).
Methods: From November 2009 to October 2013, we retrospectively considered all consecutive HF outpatients, with available LVEF, enrolled in the Cardiovascular Observatory. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.
Results: A total of 2424 patients (57% males; mean age 78±8; NYHA 3–4 20%) were considered. Of these, 1457 (60%) had HFpEF, 358 (15%) HFbEF, 609 (25%) HFrEF. At a follow-up of 28±14 months, 502 patient were dead (21%), 168 (28%) among HFrEF cases, 60 (17%) among HFbEF and 273 (19%) among HFpEF. The overall high mean age and frequent non cardiac comorbidities (median number 2) ran similarly across different HF phenotypes. In the overall population, the multivariable model included age (HR 2.41; p=0,003), male sex (HR1.63; p<0,001), NYHA class III-IV (HR 1.52; p=0.009), systolic blood pressure (SBP) <110 mmHg (HR 2.05; p<0,001), hyponatremia (HR 1.68; p=0,026), anemia (HR 1.43; p=0.001), diabetes mellitus (HR 1.46; p=0,015), betablockers (HR 0.76; p=0,006), ACEi/ARBs (HR 0.76;p=0,009). The multivariate model performed differently across the three HF phenotypes. Among predictors, SBP <110 mmHg (HR 2.45; p=0,05) and betablockers (HR 0.67; p=0.036) were significant only in HFrEF, whereas anemia (HR 1.42; p=0.027), chronic obstructive pulmonary disease (HR 1.41; p=0.028), moderate-to-severe aortic valve disease (HR 1.45; p=0.048) and ACEi/ARBs (HR 0.68; p=0.014) were significant only in HF-pEF.
Conclusions: In our cohort study of outpatients characterized by advanced age and frequent non cardiac comorbidities, covariates generally included in available HF risk models showed strikingly different predictive power according to HF phenotypes These data suggest that HF risk models could be effectively applied in real world patients across different HF phenotypes.

P6576 | BEDSIDE
Severe hyponatremia and in-hospital deterioration of sodium is associated with increased mortality in patients admitted with acute heart failure

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Introduction: Hyponatremia predicts poor prognosis in patients with acute heart failure (AHF). However, the association of severity of hyponatremia and changes of sodium (Na) level with long-term outcome has not been delineated.
Methods: Patients hospitalized for AHF composed this registry. Data of biochemistry and echocardiographic parameters were collected. Hyponatremia was defined as serum Na level <135 mEq/L. Linking to National Death Registry identified the clinical outcomes of all-cause mortality and cardiac death, with a follow duration of up to 4 years.
Results: Among 2556 patients, 360 patients (78.04±12.24 year-old, 63.6% men) had on-admission hyponatremia. The hyponatremic subjects were older, with more co-morbidities of diabetes and stroke. Along the hospitalization, 1051 subjects had decreases of Na level at discharge. The on-admission Na levels were

inversely associated with in-hospital, 90-day and 4-year all-cause death. There were incremental impacts of the Na decreases with on-admission sodium level on clinical outcomes, while subjects with hyponatremia at admission and decreasing Na level during hospitalization would have the highest mortality rate. (Figure, p<0.001) After accounting for age, sex, medications, hematocrit, and renal function, subjects with hyponatremia at admission and decreasing Na level during hospitalization have an increased risk of death (HR 2.222, 95% CI 1.292–3.283) with reference to those with normonatremia at admission and on-treatment non-dropping Na level.

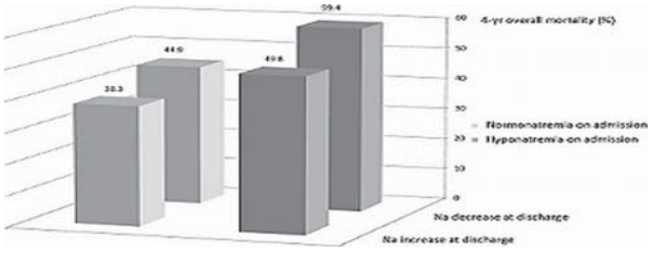

Figure 1

Conclusion: The on-admission hyponatremia is an independent predictor of in-hospital, short-term, and long-term mortality in hospitalized patients of AHF. Combined the on-admission hyponatremia with the changes of Na level during hospitalization further improved the risk classification of AHF.

P6577 | BEDSIDE

Comparison of usefulness of coronary SYNTAX score in patients with prior heart failure with preserved ejection fraction versus with reduced ejection fraction: a sub-analysis of shinano registry

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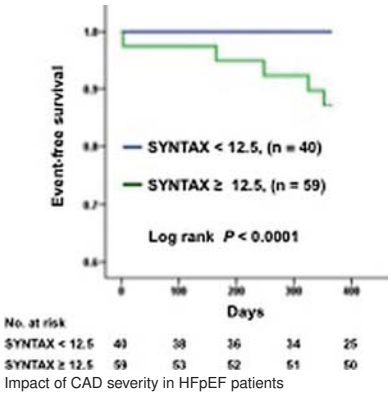
Background: Coronary artery disease (CAD) is common in patients with heart failure (HF), but little is known about the prognostic significance of coronary lesion complexity in patients with HF with preserved ejection fraction (HFpEF) versus those with reduced ejection fraction (HFrEF)
Purpose: To investigate whether coronary SYNTAX score, which is a coronary lesion complexity scoring system, could improve risk stratification in HF patients with CAD, and to compare the usefulness of SYNTAX score in patients with HFpEF vs. HFrEF.
Methods: We enrolled 200 patients (age, 73±11 years) with prior HF who underwent percutaneous coronary intervention. Patients were tracked prospectively for 12 months. The study endpoint was the composite of major adverse cardiovascular events (MACE) including all-cause death, myocardial infarction, and stroke.
Results: Adverse events were observed in 33 patients (16.5%). Ninety-nine patients were HFpEF (EF ≥50%) and 101 patients were HFrEF (EF <50%). In Kaplan-Meier analysis, patients with high SYNTAX scores (≥12.5) showed worse prognoses than those with low SYNTAX scores (<12.5) (27.2% vs. 7.4%, P<0.0001). Multivariate Cox proportional hazards analyses revealed that SYNTAX score was significantly associated with MACE (hazard ratio: 1.08, 95% confidence interval: 1.04 to 1.11; P<0.01). Furthermore, HFpEF patients with high SYNTAX scores showed worse prognoses than those with low SYNTAX scores (30.0% vs. 0%, P<0.0001), whereas HFrEF patients did not show a similar correlation with prognoses (25.0% vs. 16.3%, P=0.30).



Impact of CAD severity in HFpEF patients

Conclusions: In prior HF patients with CAD, high SYNTAX scores predicted a high incidence of MACE. SYNTAX score might be a more useful parameter to improve risk stratification in patients with HFpEF than those with HFrEF.

PROGNOSIS IV

P6578

P6579 | BEDSIDE

Prognostic value of NT-proBNP in heart failure with preserved versus reduced ejection fraction (From the Korean Heart Failure [KorHF] registry)

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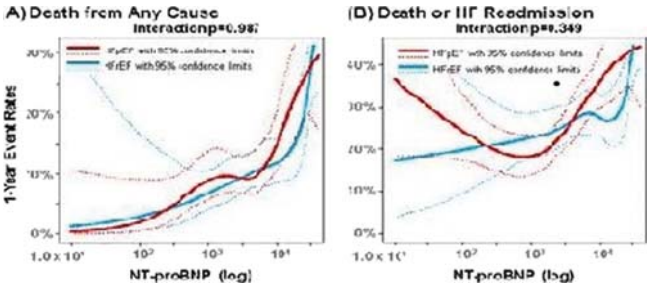
Introduction: Although plasma level of NT-proBNP is a reliable prognostic factor in patients with heart failure (HF), it is still unclear how differently it predicts adverse outcomes in HF with preserved ejection fraction (HFpEF) versus HF with reduced ejection fraction (HFrEF).
Purpose: To identify the prognostic value of N-terminal–pro-brain natriuretic peptide (NT-proBNP) in HFpEF versus HFrEF.
Methods: From the Korean Heart Failure (KorHF) registry, a prospective multicenter cohort for consecutive patients who were hospitalized for acute HF syndrome, those with valid NT-proBNP and left ventricular ejection fraction (LVEF) measurements were extracted. Patients with LVEF ≥40% were categorized as the HFpEF (N=867), and those with ≤40% as the HFrEF groups (N=1,081).
Results: Patients with HFpEF had significantly lower NT-proBNP level than those



NT-proBNP levels and clinical outcomes

with HFrEF (3,312 pg/mL vs. 5,644 pg/mL, p<0.001). Event-free survival did not differ between the two groups either in terms of death from any cause (88.3% vs. 86.4%; p=0.151) or the composite of death or HF readmission at 1 year (72.6% vs. 71.2%; p=0.375). Increasing levels of NT-proBNP was significantly associated with poor outcomes. However, the relationship was not different among the HFpEF and HFrEF groups (interaction p=0.987 for all-cause death; p=0.349 for the composite of all-cause death or HF hospitalization).
Conclusion: Plasma level of NT-proBNP is the most powerful prognostic factor in both HFpEF and HFrEF. Although patients with HFpEF have lower NT-proBNP levels, the prognosis of a patient with HFpEF expected from a given NT-proBNP level is similar with his/her counterpart with HFrEF.

P6580 | BEDSIDE
Which patient with left ventricular ejection fraction ≤40% and when die during 3 years after discharge home from acute myocardial infarction - analysis of joined PL-ACS and AMI-PL registries

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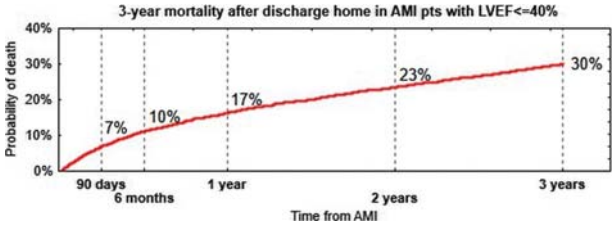
Patients with left ventricle ejection fraction (LVEF) ≤40% require close monitoring after discharge from AMI. Therefore we assessed which patient with LVEF ≤40% and when die during 3 years after discharge from AMI.
Methods: PL-ACS is a clinical registry, however it does not cover all hospitals. AMI-PL is a nationwide database of AMI, derived from the only, public, obligatory, health insurer in Poland, and provide data on hospitalizations, procedures, and deaths. We combined PL-ACS and AMI-PL data for 4461 survivors from AMI discharged home in 2009 with LVEF ≤40%.
Results: Patients with LVEF ≤40% comprised 26% of all discharged patients. Of them 87% were treated invasively. 3-year mortality after discharge was 30% and one-third of deaths were during first 6 months following AMI (figure). Predictors of 3-year mortality are presented in the table.

Table 1

	Relative risk (95% CI)		Relative risk (95% CI)
Age (per 5 years more)	1.25 (1.21–1.29)	Peripheral artery disease	1.46 (1.19–1.78)
LVEF (per 5% less)	1.23 (1.18–1.28)	History of stroke	1.47 (1.19–1.82)
Invasive treatment	0.68 (0.58–0.8)	In-hospital cardiac arrest	1.88 (1.28–2.76)
History of renal failure	1.43 (1.22–1.69)	Chronic pulmonary disease	1.40 (1.14–1.72)
NYHA class (per 1 more)	1.20 (1.10–1.32)	STEMI (vs. NSTEMI)	0.83 (0.74–0.94)
Diabetes mellitus	1.28 (1.13–1.46)	Prior CABG	0.65 (0.47–0.90)
Current smoking	1.34 (1.15–1.56)	CABG	0.57 (0.37–0.88)



Conclusion: Patients discharged home after AMI with reduced LVEF ≤40% are at high risk of death especially during first 6 months.

P6581 | BEDSIDE
Right ventricle deformation, systolic function and pressure overload which one the key prognosticator in outpatients with systolic heart failure

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Background: Right ventricle (RV) geometry and function, along with the pulmonary pressure are major predictors of the outcome in outpatients with systolic heart failure (SHF).
Aim: To evaluate which one the key prognosticator in outpatients with SHF: the RV deformation, systolic function or pressure overload.
Population and methods: 143 outpatients with SHF followed-up in a Heart failure unit, age 68.0+12.6 years old, NYHA class III (34.3%) and median Nt-ProBNP 1871pg/ml. RV systolic function was characterized by the TAPSE and RV fractional area change (RVFAC); deformation with the RV global strain (RVGS) by 2D-Strain (Vivid 7-EcoPAc 10); tricuspid ring TDI S wave (STr) and the pulmonary pressure with the estimated systolic pulmonary artery pressure (sPAP). All parameters were categorized in quartiles, and the worst used in a Cox survival Model.
Results: (1) the 3-year death rate was 36.4%. (2) Death was significantly associated with greater sPAP (p=0.009), lower TAPSE (p=0.007) and STr (p=0.001) and worst RVGS (p=0.001). (3) The ROC curve for death was associated with sPAP (AUC=0.63 p=0.027), TAPSE (AUC=0.65 p=0.003), STr (AUC=0.7 p=0.002) and RVGS (AUC=0.73 p=0.001). (3) The survival curve and greater risk of death was associated with the worst quartile of all parameters. However the TAPSE<16.8 (HR=5.8; 95% CI 1.7–19.9; p=0.005) was the independent predictor of survival.

	KM	Univariate Cox			Multivariate Cox		
	p	HR	95% CI	p	HR	95% CI	p
sPAP >49.6	0.013	2.2	1.2–4.2	0.015			NS
TAPSE <16.8	0.001	3.0	1.-5.3	0.001	5.8	1.7–19.9	0.005
RVFAC <0.29	0.026	2.1	1.1–4.1	0.03			NS
STr <13.0	0.014	3.9	1.2–13.1	0.024			NS
RVGS >–14.7	0.001	5.6	1.7–18.1	0.004			NS

Conclusion: RV systolic function, deformation and pressure overload were strong predictors of the 3-year survival of outpatients with SHF. Nevertheless, TAPSE which is an easy to perform measure was the independent predictor of death.

P6582 | BEDSIDE
KIM-1 and NAG: new predictors for long-term progression of chronic kidney disease in patients with heart failure

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Background: Patients with chronic heart failure (CHF) are often characterized by the cardiorenal syndrome (CRS). The aim of the present study was to assess whether novel markers of kidney injury are able to predict progression of chronic kidney disease (CKD) in patients with CHF.
Methods: New renal biomarkers, kidney injury molecule-1 (KIM-1), N-acteyl-ß-D-glucosaminidase (NAG) and Neutrophil Gelatinase-Associated Lipocalin (NGAL), were assessed from urine samples of 149 patients with chronic heart failure. During a 5-year-follow-up, renal function was assessed by creatinine and eGFR (MDRD) and was available for 135 patients (the other 14 patients died). Further, data regarding all-cause mortality was obtained.
Results: 35 patients (26%) developed a progression of chronic kidney disease during the follow-up period, as defined by a reduction of at least one CKD stage. No difference regarding age, sex, BMI, hypertension, diabetes or EF was present between patients with and without progressive renal disease (each p=n.s.). At baseline, creatinine concentrations and eGFR were significantly different between both groups (sCr: 1.21±0.72 vs 1.05±0.41, p=0.009; eGFR: 64.4±20.7 vs. 78.1±25.8 ml/min/1.73m^2, p=0.001). In a Kaplan-Meier-analysis, KIM-1 and NAG were predictors of progressive renal disease (both p<0.01). In a Cox regression analysis, initial eGFR (OR 0.98, 95% CI 0.96; 0.99, p=0.002) and KIM-1 > median (OR 2.5, 95% CI 1.22; 5.2; p=0.012) as well as NAG > median (OR 2.6, 95% CI 1.24; 5.45; p=0.012) were independent predictors of progressive renal disease. A ROC-analysis yielded satisfying predictive values for KIM-1 (AUC 0.65) and NAG (AUC 0,63) for progression of CKD. NGAL showed no association with progression of CKD. Further, KIM-1 and NAG were also independent predictors of a combined endpoint of progressive CKD and all-cause mortality by Cox regression analysis (each p<0.05).
Conclusions: The present study demonstrates a significant progression of renal dysfunction in patients with chronic heart failure during long-term follow-up. Further, it shows a strong association of the new renal biomarkers KIM-1 and NAG with progressive kidney disease in these patients and suggests their usefulness as biomarkers of the cardiorenal syndrome.
Acknowledgement/Funding: none

P6583 | BEDSIDE
Impact of diabetes mellitus on acute heart failure

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Background and aim: The prevalence of heart failure among diabetic patients is reported as 20%. Conversely, several heart failure registry data reported high prevalence of diabetes mellitus reaching 40%. Although, the outcomes in heart failure patients combined with diabetes mellitus (DM-HF) have been suggested worse than those without diabetes (non-DM-HF), the effect of glycemic control has not been reported yet. We aimed to investigate the impact of diabetes mellitus in short term outcomes of acute heart failure patients.
Methods: We analyzed data from the Korean Acute Heart Failure (KorAHF, n=5627) which is a registry of patients hospitalized for acute heart failure syndrome in ten regionally-representative tertiary university hospitals in Korea.
Results: 1) 40.0% had diabetes mellitus. DM-HF patients were older (70.1±11.6 vs 67.4±16.0, p<0.001), more men (55% vs 52%, p=0.017), had more hypertension (72% vs 50%, p<0.001), chronic renal disease (21.6% vs 9.5%, p<0.001), whereas had less atial fibrillation (25.2% vs 29.1%, p=0.001) than non-DM-HF.
2) Ischemia was both the leading cause (52.7%) and the most frequent aggravating factor (36.1%) in DM-HF patients, which were far more than in non-DM-HF patients (27.5% and 19.8% respectively).
3) In-hospital mortality among DM-HF patients was 60% higher than non-DM-HF patients (6.1% vs 3.9%, p<0.001). The difference remained significant after adjusting gender, age, history of hypertension, ischemic heart disease, functional status and serum creatinine.

4) Among DM-HF patients, the status of hyperglycemic control in the range of HbA1C 6–8% did not have any impact either on in-hospital mortality or short-term follow up during 6 months. However, surprisingly, DM-HF patients managed on insulin (DM-HF-Insulin, 49.7% of DM-HF patients) had far worse in-hospital mortality of 9.2% comapred with DM-HF patients managed on oral hypoglycemic agents (DM-HF-OHA) (1.5%, $p<0.001$). In-hospital mortality difference remained significant after adjusting gender, age, history of hypertension, ischemic heart disease, functional status, HbA1C and serum creatinine. If DM-HF-OHA were confined, in-hospital mortality and short-term results were not significantly different comapred with non-DM-HF patients.
Conclusions: DM-HF patients had worse prognosis than non-DM-HF patients. Hyperglycemic control status might have little impact either on in-hospital mortality or short-term follow up. Although DM-HF-OHA patients did not have worse outcome than non-DM-HF patients, DM-HF-Insulin patients have three folds higher in-hospital mortality, which warrants long-term study.
Acknowledgement/Funding: Research of Korea Centers for Disease Control and Prevention

P6584 | BEDSIDE
Heart failure epidemiology: a population-based analysis of 88,195 patients

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Introduction: Heart failure (HF) is frequent and its prevalence is increasing. Most of the studies that analyzed heart failure readmission focused on 30-day readmission or on selected patients. However, less is known on factors related to readmission or death at a population level. Our aim was to analyze clinically-related readmissions, survival and healthcare cost at a population level.
Methods: Population based study that included all the patients with diagnosis of HF in the health areas of the Catalan Health Service. Patients were divided in 3 groups: HF diagnosis made at the primary care setting, patients with a remote (>1 year) and with a recent (<1 year) HF admission. We analyzed 1-year (2013) readmissions, survival and costs.
Results: A total of 88,195 cases were analyzed, of which 14% were HF diagnosis at primary care setting, 71% with a remote HF admission and 15% with a recent HF hospitalization. Mean age was 77.4 years, 55% were women. Comorbidities were frequent, with a median of 6 comorbidities per patient. The most frequent were hypertension, ischemic heart disease, atrial fibrillation, anemia, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, depression and cancer. One-year mortality rate in the whole cohort was 14%, but was higher in patients with a recent hospitalization (24%) than in patients with remote HF hospitalization (13%) and primary care diagnosis (11%). All-cause readmission and the combination of death/HF readmission was also higher in the recent HF hospitalization group compared to the other 2 groups (48% vs 29% vs 21% and 55% vs 34% vs 26%, respectively). In multivariate regression analysis, age, gender, HF group of diagnosis, number of hospital admissions and emergency room visits the previous year were found to be independently associated with the combination of death/HF readmission. Mean healthcare cost associated with heart failure was 6,571€ and was mainly driven by hospitalization (36% of expenditure), pharmacy (22%) and primary care (14%). Health-care expenditure was higher in patients with a recent hospitalization (9,892 €/year) and 26% of this group had an expenditure higher than percentile 85. The same data were 6,402 € and 14% for patients with a remote HF hospitalization and 4,323 € and 8% for primary care HF diagnosis.
Conclusions: HF patients with a recent hospitalization due to HF are at high risk of subsequent hospitalization or death at 1 year and account for the highest healthcare cost. Although this risk and cost decreases, it is still high in patients with a remote HF admission or primary care HF diagnosis.

P6585 | BEDSIDE
Left atrial emptying function predicts long-term outcome in HFpEF patients

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Background and aim: Although many prognostic variables have been reported, the risk stratification of patients with heart failure and preserved ejection fraction (HFpEF) is still controversial. We investigated the prognostic value of various conventional Doppler echocardiographic parameters on the clinical outcomes of a sample of such patients.
Methods: This study included 139 consecutive patients (62±10 years) with congestive HFpEF. The primary outcomes were cardiac events (CE = mortality or need for hospitalization) due to acute HF signs and/or symptoms. LV end-diastolic and end-systolic dimensions, ejection fraction (EF), mitral and tricuspid annulus peak systolic excursion (MAPSE and TAPSE), myocardial velocities (s', e' and a'), left atrial (LA) dimensions, LA volume and LA emptying fraction were all measured. Mean follow-up was 20±5 months.
Results: During the follow-up period, 53 patients (38%) had CE. The hemoglobin level was lower (P=0.02), LV mass index was higher (P=0.002), LA was larger (p=0.002), LV EDD (0.003) and LV ESD (p=0.02) were greater, E/e' lower (P=0.01), LA emptying fraction was lower ($P<0.001$), in patients who had cardiac events compared to those who did not. Multivariate analysis identified age (OR=0.982, 95% CI 0.869–0.992; P=0.027) and LA emptying fraction (OR=0.931, 95% CI 0.869–0.997; P=0.041) as independent predictors of CE. A LA emptying fraction ≥60.5% was 70% sensitive and 65% specific (AUC 0.74, $p<0.001$) in predicting CE.
Conclusions: In medically treated patients with chronic HFpEF, left atrial function, but not LA diameter, was associated with increased risk of cardiac events. This finding highlights the need for routine LA function monitoring for better optimization of medical therapy in HFpEF patients.

P6586 | BEDSIDE
Serum relaxin as a prognostic biomarker in acute heart failure

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Background: Relaxin has been implicated in many cardiovascular physiologic and pathologic processes. It mediates vasodilation and natriuresis, and has anti-inflammatory as well as anti-fibrotic actions. Recent trials strongly suggest that its administration may be promising in acute heart failure (HF). Endogenous cardiac production of relaxin seems to be increased in HF as a compensatory mechanism, yet the prognostic impact of its circulating levels is unknown.
Purpose: We aimed to determine the prognostic potential of serum relaxin in acute HF.
Methods: We selected patients from a registry of acute HF patients. These patients were followed during hospital stay and for 6-month after discharge. The main outcome was all-cause death. Admission serum relaxin was measured using an ELISA kit (Immunodiagnostik, Germany, detection limit 0,5pg/ml). If relaxin levels were below the detection limit, they were set at 0.4pg/ml. Relaxin was dichotomized according to the median value of its distribution. The ability of relaxin to predict death was analysed using Cox-regression analysis. One to one adjustments were made considering variables with known prognostic implications.
Results: We evaluated relaxin serum levels in 81 acute HF patients. Median age was 82 years, 37% of the patients were male and 63% had systolic dysfunction. Median serum relaxin was 36.1 pg/mL (range 0.4–1041.8). Twenty patients had relaxin levels below the detection limit. Patients with relaxin levels above the median were older (median 83 vs. 79 years, p=0.01) and less likely to be treated with a beta-blocker (60.0% vs. 32.5%, p=0.01) or a statin (72.5% vs. 45.0%, p=0.01). No differences were observed between groups regarding admission BNP (median 1143.0 vs. 1289.2 pg/ml, p=0.91), NYHA class, creatinine, or echocardiographic parameters such as ejection fraction (EF) or left atrium size. One patient died in-hospital and 12 died after discharge. Patients with relaxin levels above the median had a hazard ratio of death of 3.76 (95% CI 1.03–13.67, p=0.04). This association was independent of admission BNP and remained significant after adjusting for sex, EF or creatinine. This trend has also remained after adjusting for age or HF-modifying therapy, although it did not reach statistical significance (p-values 0.09 or 0.08, respectively).
Conclusions: Our results suggest that serum relaxin seems to be a BNP-independent predictor of death in acute HF patients. These results provide a new insight into the importance of endogenous relaxin in HF, but need further validation in a larger cohort of patients.

P6587 | BEDSIDE
Additive effect of reduced left ventricle ejection fraction and functional status at discharge home from acute myocardial infarction on 3-year rehospitalizations due to heart failure and mortality

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Heart failure is one of the main causes of poor outcomes after discharge home in acute myocardial infarction (AMI). The aim of this analysis was to assess relationship of left ventricle ejection fraction (LVEF) and functional status (NYHA class) at discharge to 3-year outcomes after acute phase of AMI.
Methods: We used the Polish Registry of Acute Coronary Syndromes (PL-ACS) database (for baseline characteristics of AMI patients from year 2009) linked to the database of the only health insurer in Poland for 3-year follow-up data concerning rehospitalizations and total mortality. 12692 patients with AMI (48% NSTEMI and 51% STEMI), with known both LVEF and NYHA class were discharged home.
Results: The distribution of LVEF was: ≥45% – 70%, 36–44% – 15%, 26–35% – 10%, ≤25% – 5%, and NYHA was: I – 59%, II – 34%, III or IV – 7%. During 3 years 1596 (12.6%) of patients were rehospitalized due to heart failure and 2014 (15.9%) died. We found and additive effect of LVEF and NYHA class on both

rehospitalizations due to heart failure and mortality during 3 years following discharge (table). In multivariate analyses adjusted for baseline characteristics and parameters from the acute phase of AMI, both LVEF and NYHA class were significant predictors of rehospitalizations due to heart failure (LVEF HR=1.58, 95% CI: 1.50–1.66, p<0.0001; NYHA class HR=1.29, 95% CI: 1.19–1.40, p<0.0001) and 3-year mortality (LVEF HR=1.49, 95% CI: 1.42–1.56, p<0.0001; NYHA class HR=1.25, 95% CI: 1.16–1.34, p<0.0001).

	Rehospitalizations due to heart failure			Mortality		
	NYHA I	NYHA II	NYHA III or IV	NYHA I	NYHA II	NYHA III or IV
LVEF ≥45%	5.8%	10.2%	22.3%	8.4%	13.1%	29.9%
LVEF 36–44%	12.1%	16.4%	35.8%	15.1%	22.5%	41.8%
LVEF 26–35%	26.2%	29.5%	39.4%	27.3%	33.6%	44.2%
LVEF ≤25%	29.1%	42.8%	43.9%	42.7%	40.0%	58.3%

Conclusion: Functional status at discharge home from AMI has an important additional effect to left ventricle ejection fraction for long term outcomes.

TREATMENT OF HYPERTENSION II

P6588 | BEDSIDE
Nine-year target systolic blood pressure less than 120 mmHg for more than 65 aged hypertension patients with chronic renal disease

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Background: Many studies demonstrate that systolic blood pressure (SBP) ≧140 mm Hg does not provide renal protection in renal disease with hypertension, but SBP≦120 mmHg may be able to slow progress of renal disease. However, target SBP≦150 mmHg in elderly hypertension patients was recommended in Chinese hypertension guideline in 2005.The long-term safety and efficacy of SBP≦120 mmHg in elderly hypertension patients with chronic renal disease is hardly reported.
Methods: In a prospective, controlled open-label studies, the authors have evaluated the safety and efficacy of nine-year treatment on progress of renal disease and risk of development of cardiovascular disease in 122 >65 aged hypertension patients with chronic renal disease III to IV stage and macroproteinuria. Before randomization, all patients have already been treated for one-year with angiotensin converting enzyme inhibitors (ACEI) or angiotensin AT1 receptor blockade (ARBs) and other antihypertensive drugs, but their SBP are above 140 mmHg,less than 150 mmHg. Blood pressure, serum creatinine (Cr) and potassium were monitored every 14 days in the period of follow-up by physician and healthcare nurse and more frequent patient-physician encounters will be improve that patients monitored their blood pressure every day at home and adjusted their own medication according to pre-agreed rules.
Results: By the end of nine year,medication possession ratio between two groups was similar (94% vs 94%), mean blood pressure in treatment group was 118/68±6/3 mmHg and in control was 149/74±13/9 mmHg, Cr clearance increased from 51±2.0 to 65±3.2 ml/min (p<0.001)in the group of strict control of SBP,by contrast, Cr clearance decreased significantly from 52±1.9 to 30±2.8 ml/min (P<0.01)in the controls. During this time, urine protein excretion decreased from 1.4±0.5 to 0.2±0.2g/24 hours (P<0.0001) in the treatment group, but urine protein excretion decreased slightly (from 1.3±0.4 to 1.1±0.9g,P>0.05)in the controls. Fourteen patients had got ACS, 24 stroke, 14 renal dialysis (4 from III and 10 from IV stage) and 15 died (7 in SCD and 6 in heart failure and 2 in non-cardiac reasen) in controls, and five patients had got ACS, 9 stroke, 2 renal dialysis (all from IV stage) and 7 died in non-cardiac causes in the treatment group. Incidence of hyperkalaemia was similar between two groups.
Conclusions: SBP≦120 mmHg is safe and was more apparently in decreasing proteinuria, slowing the progress of renal disease and reducing the risk of development of cardiovascular events in elderly hypertensive patients with chronic renal disease and proteinuria.

P6589 | BEDSIDE
Effect of metformin on ventricular remodeling in patients with primary hypertension and type 2 diabetes mellitus

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Objective: To explore the effects of metformin on left ventricular remodeling in patients with primary hypertension and type 2 diabetes mellitus as well as the effect of hypertension duration and duration of drug usage.
Methods: We retrospectively analyzed the clinical and echocardiographic data of 176 patients with primary hypertension and type 2 diabetes mellitus admitted to our hospital from January to December 2012. The follow-up period was 6 months to 2 years. The patients were classified into two groups according to the usage of metformin: metformin group (n=84) and control group (n=92). Clinical data and echocardiography findings were evaluated both at baseline and follow-up. Subgroup analysises were used to assess the effect of hypertension duration and duration of drug usage.
Results: (1) At baseline, there was no significant difference in interventricular septum depth (IVSD), left ventricular posterior wall depth (LVPWD), and left ventricular mass index (LVMI) between the two groups. At the follow-up period, IVSD (P=0.001), LVPWD (P=0.04) and LVMI (P=0.01) were lower in metformin group compared with control group. Multiple linear regression indicated that metformin had significant influence on LVPWD (B=–0.69, standard error=0.30, t=–2.31, P=0.02, 95% confidence interval –1.28 to –0.10) and LVMI (B=–6.38, standard error=2.79, t=–2.14, P=0.04, 95% confidence interval –12.37 to –0.71). At the follow-up period, LVMI was lower in both metformin groups compared with control group. Besides, LVMI was the lowest in the group of which the patients took metformin for more than one year. It was significant lower than that in control group (P=0.04). (2) For patients whose hypertention duration was shorter than 5 years, at the follow-up period, LVMI (P=0.04) was lower in metformin group compared with control group. For patients whose hypertention duration was not shorter than 5 years, at the follow-up period, IVSD (P=0.01) and LVMI (P=0.02) were lower in metformin group compared with control group.
Conclusions: Metformin may attenuate left ventricular hypertrophy of patients with primary hypertension and type 2 diabetes mellitus. In patients with longer hypertension duration and longer duration of metformin use, metformin may show more effects on the attenuation of left ventricular hypertrophy of patients with primary hypertension and type 2 diabetes mellitus.
Acknowledgement/Funding: Supported by National Natural Science Foundation of China (81030001,81300067)

P6590 | BEDSIDE
Randomized study to determine the effect of unmonitored diet and exercise education on blood pressure (the LSM study)

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Background: Life style modification, such as exercise therapy and Dietary Approaches to Stop Hypertension (DASH) diet, has been shown to be effective for treatment of hypertension. However, most of the clinical studies regarding life style modification have been done in a monitored setting when in the real word setting, unmonitored diet and exercise are recommended to the patients.
Purpose: To evaluate how unmonitored recommendation of Korean DASH diet and exercise education affects blood pressure in patients with prehypertension or mild hypertension. Subjects wild mild hypertension were defined as patients with office blood pressure between 140–160/90–100mmHg who were taking either 1 or no medications.
Methods: A total of 76 patient, who were aged over 20 and diagnosed as either prehypertension or mild hypertension, were randomly assign to the control (C) group (n=26), the diet education (D) group (n=25), and the diet and exercise education (D+Ex) group (n=26). The D group and the D+Ex group both received DASH diet education, and the D+Ex group received exercise education. The intervention lasted for 8 weeks, and office BP, central BP, and 24-hour ambulatory BP were examined before and after the study period. The trial was registered at ClinicalTrials.org (NCT01637909).
Results: Although office BP showed tendency to be reduced in the D+Ex group and the D group compared to the C group, it was not statistically significant. The D+Ex group showed significantly decreased 24 hour average ambulatory SBP (systolic BP, –5.5±7.2 vs. –1.9±8.1 vs. 1.1±7.1 mmHg, P=0.011; diastolic BP, –2.9±5.0 vs. –0.9±5.1 vs. 0.5±5.1, P=0.067) and daytime average SBP/DBP (systolic BP, –5.9±9 vs. –1.3±8.1 vs. 0.9±8,2 mmHg, P=0.02; diastolic BP, –4.4±6.9 vs. –0.9±5.2 vs. –0.1±5.8, P=0.033). However, there was no significant difference in nocturnal ambulatory BP (systolic BP, –4.0±9.9 vs. –3.8±12.6 vs. 0.5±12.6 mmHg, P=0.322; diastolic BP, –1.3±7.2 vs. –1.2±7.2 vs. 0.5±8, P=0.652). Central aortic pressure showed a tendency to being reduced in the D+Ex group and the D group but without statistical significance.
Conclusion: Unmonitored life style modification through diet and exercise, but not diet alone, was effective for lowering blood pressure. Life style modification emphasizing both dietary modification and exercise should be accentuated.
Acknowledgement/Funding: This stydy was supported by an industrial research grant from Sanofi Aventis.

P6591 | BEDSIDE
Influence of fixed-dose combination perindopril/amlodipin on target organ damage in patients with arterial hypertension

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To evaluate the antihypertensive effectiveness and changes of target organ damage in patients with arterial hypertension (AH) on fixed dose combination (FDC) (perindopril (P)/amlodipin (A)) treatment.
There were included 30 patients (age>30 yrs, untreated hypertensives with BP≥160/100 and ≥200/120 mmHg or who were on monotherapy (except P), but their office BP was ≥140/90 and ≤200/120 mmHg), whom were evaluated office systolic (SBP) and diastolic (DBP) blood pressure (BP), 24-h SBP and 24-h DBP, central SBP (cSBP) and aorta pulse wave velocity (PWV) by Sphygmocor, EchoCG with Tissue Doppler, albuminuria, intima-media thickness (IMT), ankle-brachial index (ABI), biochemical blood analysis. Follow-up period was12

months. After wash-out period P/A administered in dose 5/5 mg with up-titration to 10/10mg every 2 weeks. Indapamid was added as the third drug. Primary endpoints were BP lowering (office, systolic, central), significant (≥SD) dynamic of target organ damage signs, tolerance of FDC.
Baseline FDC were administered to 34 pts, but 4 were excluded due to intolerance (n=1) or their personal reasons. Office SBP/DBP decreased from 156.4±3.8/96.3±2.2 till 135.3±1.3/76.2±1.1 mmHg ($p<0.001/0.001$), 24-hSBP/DBP from 140.2±1.9/86.6±2.2 till 117.8±1.4/74.2±1.1mmHg ($p<0.001/0.001$), cSBP from 142.8±2.5 till 118.3±2.7 mmHg ($p<0.001$). Target BP was achieved in all patients. Effective BP control followed by positive target organ changes (table). The changes of E/E', E/A and albuminuria did not correlate with office BP lowering, but with aorta PWV and Aix75 decreasing. We did not note any significant changes of biochemical patterns.

Patterns	Baseline	12 months	Patterns	Baseline	12 months
Aorta PWV, m/s	11.9±0.7	9.4±0.8‡	E/A	0.93±0.06	1.3±0.08‡
ABI	1.00±0.05	1.1±0.08	E/E'	9.9±0.2	7.6±0.5‡
Albuminuria, mg/24-h	53.3±5.6	15.8±3.2‡	Cornel index, mm x ms	2440.1±67.9	1987.2±66.8‡
IMT, mm	1.1±0.03	1.0±0.04	Aix75, %	26.8±1.9	11.2±1.7‡
LVMI, g/m^2	108.8±5.5	88.3±5.3‡	Left atrium, mm	41.1±0.2	38.1±0.3‡

‡$p<0.05$.

The treatment based on FDC (P/A) was effective not only in decreasing of office and ambulatory BP, but central SBP too. It led to decreasing of target organ damage. Diastolic left ventricular function and renal damage improving were connected with much decreasing arterial stiffness and aorta augmentation.

P6592 | BEDSIDE
Prevalence, treatment and control of hypertension in middle-aged Mexican adults

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Background: Hypertension is common in Mexican adults, but the extent of medication among hypertensives, and of blood pressure control among those receiving medication, is unknown. The Mexico City Prospective Study is a blood-based cohort of 150,000 adults aged ≥35 years when recruited in 1998–2004.
Methods: The baseline questionnaire, completed by 52,644 men and 107,111 women, asked about previous doctor diagnoses of hypertension and current medication. Blood pressure was measured 3 times in the seated position. "Hypertension" was defined as a recall of a doctor diagnosis, blood pressure lowering drug use, average SBP≥140 mmHg or average DBP ≥90 mmHg. Logistic regression assessed the odds of receiving treatment for hypertension and the odds of such treatment successfully controlling blood pressure (ie, SBP <140 mmHg and DBP <90 mmHg).
Results: Mean blood pressure increased with age in both sexes, from 120/80 mmHg at ages 35–44 to 138/85 at ages 75–84. Consequently, the prevalence of "hypertension" increased strongly with age from 25% at ages 35–44 to 61% at ages 75–84 in males and, even more sharply, from 20% at ages 35–44 to 72% at ages 75–84 in females. Among those with hypertension, 59% of males and 38% of females had no previous diagnosis of it and were not taking any BP-lowering drug while 30% of males and 44% of females were taking one or more blood pressure lowering drug. Among those with hypertension, the prevalence of blood pressure lowering drug use increased sharply with age, with a lower prevalence at every age for males compared with females. Among those who were taking a blood pressure lowering drug, blood pressure was "controlled" for 39% of males and 37% of females, which did not vary markedly by age in males, but was somewhat higher for younger females than older females. In addition to older age and female sex, hypertension was more likely to be treated (and treated hypertension more likely to be controlled) among those with a higher level of education. Treatment of a hypertensive participant with a blood pressure lowering drug was also more likely for those having insurance provided by the largest health care provider (IMSS) than for those who had other insurance or no insurance.
Conclusions: Elevated blood pressure is common in middle-aged Mexican adults and is often untreated. Future prospective analyses of this cohort will investigate the full effects of blood pressure on cause-specific mortality.
Acknowledgement/Funding: The Wellcome Trust

P6593 | BEDSIDE
Use of blood pressure salt sensitivity determination to optimize anti-hypertensive therapy in patients with complicated arterial hypertension

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Purpose: Evaluate the use of BP salt sensitivity determination to optimize antihypetensive therapy in patients with complicated arterial hypertension.
Methods: 66 Patients (20 men and 46 women, avg. age 57.7±1.0) with arterial hypertension and ischaemic stroke (1 to 7 years ago) were examined. Hypertension duration – 9.9±0.9 years. The patients were randomized into 3 groups (22 people each). Group 1 patients were on lisinopril for 3 months (10–20 mg a day), group 2 – on felodipine (5–10 mg), group 3 – on a combination of enalapril 20 mg and 12.5 mg of hydrochlorthiazide. 24-Hour BP monitoring was conducted in patients twice by a common method using ABPM-04. Salt sensitivity of BP was evaluated by the (Weinberger M.N., 1986) method. Daily Na+ excretion was measured by ion-selective potentiometry.
Results: Salt-sensitive (SS) type of BP was identified in 33 (50%) patients, salt-resistant (SR) – in 33 (50%). BMI in SS proved to be higher than in SR – 30.8±0.7 and 26.6±1.0 kg/m^2, ($p<0.05$). Daily Na+ excretion in SS was 229.3±15.2 mmol vs 188.1±11.2 mmol in SR ($p<0.05$), indicating higher dietary Na intake. After 3 months of therapy, avg. SBP in Group 1 patients decreased from 144.3±1.4 to 128.8±1.9 ($p<0.001$), avg. DBP – from 85.0±1.5 to 76.6±1.6 mm Hg ($p<0.01$). Avg. SBP and avg. DBP decrease was significantly greater in SR patients than in SS – 17.6±1.9 vs 11.6±1.7 ($p<0.05$) and 9.1±1.1 and 5.4±1.0 mm Hg, respectively ($p<0.05$). In Group 2, avg. SBP decreased from 143.1±2.1 to 130.5±2.4 ($p<0.01$), avg. DBP – from 81.7±1.5 to 74.3±1.8 mm Hg ($p<0.05$), with the absolute decrease of BP in SS patients being more significant than in SR – avg. SBP decreased by 16.1±2.8 and 9.6±1.9 ($p<0.05$), avg. DBP – by 8.8±1.9 and 5.7±1.5 mm Hg ($p<0.05$). Therapy of group 3 patients with enalapril and hydrochlorothiazide showed the most considerable BP decrease – avg. SBP from 146.6±3.4 to 128.8±3.0 ($p<0.05$) and avg. DBP – from 82.7±2.4 to 71.2±2.0 mm Hg ($p<0.05$). In SS patients, avg. SBP decreased more significantly than in SR – by 22.7±3.7 vs 13.9±3.1 ($p<0.05$), avg. DBP – by 13.9±1.8 vs 7.2±1.6 mm Hg ($p<0.05$).
Conclusions: 1. The studied anti-hypertensive drugs demonstrated different effect depending on the BP response to the salt load – lisinopril showed the highest effect in SR patients, felodipine and the combination of enalapril and hydrochlorthiazide had a more pronounced anti-hypertensive effect in SS patients. 2. Determination of salt sensitivity of BP can be used to optimize the selection of individual anti-hypertensive therapy.

P6594 | BEDSIDE
Evaluation of β-thalassemia minor on metabolic profile in patients with newly diagnosed hypertension

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Purpose: β-Thalassemia minor (Tm) has long been deemed to confer cardiovascular protection. Thus, besides serum lipids the rest of the components of cardiovascular risk as well as the metabolic profile of Tm subjects in general have not been addressed.
Methods: We evaluated metabolic parameters and risk-prediction equations in 23.680 consecutive subjects, that is, 11.192 women and 12.488 men, with newly diagnosed hypertension according to the presence or absence of Tm.
Results: The two groups did not differ in gender distribution, age, body mass index or systolic or BP, but Tm patients had a higher pulse pressure (p=0.01). In contrast, hypertensive patients with Tm had a better lipidemic profile with significantly lower low-density lipoprotein (LDL, p=0.009), total cholesterol and triglycerides, and higher high-density lipoprotein levels (all $p<0.001$), as well as lower waist-to-hip and waist-to-stature ratios (all $p<0.001$) compared with hypertensive patients without Tm. There was also a tendency for a lower prevalence of diabetes mellitus in Tm patients. As a result, Tm patients had a lower overall prevalence of metabolic syndrome (26% vs39%,$p<0.001$).
Conclusions: Tm is followed by a favorable cardiovascular and metabolic profile, beyond the well-known differences in serum lipids. Moreover, although gender differences do exist, women with Tm seem to be equally, if not more, protected as men.

P6595 | SPOTLIGHT
Serum uric acid and the risk of development of hypertension in the urban population

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Objective: To analyze the relation between serum uric acid levels, and development of hypertension in a large adult population using the data from Belarusian national representative survey.
Design and methods: We conducted a 5-year prospective analysis of 3500 individuals living in a district of Vitebsk in 2007/2008 (coverage of the survey was 97.9%), 2010/2011 (coverage of the survey was 77.8%) and 2012/2013 (coverage of the survey was 84.3%). HT were evaluated according to the WHO/ISH (1999). The survey included standard questionnaires for detection of cardiovascular risk factors, measurements of blood pressure, electrocardiography, serum C-reactively protein, uric acid and cholesterol data.
Results: There were 2170 persons with normal blood pressure and 1257 persons with hypertension in the studied population. Men and women were similar of mean age. In 5 years 285 new cases of hypertension developed. There was revealed significant positive association between IV quartile of serum uric acid level (339–527 mmol/l) and the frequency of new cases of hypertension adjusted for age and sex (df=1; χ^2 Wald=5,1; $p<0,05$). According to multifactorial regression analysis high uric acid level (>338 mmol/l) ($p<0.001$) the same as systolic blood level (>120 mmHg) and high body mass index level (>25.7 kg/m^2) ($p<0.001$) are the

most significant factors affecting the frequency of new cases of hypertension in the studied population.
Conclusions: The results of our study showed that serum uric acid level is a risk factor of developing hypertension in Belarusian urban population.

P6596 | BEDSIDE
Association of urinary sodium excretion with blood pressure and cardiovascular clinical events in South America: The PURE study

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Background: Sodium intake is reported to be a modifiable determinant of hypertension, a principal risk factor for cardiovascular disease and mortality. Information on the relationship of sodium intake with blood pressure and clinical events in populations outside North America and Europe is limited, despite variation in sodium intake across geographic regions.
Purpose: Our aim is to assess the association of sodium intake with blood pressure, cardiovascular events and mortality in a cohort from four South American countries.
Methods: We studied 17,033 individuals, aged 35 to 70 years, from four South American countries (Argentina, Brazil, Chile and Colombia) participating in a large international prospective cohort. Measures of sodium excretion (SE) were estimated from a morning fasting urine and were used as a surrogate for intake. We assessed the association of SE with blood pressure and the composite outcome of death and major cardiovascular events.
Results: Mean SE was 4.70±1.43 g per day. 2.8% of participants had a SE of less than 2.3 g per day, and 0.5% below 1.5 g per day. For each gram of estimated SE there was an increment of 1.52 mm Hg in systolic blood pressure ($P<0.001$) and an increment of 0.58 mm Hg in diastolic blood pressure ($P<0.001$). This positive association was nonuniform with steeper slope at a higher SE level (more than 5 g/day) compared to the slope at moderate (3 to 5 g/day) and low (less than 3 g/day) SE, for both systolic and diastolic blood pressure ($p=0.002$ and $p<0.001$ for interaction, respectively). With a median follow-up of 4.7 years, the primary composite outcome occurred in 568 participants (3.4%). Compared with SE of 5 to 6 g/day (the reference category), SE of greater than 7 g/day was associated with increased risks of the primary composite outcome (OR 1.73; 95% CI 1.24 - 2.40; $p<0.001$), death from any cause (OR 1.87; 95% CI 1.23 - 2.83; $p=0.003$), and major CV disease (OR 1.77; 95% CI 1.12 to 2.81; $p=0.014$) on multivariable analyses. SE of less than 3 g/day was associated with a nonsignificant increased risk of the primary composite outcome (OR 1.20; 95% CI 0.86 - 1.65; $p=0.26$), death from any cause (OR 1.25; 95% CI 0.81 to 1.93; $p=0.29$), and a significant increase in major CV disease (OR=1.50; 95% CI: 1.01 to 2.24; $p=0.048$), compared with SE of 5 to 6 g/day.
Conclusions: Our results support a positive, nonuniform association between estimated urinary SE and blood pressure, and a J-shaped pattern of association between SE and clinical outcomes in this South American cohort.
Acknowledgement/Funding: Heart and Stroke Foundation of Ontario, the PHRI, the CIHR, unrestricted grants from several pharmaceutical companies.

P6597 | BEDSIDE
The association between urinary sodium to potassium ratio and blood pressure by salt consumption level: the Takahata study

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Background: Previous epidemiological studies revealed that urinary Na-K ratio [UNa/K] would correlate to blood pressure (BP), however salt consumption levels might modulate the correlation between Na-K balance and BP.
Purpose: We aimed to investigate the effects of UNa/K on BP by their salt consumption level in general Japanese population.
Methods: We recruited 3519 participants in 2004–6 at Takahata town, Yamagata, Japan. We excluded subjects with use of antihypertensive drugs in this analysis. First-void morning urines were collected, and estimated 24 hours urinary Na and K excretions were calculated by Kawasaki's equation. Linear regression analyses were used to calculate the coefficient of Na/K for blood pressure with the adjustment for considerable factors. Furthermore, additional analysis divided by their salt consumption level was performed.
Results: A total of 2174 participants (median age 60, male 46.1%) were eligible to analyze. The estimated median (interquartile range) dairy salt consumption was 12.5 (10.3–14.8) g in this cohort. UNa/K showed positive linear association for systolic and diastolic BP (Coefficient [CE]: 3.388, Standard error [SE]: 0.586, $P<0.0001$, CE: 1.635, SE: 0.397, $P<0.0001$, respectively). Nevertheless, this association was weakened in subjects with salt consumption less than median level (shown in the table below).
Conclusion: Yet UNa-K was significantly associated with BP level in this East Asian cohort, this association was attenuated in subjects with low sodium diet.

UNa/K for BP by their salt intake level

	All			Salt intake ≥12.5/day			Salt intake <12.5g/day		
	Coefficient	SE	P-value	Coefficient	SE	P-value	Coefficient	SE	P-value
SBP, UNa/K									
Univariate	3.724	0.607	<0.001	3.836	0.980	<0.001	0.815	1.028	0.427
Multivariate	3.388	0.586	<0.001	4.039	0.963	<0.001	1.981	0.973	0.042
DBP, UNa/K									
Univariate	1.893	0.400	<0.001	1.433	0.635	0.024	0.241	0.688	0.726
Multivariate	1.635	0.397	<0.001	2.074	0.646	0.001	0.979	0.667	0.143

The result of linear regression analysis of each 1 UNa/K unit increase for BP. In multivariate model, we adjusted for sex, age, BMI, smoking, alcohol, diabetes, total cholesterol and urinary albumin-creatinine ratio.

This finding inferred that the impact of K for BP might vary according to sodium consumption level.

P6598 | BEDSIDE
Low testosterone levels and increased intima media thickness: importance of lipid profile in hypertensive men

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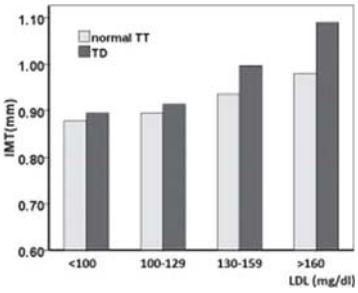
Purpose: Carotid intima media thickness (IMT) is a marker of subclinical vascular damage in patients with essential hypertension. Low testosterone has been associated with increased carotid IMT. We investigated whether this association could be mediated or modified by hypertension severity as well as lipid profile.
Methods: Total testosterone (TT) levels were measured in 287 non-diabetic hypertensive men (mean age 55±7 yrs) with no evidence of clinical atherosclerosis. Testosterone deficiency (TD) was defined when TT levels were below 3.4 ng/ml. The presence of carotid plaque and IMT were evaluated by ultrasonography.
Results: 86 (30%) hypertensive patients had TD. Analysis with and without adjustment for age and blood pressure level showed that carotid IMT was inversely and significantly correlated with TT. This association depended on LDL levels (P for interaction <0.05). Subjects were categorized according to LDL levels [Group 1: (<100 mg/dl), Group 2: (100–129 mg/dl), Group 3: (130–159 mg/dl) and Group 4: (>160 mg/dl)]. Among hypertensive patients with LDL 130–159 mg/dl and >160 mg/dl, patients with TD had significantly higher mean IMT compared to subjects with TT concentration above the cut off level for biochemical definition of TD (1.02 vs 0.94 mm, $P<0.05$ and 1.17 vs 0.97 mm, $P<0.01$, respectively, figure). The differences remained significant after adjustment for age and mean blood pressure (all $P<0.05$). By contrast, among men with either LDL<100 mg/dl or 100–129 mg/dl, mean IMT was similar in both groups (P = NS).



LDL, testosterone levels and carotid IMT

Conclusions: In hypertensive men, TD is associated with increased carotid IMT only in those with LDL levels greater than 130 mg/dl.

P6599 | BEDSIDE
Relationships between periodontal disease and hypertension and vascular dysfunction - importance of immunosenescent CD8+ T cells

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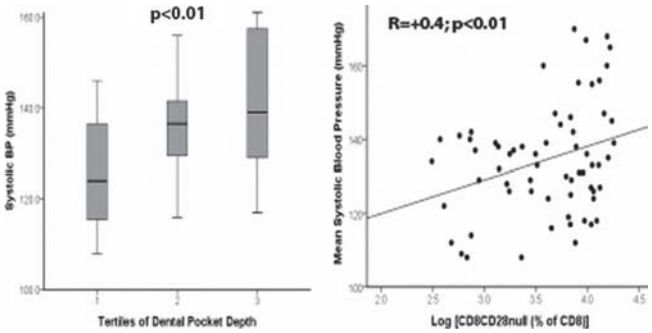
Periodontitis may be associated with cardiovascular disease including hypertension, which is particularly interesting taking into account recent evidence of the role of the immune system in hypertension. We aimed to investigate the relationships between hypertension and periodontitis severity in the context of chronic immune system activation.
Methods: We studied 87 subjects with concomitant periodontitis and hypertension. Periodontal gingival pocket depth, bleeding index and CAL. 24 hour blood pressure (ABPM) and endothelial function (flow-mediated dilatation) were determined. T cell and monocyte immune signature was studied in blood by flow cytometry.
Results: 24 hour/daytime systolic and diastolic blood pressures were significantly correlated with the tertiles of pocket depth (Figure; $p<0.01$). Severity of periodontitis was associated with endothelial function (ANOVA; $p<0.01$). These relation-



BP and periodontitis and CD8CD28null Tc

ships remained significant in multivariate analysis accounting for major clinical factors and treatments. Periodontitis severity was not associated with changes in classical, naïve, effector or memory T cells or with CD14+CD16+/– monocytes. However, periodontal pocket depth was significantly related to prevalence of immunosenescent CD8+T cells (CD8+CD28nullCD57+;$p<0.01$), which had been linked to hypertension. There was a significant positive correlation between prevalence of these cells and blood pressure (Figure, $R=+0.4$;$p<0.01$) and an inverse correlation with endothelial function (FMD;$R=-0.5$;$p<0.01$). These relationships remained significant in multivariate analysis accounting for age, sex and clinical factors.

Conclusions: Severity of periodontitis affects hypertension control and vascular dysfunction. Increased peripheral blood immunosenescent CD8+ T cells may provide link between these pathologies.

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