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HEART FAILURE: BIOMARKER BULLET POINTS

2818 | BEDSIDE
Novel biomarkers to predict cardiovascular admission in patients with pharmacologically optimised chronic heart failure

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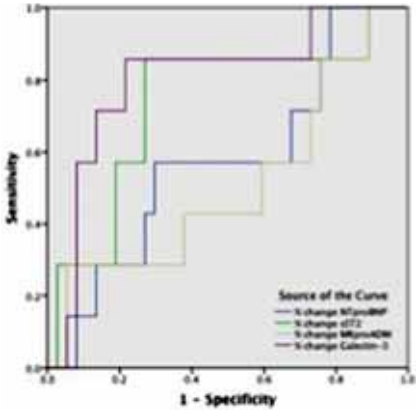
Background: The evidence for using the B-Type Natriuretic Peptides to predict decompensation in heart failure has provided mixed results. We examined serial concentrations of three novel biomarkers sST2 (an IL-1 receptor family member), Galectin-3 (a soluble β-galactosidase-binding lectin), and Mid-regional pro-adrenomedullin (MRproADM) (a vasodilatory natriuretic peptide), to ascertain superiority over NTproBNP in predicting cardiovascular admission.
Methods: We prospectively studied 50 patients with stable CHF due to LV systolic dysfunction. All patients were on optimum doses of prognostically indicated medications and in NYHA Class I-III. Mean age was 67.3 years (SD 11.568), 82% were male and 48% had IHD. Mean LVEF was 30.7%. Patients were followed for a period of 6 months with samples drawn at baseline, 1 month, 3 months and 6 months.
Results: Median concentrations at baseline for NTproBNP, sST2, Galectin-3 and MRproADM were 300pg/ml (IQR 80.8-1282), 17.6ug/L (IQR 13.3-22.5), 7.9ug/L (IQR 6.9-9.3) and 0.73nmol/L (IQR 0.58-0.95) respectively.
On ROC analysis, AUC for % change in the respective biomarkers and CV admission was 0.803 (p=0.012) for Galectin-3, 0.734 (p=0.052) for sST2, 0.506 (p=0.962) for MRproADM and 0.571 (p=0.553) for NTproBNP. Comparable results were found for absolute changes in biomarker concentrations with AUC of 0.807 (p=0.011), 0.734 (p=0.052), 0.546 (p=0.700) and 0.579 (p=0.511) respectively.



ROC analysis for % change.

Conclusion: Both sST2 and Galectin-3 are better predictors of CV admission than NTproBNP. Galectin-3 in particular demonstrates a significant ability for this use. Conversely, MRproADM is less predictive than NTproBNP, indicating it may have no role in monitoring heart failure patients. Further work in a larger sample to validate these findings is warranted.

2819 | BEDSIDE
Serial measurements of high-sensitive cardiac troponin T predict prognosis of ambulant chronic heart failure patients: results of the Bio-Shift study

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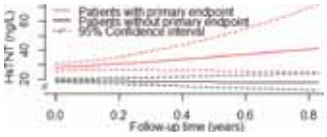
Purpose: The prognostic value of high-sensitive cardiac troponin T (Hs-cTnT) in chronic heart failure (CHF) patients has been investigated, but most studies evaluated single or few measurements only. We aimed to examine longer term Hs-cTnT patterns in CHF patients, and their value for assessing prognosis.
Methods: From 2011 to 2013, 263 ambulant CHF patients were included in 2 hospitals. Hs-cTnT was measured at baseline and every 3 months. The primary endpoint (PE) comprised heart failure (HF)-hospitalization and cardiovascular mortality. The association between Hs-cTnT pattern and the PE was assessed by a statistical method that combines a mixed model, describing temporal evolution of Hs-cTnT, with Cox proportional hazards regression.
Results: Mean age was 67 (SD 13) years, 72% were men and 27% were in NYHA class III–IV. During a median follow-up of 1.0 (IQR 0.6-1.4) years 885 blood samples were drawn, with a median of 3 (IQR 2-5) per patient. The PE was reached in 41 patients (16%). Median baseline Hs-cTnT was 17 (IQR10-32) ng/L,which was higher in patients with PE than in those without (28 (IQR 21-50) ng/L vs. 15 (IQR 9-30) ng/L; age- and sex adjusted hazard ratio (HR) for doubling of baseline Hs-cTnT: 1.71; 95% CI 1.27-2.32). In patients with a PE, age- and sex adjusted Hs-cTnT increased linearly over time (figure). The median of the last Hs-cTnT before a PE was 45 (IQR 22-69) ng/L. The temporal Hs-cTnT pattern was associated with increased risk of PE: doubling of Hs-cTnT over time resulted in 1.71 times increased risk (95% CI 1.32-2.26).



Temporal patterns of Hs-cTnT.

Conclusions: Temporal patterns of Hs-cTnT are associated with HF-hospitalizations and cardiovascular mortality in CHF patients. Hs-cTnT increased linearly before an event, whereas in stable patients the Hs-cTnT pattern remained steady over time.

2820 | BEDSIDE
Renalase in patients with heart failure

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Introduction: There are known correlations between renalase and renal failure, however there are few reports evaluating renalase in patients with heart failure (HF).
Purpose: The aim of this study was to assess serum renalase concentration in patients with heart failure.
Methods: The study included 130 patients who underwent heart transplantation (HTx), 114 patients with HF due to coronary artery disease (CAD) or dilated cardiomyopathy (DCM) without heart transplantation (no-HTx) (EF≤40%), and 27 healthy volunteers.
Results: In 130 HTx patients mean age was 53.2±14.1, in 114 no-HTx patients mean age was 69 years (27.2;85.3) with men constituting 82.5% of the group. In no-HTx group CAD was present in 86% of patients, DCM in 26.3% of patients, hypertension in 70.2% of patients, DM type 2 in 31.6% of patients and CKD in 29.8% of patients. The eGFR<60 ml/min/1.73m^2 was found in 30.7% of no-HTx patients, mean BMI was 27.47±3.95. In no-HTx group 3.5% of patients were in NYHA I class, class II-48.25%, ≥class III-48.25%. In no-HTx patients mean serum renalase concentration was 8.93±2.9μg/ml, mean EF- 26.5% (13;40), mean serum BNP- 293.5pg/ml (23;3352), mean serum creatinine- 1.04mg/dL (0.68;6.05), mean eGFR- 72.39±24.23mg/ml/1.73m^2. In the HTx group mean serum renalase concentration was 8.41±5.47μg/ml, mean EF- 55.7±9.86%, mean NT-proBNP- 165.7pg/ml (17.2;3975.8), mean serum creatinine- 1.74±1.14mg/dl, mean eGFR- 54.5±27.89 ml/min/1.73m^2. In both groups serum renalase concentration was significantly higher compared to the control group [8.93±2.9μg/ml vs. 3.86±0.73μg/ml vs. 8.41±5.47μg/ml,p<0.001]. Positive correlation was found between serum renalase and serum creatinine concentration in no-HTx patients (R: 0.349, p: 0.00223) and in patients after HTx (R: 0.85, p<0.001) and positive correlation between serum renalase concentration and patients age in noHTx and HTx grups (R: 0.234, p: 0.0344 vs. R: 0.25, p<0.01). Negative correlation was found between serum renalase concentration and eGFR in no-HTx patients (R:-0.37959,p:0.000851) and in HTx patients (R:-0.58,p<0.001). In HTx patients there was a significant correlation between serum renalase concentration and EF (R: 0.26, p<0.01) or serum NT-proBNP (R: 0.41, p<0.001) and NYHA class (R: 0.31, p<0.001), without significant correlation in no-HTx patients.
Conclusions: HTx patients are characterized with better left ventricle systolic function but worse renal function compared to no-HTx patient. Higher serum renalase concentration in both groups was related to impaired renal failure, and in HTx group also with left ventricle function.

2821 | BEDSIDE
Tumor Necrosis Factor (TNF-a) gene polymorphisms and cardiac sarcoidosis

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Background: The induction of Th1 and suppression of Th2 response is predominant in sarcoidosis granuloma formation and strongly associated with TNF-α production. Polymorphisms in the promoter region of the TNF-a gene result in high and low TNF-a producers. Frequency of the rare TNF-a -308 allele was significantly higher in Japanese patients with cardiac sarcoidosis. Cardiac sarcoidosis (CS) is the leading cause of sarcoidosis mortality and remains underdiagnosed. The identification of genetic predisposition could play a critical role in the identification of underlying subclinical forms of CS. The present study was con-

ducted to investigate possible correlations between the emergence of CS and the -1.031(T/C), -857(C/T), -308(G/A), and -238(G/A) TNF-α gene polymorphisms in a well-defined Greek cohort.
Methods: One-hundred and seventy three sarcoidosis patients (42 with CS) were recruited. Diagnosis of sarcoidosis was established when clinicoradiological findings were supported by histologic evidence. CS was determined according to standard criteria. DNA was isolated from peripheral blood with the NucleoSpin Blood Kit (Macherey-Nagel, Germany). The -1031(T/C), -857(C/T), -308 (G/A) and the -238 (G/A) polymorphisms of TNFα gene were genotyped as previously described
Results: There was no significant difference between the panel of patients with cardiac and non-cardiac sarcoidosis concerning the -1.031(T/C) and -238(G/A) TNFα polymorphisms. Regarding the -857 (C/T) polymorphism, the TT genotype and the T allele were found to be over-represented in sarcoid patients with CS (p=0.02 and 0.012, respectively). AA genotype of the -308 (G/A) as well as the A allele were also found significantly more frequently in patients with CS (p=0.014 and 0.012 respectively). From the investigated TNFα promoter polymorphisms, 9 main haplotypes were deduced. Haplotypes 3 and 5, including A nucleotide position -308, and T nucleotide at position -857 respectively, were significantly over-represented in the sarcoidosis group with cardiac involvement.
Conclusions: To date, still we do not know what predisposes some sarcoidosis patients to develop cardiac involvement. We showed that TNFα -857T and -308A variants are associated with cardiac involvement in Greek patients with sarcoidosis

2822 | BEDSIDE
Albuminuria as an independent predictor for in-hospital worsening renal function in acute decompensated heart failure

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Purpose: Worsening renal function (WRF), frequently seen in patient with heart failure during hospitalization, is known as a factor associated with poor prognosis. Although albuminuria is considered an early sign of renal disorder, little is known about the significance of albuminuria to WRF in acute decompensated heart failure (ADHF). Thus, we assessed the potential usefulness of albuminuria for predicting WRF in patients with ADHF.
Methods: We examined 280 consecutive ADHF patients who admitted to our hospital between January 2013 and December 2013 from prospective registry. We excluded 8 patients receiving dialysis treatment. WRF was defined as an increase in serum creatinine levels $\geqq$0.3 mg/dl from baseline to discharge. We performed blood and spot urine examination $\leqq$24 hours after admission and at discharge. Albuminuria was expressed as the urine albumin/creatinine ratio (UACR) $\geqq$300mg/gCr.
Results: The overall prevalence of WRF in ADHF was 39 patients (15%). WRF were more commonly observed in patients with older age, lower hemoglobin level, higher incidence of hyperuricemia, chronic kidney disease (CKD) and previous heart failure hospitalization. There were no significant differences between the two groups in terms of sex, body mass index (BMI), incidence of hypertension, ischemic heart disease, re-exacerbation of heart failure during hospitalization, weight change from admission to discharge, cardiovascular medications, left ventricular ejection fraction (LVEF), serum troponin-I, creatinine, blood urea nitrogen (BUN) and plasma brain natriuretic peptide (BNP) levels on admission. Multivariate logistic regression analyses showed that albuminuria (odds ratio 5.0, 95% CI 1.5-16.8, p=0.007) was an independent determinant for WRF, among variables including age, LVEF, systolic blood pressure, estimated glomerular function rate (eGFR), serum sodium and hemoglobin levels, and intravenous furosemide dose for initial 24 hours.
Conclusions: Albuminuria on admission rather than baseline eGFR or history of CKD may be a useful predictor of WRF during hospitalization in patients with ADHF.

2823 | BEDSIDE
Clinical impact of quantitative and qualitative alterations in the extracellular matrix (ECM) in human cardiomyopathy

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Purpose: Cardiac fibrosis is known to be a hallmark of myocardial remodeling. Quantitative and qualitative alterations in the extracellular matrix (ECM) in human cardiomyopathy are, however, unclear. This study aimed to analyze the ECM alterations by measuring the pathological and serological markers in the human cardiomyopathy.
Methods: In the pathological analysis, 113 patients of non-ischemic cardiomyopathy who underwent LV endomyocardial biopsy (EMB) were divided into three groups; A: mild fibrosis group, B: moderate fibrosis group, C: severe fibrosis group, according to the %fibrosis area in the EMB tissues. In the serological analysis, serum procollagen type I amino-terminal peptide (PINP), carboxyl terminal telopeptide of collagen I (ICTP), procollagen type III (PIIINP) and type IV collagen 7s were measured as turnover markers of collagen I, III and IV in 75 patients (45; dilated cardiomyopathy, 30; controls). Relationships between fibrosis and cardiac function were determined in each analysis.
Results: %fibrosis area ranged from 0 to 11% in the group A, 12 to 30% in the group B and 30 to 99% in the group C. Ejection fraction (EF) was 43.8±13.4%, 40.2±12.9% and 33.7±14.0% in the group A, B and C, respectively (A vs. C, $P<0.01$). LV end-diastolic volume index was 95.1±25.4ml/m^2, 107.3±42.1ml/m^2 and 128.5±43.9ml/m^2 in the group A, B, and C, respectively (A vs. C, $p<0.001$; B vs. C, $p<0.05$). Absolute increase of EF at 1 year was negatively correlated with %fibrosis ($r=-0.31$, $P<0.05$). Reverse remodeling defined as an absolute increase of EF $\geq$10% to a final value of >45% was observed in 71.4% patients in the group A, in 42.9% patients in the group B, in 35.0% patients in the group C, (A vs. C, $p<0.05$). Among the collagen turnover markers, ICTP, PIIINP and type IV collagen 7s were significantly higher in the patients with DCM than in the control patients (11.4ng/ml vs. 3.3ng/ml, $p<0.0001$; 0.91U/ml vs. 0.57U/ml, $p<0.005$; 6.0ng/ml vs. 4.0ng/ml, $p<0.0001$, respectively). ICTP and PIIINP were correlated with renal function whereas, only type IV collagen 7s was significantly correlated with parameters of cardiac function (EF; $r=-0.41$, $p<0.001$, LV systolic diameter; $r=0.32$, $P<0.05$, BNP; $r=0.43$, $P<0.001$). Immunohistochemistry for type IV collagen revealed strong staining in the basement membrane surrounding the cardiac myocytes, which was prominently disrupted in the hearts with severe LV remodeling.
Conclusion: Cardiac fibrosis in LVEMB is associated with worsening hemodynamic parameters. Among the ECM alterations, disruption of the basement membrane may be related with LV remodeling.

2824 | BENCH
Important role of receptor for advanced glycation end products and its ligand high mobility group box 1 in inflammatory cardiomyopathy

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Purpose: Inflammatory cardiac mechanisms contribute to progressive heart failure, an increasingly prevalent disorder with considerable morbidity and mortality. High mobility group box 1 (HMGB1) is a multifunctional protein which can stimulate inflammatory cells directly or by forming immunostimulatory complexes. HMGB1 acts hereby at least in part via RAGE (receptor for advanced glycation end products) and initiates an immune response. The aim of this study was to analyze the innate danger signal HMGB1 and its binding partner RAGE in the pathogenesis of inflammatory cardiomyopathy.
Methods: A/J-wild type (wt) and A/J-RAGE knockout mice (ko) were immunized with murine cardiac troponin I (TnI) or control-buffer. Furthermore adenoviral mediated cardiac specific overexpression of HMGB1 was performed in this mice, which were also immunized. We evaluated mechanical parameters of cardiac function and measured the concentration of Troponin T (TnT), HMGB1 and antibody titers against TnI in serum. Additionally we analyzed the protein expression and histopathological changes of the myocardium.
Results: TnI-immunized wt-mice developed severe inflammation, cardiomegaly and reduced ejection fraction (EF) of the heart. TnI immunization showed two times higher HMGB1-levels in serum which correlated with increased concentration in myocardium. In contrast TnI-immunized ko-mice showed significantly lower antibodies against TnI and reduced TnT-levels. There was almost no significant inflammation or fibrosis in hearts of TnI-immunized ko-mice compared to wt-mice. Cardiac function was also preserved in ko-animals.
Surprisingly, cardiac HMGB1-overexpression alone, without TnI immunization, also led to sustained cardiac inflammation and fibrosis in both wt- and ko- mice. This was associated with significantly reduced ejection fraction in animals of these groups (EF: wt/HMGB1: 41±9 and ko/HMGB1: 53±9, %) compared to Luciferase-vector (Luc) treated control mice (EF: wt/Luc: 87±1 and ko/Luc: 86±1, %). Five times higher serum levels of TnT were assessed in both HMGB1 treated groups compared to littermate controls.
Conclusions: Our study suggests that HMGB1 and its receptor RAGE are important components in the pathogenesis of TnI induced autoimmune myocarditis. Furthermore HMGB1 is capable to induce severe inflammation, fibrosis and congestive cardiac failure on its own and this effect seems to be in part RAGE-independent. Both proteins have a key role in inflammatory mechanisms and blockage of one of these molecules might represent a novel therapeutic strategy in the treatment of inflammatory cardiomyopathy.

2825 | SPOTLIGHT
Comparision of sST2 and galectin-3 for risk prediction relative to renal function in hospitalized patients with heart failure

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Purpose: To investigate whether risk prediction relative to renal function was different between sST2 and galectin-3 in hospitalized patients with heart failure (HF).
Methods: We consecutively enrolled 1161 patients hospitalized for HF, and followed up for 1 year. Multivariable fractional polynomials (MFP) were used to evaluate the interaction between two variables in predicting death. Multiple Cox re-

gression, discrimination, reclassification and calibration analyses were used to evaluate the prognostic value of sST2 and galectin-3 relative to clinical risk factors. The endpoint was all-cause death.

Results: 174 patients died during follow-up. MFP showed the prognosis of sST2 did not interact with estimated glomerular filtration rate (eGFR), whereas identical galectin-3 concentration was more predictive in patients with eGFR >60 mL/min/1.73m^2 (n=735) than ≤60 mL/min/1.73m^2 (n=426). After stratifying patients by eGFR of 60 mL/min/1.73m^2, the area under the curve (AUC) for sST2 (0.77) was similar to galectin-3 (0.76) in patients with high eGFR (P=0.66), but higher than galectin-3 when eGFR was lower (AUC of 0.75 vs. 0.62, P=0.001). As assessed by AUC, net reclassification improvement, and integrated discrimination improvement, sST2 improved risk prediction to reference model, irrespective of renal function. However, incorporation of galectin-3 only yielded additional prognostic value in patients with eGFR >60 mL/min/1.73m^2.

Biomarkers for predicting mortality

	Reference model (95% CI)	Model with sST2 (95% CI)	P value	Model with galectin-3 (95% CI)	P value
Patients with eGFR >60mL/min/1.73m^2					
AUC	0.82 (0.77–0.87)	0.85 (0.81–0.90)	0.008	0.86 (0.81–0.90)	0.003
IDI	Reference	0.05 (0.01–0.10)	0.026	0.04 (0.003–0.07)	0.03
H-LS	P=0.12	P=0.33		P=0.59	
Patients with eGFR ≤60mL/min/1.73m^2					
AUC	0.76 (0.70–0.81)	0.80 (0.75–0.86)	0.005	0.76 (0.71–0.81)	0.60
IDI	Reference	0.09 (0.04–0.14)	0.001	0.01 (–0.01–0.03)	0.49
H-LS	P=0.39	P=0.78		P=0.41	

CI = confidence interval; AUC, area under the curve; IDI: Integrated discrimination improvement; H-LS, Hosmer-Lemeshow stastic.

Conclusions: The prognostic value of sST2 was similar to galectin-3 in hospitalized patients with HF when eGFR >60 mL/min/1.73m^2; however, the predictive ability of galectin-3 declined when eGFR≤60 mL/min/1.73m^2.

2826 | BENCH
Anti-beta3-adrenoceptor antibodies possess partial agonist effect but do not affect the beta1-adrenoceptor-mediated inotropy and the beta3-adrenoceptor-mediated vasorelaxation in Lewis rat

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Purpose: To evaluate whether anti-β3–adrenergic receptor (AR) antibodies (ABs) possess β3–AR agonistic effect and whether active immunization producing β3–ABs and β1 and 3–ABs has deleterious effects on cardiac and vascular reactivity in Lewis rats.

Methods: Lewis rats were immunized for 3 months with peptidic sequences corresponding to the second extracellular loop of β3–AR and β1 and 3–AR. The β3–ABs were characterized by Enzyme-linked immunosorbent assay and their agonistic effect was evaluated on electrically field-stimulated isolated cardiomyocytes from adult rabbit by measuring the cell shortening. Moreover, inotropy studies and isolated aorta and mesenteric arteries studies were also conducted on immunized rats.

Results: SR58611A (10 nM), a preferential β3–AR agonist, induced a decrease of cell shortening (-39.6±4.4% (n=11)) in rabbit isolated cardiomyocytes. This decrease was significantly inhibited by preincubation with purified β3–ABs (25 μg/mL) ($p<0.001$). Moreover, the application of β3–ABs (25 μg/mL) induced a decrease of cell shortening (-18.5±3.9% (n=10)) which was partially blocked when the cardiomyocytes were preincubated with the L–748337 (1 μM), a selective β3–AR antagonist ($p<0.05$).

The cell shortening of cardiomyocytes from rats immunized against the β1–AR, in response to isoprenaline (10 nM), was significantly decreased ($p<0.05$) compared to control rats. In contrast, this effect was conserved in rats immunized against β3/β1–AR. Vasorelaxations induced by acetylcholine and SR58611A in both aorta and mesenteric arteries were unaltered by β3–AR and β1 and 3–AR immunization.

Conclusion: These results showed for the first time that β3–Bs induced a β3–AR partial agonist-like activity. They would not have a cardiovascular pathogenic action but would offset the cardiac and endothelial dysfunctions caused by β1–ABs.

NEW PREDICTORS OF OUTCOME IN CONGENITAL HEART DISEASE

2831 | BEDSIDE
Hypoalbuminemia predicts outcome in adult patients with congenital heart disease

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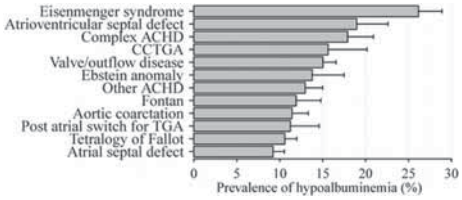
Background: In patients with acquired heart failure, hypoalbuminemia is associated with increased risk of death. The prevalence of hypoproteinemia and hypoalbuminemia and their relation to outcome in adult patients with congenital heart disease (ACHD) remains, however, unknown.

Methods: Data on ACHD patients who underwent blood testing in our centre within the last 14 years were collected. The relation between laboratory, clinical or demographic parameters at baseline and mortality was assessed using Cox proportional-hazards regression analysis.

Results: A total of 2972 ACHD patients were included. Mean age was 32.8yrs. [23.0-44.5] and 50.1% were male. Median plasma albumin concentration was 41.0 g/L [38.0-44.0], total protein 70.0g/L [66.0-74.0] and ALT 21.0IU/L [16.0-29.0]. Hypoalbuminemia (<35g/L) was present in 13.9% of pts. (Figure), hypoproteinemia (<60g/L) in 9.0% and abnormal ALT (>40U/L) in 10.3%. After a median follow-up of 5.8 years [3.4-9.8] 332 (11.2%) patients died. Hypoalbuminemia (HR 2.97, 95% CI 2.35- 3.75, P<0.0001) and hypoproteinemia (HR 1.82, 95% CI 1.35-2.46, P<0.0001) were strong predictors of outcome. In a multivariate analysis, including serum BNP, sodium, creatinine, ALT and after adjusting for functional class and disease complexity, only serum albumin and creatinine remained in the risk stratification model.



Prevalence of hypoalbuminemia

Conclusions: Hypoalbuminemia is common in ACHD patients and is related to 3-fold risk of death. It should be included in future risk stratification algorithms and may help improve management in selected groups of ACHD patients.

2832 | BEDSIDE
High-sensitive troponin-T in adult congenital heart disease

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Purpose: Adults with congenital heart disease (CHD) are at risk of developing heart failure and early mortality. High-sensitive troponin-T (hs-TnT), a marker of myocardial damage, is associated with cardiac dysfunction and worse prognosis in acquired chronic heart failure. We aimed to assess the value of hs-TnT in adults with CHD, and determine its relationship with cardiac function.

Methods: Extensive 2D-echocardiography and electrocardiography were performed and venous blood samples were taken on the same day in consecutive CHD patients. Included diagnoses comprised congenital aortic stenosis (AoS), aortic coarctation (CoA), tetralogy of Fallot (ToF), transposition of the great arteries (TGA) corrected by Mustard surgery or by arterial switch operation (ASO), congenitally corrected (cc) TGA and Fontan circulation.

Results: We included 391 patients (age 34±12 years, 58% male, 90% NYHA class I). Median hs-TnT was 4.7 (range <3–114.2)ng/L, hs-TnT was elevated (>14 ng/L) in 10% of all patients. Highest hs-TnT levels were seen in patients with a systemic RV; lowest hs-TnT levels in patients with ASO. Hs-TnT was higher in men than women ($p<0.001$), and in patients in higher NYHA class ($p<0.001$). Higher log-transformed hs-TnT level was associated with older age ($r=0.407$, $p<0.001$). All other significant associations between log-hs-TnT and echocardiographic parameters are presented in Table 1. Log-hs-TnT correlated positively with log-NT-proBNP levels ($r=0.416$, $p<0.001$).

Loghs-TnT & echocardiographic parameters

	β	p-value	β*	p-value
LA diameter	0.050	<0.001	0.029	<0.001
LV end-diastolic diameter	0.031	<0.001	0.035	0.003
RV annulus diameter	0.040	<0.001	0.042	<0.001
Pulmonary hypertension	1.153	<0.001	0.937	<0.001
Systolic systemic ventricular function	0.298	<0.001	0.160	0.001

*Adjusted for age, sex and NYHA.

Conclusions: Hs-TnT is elevated in 10% of adults with CHD, suggesting ongoing myocardial damage. Hs-TnT could contribute to monitoring ventricular function and identify deterioration in cardiac function. Higher hs-TnT levels seem strongly associated with elevated pulmonary pressures. Therefore, elevated hs-TnT in adults with CHD should be interpreted with caution in the emergency department. Follow-up data is needed to determine the additional prognostic value in these patients.

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Clinical predictors of mortality in adults with right-sided congenital heart disease

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Purpose: Patients with right-sided congenital heart disease (CHD) experience increased risk of mortality and morbidity in adulthood, due to longstanding pressure and volume overload of the right ventricle (RV). This study was designed to identify which patients with right-sided CHD are at highest risk of mortality.
Methods: Adults with right-sided CHD, followed between 2002 and 2012 in three congenital heart centers were identified. Right-sided CHD included atrial septal defect, Ebstein's anomaly, Fontan circulation, Tetralogy of Fallot, pulmonary stenosis and Eisenmenger syndrome. Clinical characteristics, electrocardiography, echocardiography (TTE), cardiovascular magnetic resonance imaging (CMR) and outcome data were analysed. Cox proportional hazards analysis was used to assess the most valuable determinants of mortality.
Results: In total 1.274 patients (27% of the total registered CHD population) with right-sided CHD were identified, with a mean age 32 years. Of these patients 77 died (6%, mean age 45 years), during a mean follow-up of 7.1 years. Symptomatic patients (NYHA functional class ≥II) (HR 4.7; p<0.01) and RV ejection fraction measured by CMR (HR 0.6; p=0.04), were the strongest predictors for mortality, corrected for underlying diagnosis. Symptomatic patients with an RV ejection fraction <40% were most likely to suffer from all-cause mortality, with an annual mortality rate of 1.8% versus 0.3% in patients without these risk factors.

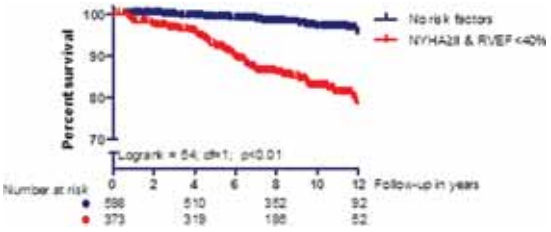

Figure 1. Kaplan-Meier analysis.

Conclusion: Symptomatic patients with right-sided CHD and RV ejection fraction below 40% have a higher annual mortality rate than patients without these risk factors. Regular follow-up and cardiovascular magnetic resonance imaging are important in the risk assessment of these patients.

2834 | BEDSIDE

Predicting survival of patients with cyanotic congenital heart disease: The value of cardiopulmonary exercise testing. Results from an international multicentre study

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Background: Patients with cyanotic congenital heart disease (CHD) are at risk of increased mortality. Few predictors of adverse outcome exist. Cardiopulmonary exercise testing (CPX) has been established as a prognostic tool in CHD patients – in general, but the value in cyanotic patients remains unclear. We analyzed the prognostic value of CPX in a large cohort of cyanotic patients.
Methods: Cyanotic patients who underwent CPX at five major centres were included. Cyanosis was defined as oxygen saturation <90% during exercise or at rest. Cox proportional-hazards analyses were performed to identify predictors of all cause mortality.
Results: 582 patients were included (52% males, age 27.3±14.2 years, 39% cyanosis at rest). During a follow-up of 4.6 years, 69 patients died. Univariate predictors were older age (HR 1.25, p=0.003), NYHA-class >1 (HR 4.0, p=0.0002), lower peak VO2 (HR 0.90, p<0.0001), lower anaerobic threshold (HR 0.90, p=0.0005), higher VE/VCO2 slope (HR 1.02, p<0.0001), lower resting O2-saturation (HR 0.95, p<0.0001), lower heart rate increase during exercise (HR 0.84 /10 bpm, p<0.0001), and lower O2-saturation during exercise (HR 0.97, p=0.0001). On multivariable analysis, peak VO2 was the only significant predictor (HR 0.88, p<0.0001). Figure 1 shows survival by quartiles of peak VO2.
In patients with resting cyanosis, lower peak VO2 (HR 0.92, p=0.002), higher VE/VCO2-slope (HR 1.02, p=0.01), lower anaerobic threshold (HR 0.90, p=0.02) and lower heart rate increase (HR 0.82 /10 bpm, p=0.001) were predictive. On multivariable analysis lower peak VO2 was the only predictor.

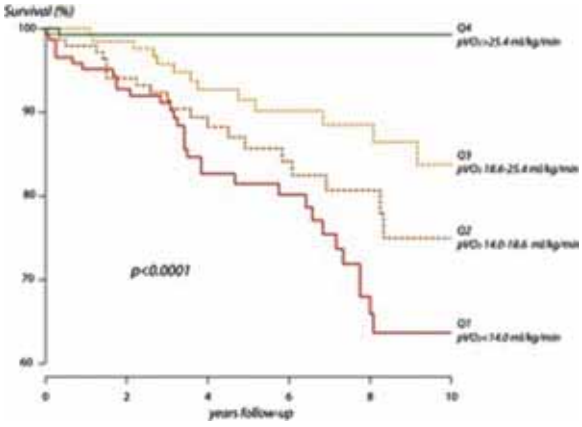

Figure 1

Conclusion: Our study confirms the predictive value of peak VO2 in cyanotic patients with CHD and suggest that CPX can be used for risk stratification independently of cyanosis.

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Depressive symptoms requiring antidepressant drug therapy in adult congenital heart disease, relate to gender and disease severity and are independently associated with higher mortality

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Background: Symptoms of depression are not uncommon in adults with congenital heart disease (ACHD) and reduce quality of life. However, the frequency of the requirement of antidepressant drug (ADD) therapy in this growing population has so far not been studied and the impact of depression on survival remains largely unknown.
Methods and results: We retrospectively identified all ACHD patients who were treated with ADDs between 2000 and 2011 at our centre. Patients receiving ADDs for migraine or indications other than depression were excluded. Start of ADD therapy was ascertained for all patients and patients were censored when therapy was terminated.
Out of 7,108 patients under active follow-up, 212 patients (3.0%) were on ADD therapy. The majority were treated with selective serotonin reuptake inhibitors (SSRIs, 73.6%), while only 17.0% received tricyclic antidepressants. Almost twice as many female patients (3.9%) were treated with an ADD compared to males (2.0%). The percentage of patients on ADD increased with disease complexity (simple lesions 2.1%, medium complexity 3.4%, high complexity lesions 5.2%, p<0.0001). Over a median follow-up time of 10.0 years (IQR 5.3-12.5 years) 409 patients (5.8%) died. Patients with ADD therapy were more likely to die compared to patients without AAD therapy (Hazard ratio [HR] 2.0 [95% CI 1.3 – 3.1], p=0.002). The association between ADD therapy and mortality was independent of disease severity, age, socioeconomic class and gender. Male patients treated with ADD had a 3.5-fold higher risk of mortality compared to males not requiring such therapy (HR 3.5 [95% CI 2.0-6.1], p<0.0001), while the association between ADD drugs and mortality was weaker in females (HR 1.3). Mortality risk on ADD therapy was statistically independent of the use of non-psychogenic QT-prolonging drugs, and no significant interaction between treatment with QT-prolonging drugs and ADDs was found (p>0.05 for both).
Conclusions: Severe depression requiring drug therapy is relatively rare in adults with congenital heart disease but is associated with significantly increased mortality and this effect is particularly evident in male patients. Patients requiring ADD may, therefore, benefit from special medical attention. In addition, this especially vulnerable subgroup of patients may benefit form a close collaboration between ACHD specialists and psychiatrists.

2836 | BEDSIDE

Attendance of outpatient clinic appointments amongst adults with congenital heart disease: predictors and relation to outcome

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Background: Adult Congenital Heart Disease (ACHD) guidelines advise life-

long, regular, follow up in predefined intervals in ACHD patients. However, limited data exist to support this position. We aimed to examine whether compliance to regular outpatient clinic appointments vs. non-attendance has an impact on outcome.
Methods and results: We examined 4461 adult patients and their records under follow up at our ACHD center between 1991-2008. Clinic attendance was quantified from electronic hospital records. For survival analysis we included clinic appointments before 2008 with follow up starting at the last attended visit before 2008. Overall 24% of scheduled clinic appointments were not attended. The main predictors of clinic non-attendance (CNA) were non-caucasian ethnicity, lower socioeconomic status, younger age, number of previous CNAs and the lack of planned additional investigation/s (e.g. echocardiography) scheduled for the same visit. During a cumulative follow-up time of 48,828 patient-years 366 patients died. Both, the number of CNAs (HR=1.08, 95%CI 1.05-1.12 per CNA, P<0.001) and the ratio of CNA to follow up period (HR=1.23, 95%CI 1.04-1.44 per CNA/year, P=0.013) emerged as independent predictors of mortality, also after adjustment for patients' age, disease complexity, functional class and socioeconomic status.
Conclusions: Patient adherence to scheduled ACHD outpatient-clinic visits is associated with better survival. Identifying patients at increased risk of CNA in a single tertiary centre was feasible. Our novel data provides previously lacking evidence in support of periodic assessment of ACHD patients at tertiary clinics. Non-attenders should be specifically targeted and receive counselling to modulate their increased risk of death.

2837 | BEDSIDE
Percutaneous interventions in Fontan circulation and the prognostic implications of having a left or right systemic ventricle

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Purpose: Our aim is to describe the percutaneous interventional procedures (PIP) performed in a cohort of Fontan patients, and the prognostic implications of the need of these procedures and the presence of a left or right systemic ventricle.
Methods: Retrospective study of patients with Fontan circulation completed at our center between 1995 and 2013. We analyzed the different types of PIP performed, the overall survival and the survival free from PIP.
Results: Of the 91 patients analyzed (15.5±5.4 years of age, 62.6% males), 46 (50.5%) required at least one interventional catheterism. The most frequent procedures were pulmonary artery angioplasty (27 procedures), angioplasty of the inferior cavopulmonary connection conduit (9 procedures), and collateral vessels embolization (7 procedures). Estimated survival at 10, 20 and 30 years of follow-up was 96.2%, 94.7% and 89.4%, respectively, and did not differ between patients who needed or not needed PIP (Figure). Estimated survival free from PIP of the entire cohort was 16.1 years (95% CI: 14.2–18.1 years). There were 4 deaths in the group of patients who underwent PIP and 2 deaths in the group without PIP (p=0.32). All 6 deaths occurred in the group of patients with a right systemic ventricle. Patients with a right systemic ventricle needed more frequently PIP than patients with a left systemic ventricle (61.2% Vs. 38.1%, p=0.028) and had a lower overall survival (Fig. 1) and survival free from PIP (13.7 years Vs. 18.9 years, p=0.015).
Conclusions: The need of PIP did not increase mortality in our cohort of Fontan patients. Patients with a right systemic ventricle had a lower overall survival and survival free from PIP than patients with a left systemic ventricle.

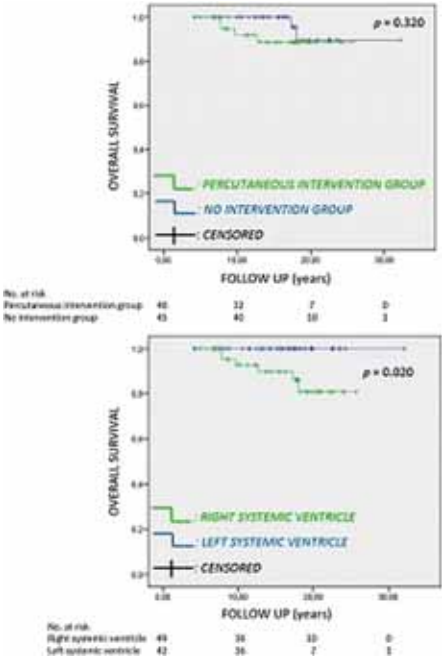

Figure 1. Overall survival.

2838 | BEDSIDE
Cardiac MRI derived measures of biventricular dyssynchrony correlate with myocardial deformation, ventricular function and objective exercise capacity in patients with repaired tetralogy of Fallot

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Background: Electrical asynchrony with prolonged QRS duration is common in patients after repair of tetralogy of Fallot (rToF) and has been linked to increased risk of sudden cardiac death and right ventricular (RV) dysfunction. We investigated biventricular myocardial dyssynchrony using cardiac magnetic resonance imaging (cMRI) and feature tracking analysis (FT) in a large ToF cohort and compared it to myocardial deformation parameters, conventional parameters of ventricular dysfunction and clinical parameters.
Methods: Between 2005 and 2008 rToF patients underwent standardized cMRI investigations as part of a nationwide study of the German Competence Network for Congenital Heart Disease. In all patients conventional parameters of ventricular function and volumes were measured. We prospectively assessed myocardial deformation and analysed regional wall motion abnormalities of the RV and the left ventricle (LV) using cMRI-FT (TomTec, Germany). The main measure of dyssynchrony was the maximal time difference (wall motion delay) of the regional strain as a parameter of mechanical biventricular dyssynchrony. In addition, clinical parameters and measures of cardiopulmonary exercise capacity were available at the time of cMRI.
Results: Overall 345 patients (56% male, mean age 17.5±8.3 yrs., pulmonary regurgitation degree 2.8±1.1; RVEDVI 121±33ml/m^2, RV EF 50±9%; LV EF 57 ±9%) were included. Parameters of biventricular wall motion delay correlated significantly with global FT-strain parameters (r-values between 0.23 and 0.43, p<0.0001 for all imaging planes assessed). Furthermore, we found a significant correlation between circumferential RV motion delay and QRS duration (r=0.15, p=0.006). Higher LV and RV wall motion delay parameters were also associated with lower peak oxygen consumption (r= -0.12 and -0.13, p<0.05, respectively) and a worse LV and RV ejection fraction (r= -0.14 and -0.20, p<0.02, respectively).
Conclusions: Assessment of parameters of mechanical dyssynchrony is feasible using cMRI-FT in contemporary ToF patients. Parameters of mechanical dyssynchrony correlate with electrical asynchrony, biventricular function and objective exercise capacity in this setting. These novel parameters may be of prognostic value and should be included in future outcome studies.

2839 | BEDSIDE
Risk factors associated with mortality in the surgical treatment of 588 patients with the simple total anomalous pulmonary venous connection

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Objective: To analyse the surgical results and the risk factors of mortality of patients with total anomalous pulmonary venous connection.
Methods: A total of 588 patients with surgically corrected TAPVC from October 1996 to September 2013 admited to our hospital were enrolled in this study.Patients only with VSD, ASD and PDA were included.Data reviewed include age, weight, anatomic type, operative data...
Results: The median age and weight at repaire was 4.35 years old and 12.1 kg. The TAPVC anatomy was supcardiac in 290 (49.3%), cardiac in 238 (40.5%), infracardiac in 20 (3.4%), and mixed in 40 patients (6.8%). Overall in-hospital surgical mortality for simple TAPVC was 5.8% (34/588). Mortality was 11.1% (30/270) from 1996 to 2007, and 1.3% (4/318) from 2008 to 2013. The number of in-hospital deaths was 34, consisting of supcardiac in 15, cardiac in 12, infracardiac in 1, and mixed in 6 patients. The causes of death were respiratory failure (18 patients), serious low cardiac output syndrome (9 patients), sudden cardiac arrest (3 patients), toxic shock syndrome (1 patient) and MODS (3 patients). There was a significant decrease in mortality when comparing 1996 to 2007 with 2008 to 2013 (P<0.01). Significant risk factors for mortality were young age (P<0.01), low weight (P<0.01), long CPB time (P=0.002), long OCCLD time (P=0.002) and cardiac connectin type (P<0.01).
Conclusion: Operative results of TAPVC have dramatically improved in the past 17 years. However patients having young age, low weight, long CPB time, long OCCLD time increased operative mortality. Specific subtypes still experience significant mortality.

2840 | BEDSIDE
Cancer: another threat for adults with congenital heart disease

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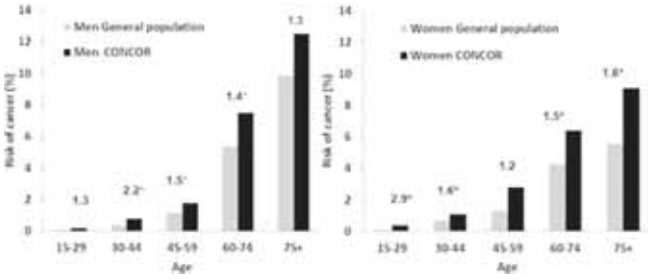
Background: Survival from congenital heart disease (CHD) has improved dramatically due to improved treatment. However, clinical observations reveal the impression that malignancies would be more prevalent in this relatively young population with a generally healthy lifestyle. Data on this topic are scarce.
Purpose: The primary objective is to evaluate the risk of cancer among adults with CHD.
Methods: To determine the risk of cancer in adult patients with CHD all patients included in the CONgenital CORvitia Dutch national registry (CONCOR) between 2001 and 2013 were linked to the national cancer registry. 5-years prevalence in 2012 was determined among CONCOR patients who were alive at 1-1-2012, based on ICD-10 diagnosis of malignancies in the 5 years prior to 2012.
Results: In total, 640 cancers were found in 573 CHD patients among the cohort of 14.326 patients. As displayed in figure 1, especially in the younger age groups in both men (30 to 44 years: RR 2.2, 95%CI 1.1-4.3) and women (15 to 29 years: RR 3.1, 95% CI 1.4-6.7) the risk of cancer was significantly higher than in the general population. Breast cancer was the most frequent type of cancer in women (40%) and prostate cancer in men (19%). Lung cancer was the least frequent (2% in women, 6% in men, 4% in total) type of cancer in adults with CHD. In addition to the increased risk for cancer, the age at occurrence was also lower in adults with CHD. For example, the average age at diagnosis for breast cancer was 52 years in CHD compared to 60 years in the general population. For lung cancer this was 58 years versus 65 years.



5-year prevalence of cancer

Conclusion: Cancer prevalence is higher than expected among adults with CHD. Further research needs to define risk of cancer by type of CHD and the association with radiation and genetic predisposition.

HYBRID IMAGING: THE FUTURE?

2845 | BEDSIDE
Novel hybrid positron emission tomography - magnetic resonance (PET-MR) multi-modality inflammatory imaging has improved diagnostic accuracy for detecting cardiac sarcoidosis

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Background: Cardiac sarcoidosis (CS) is associated with poor outcomes, but detection remains difficult. Few studies evaluate 18-fluorodeoxyglucose positron emission tomography (PET) and cardiac magnetic resonance imaging (MRI) for CS diagnosis. None examine a novel hybrid PET-MR approach. We sought to examine the diagnostic accuracy of hybrid PET-MR imaging for CS detection.
Methods: 51 consecutive patients with biopsy-proven or clinically suspected CS (age 48±13 years, 32% males) underwent hybrid PET-MR imaging. 18-FDG tracer uptake and late gadolinium enhancement (LGE) were qualitatively assessed on a binary scale and quantitatively by measuring standardised uptake value (SUV) and % LGE detected in each myocardial segment. Sensitivity and specificity of PET-MR for CS diagnosis was calculated. Inter-modality agreement was performed by the Cohen κ method. Coefficient of variance (COV) was performed to determine whether SUV quantification analysis discriminated between CS presence and absence.
Results: 37 (73%) of the patients had confirmed sarcoidosis; 46% were histologically proven and 59% had cardiac involvement according to JMHW guidelines. FDG uptake on PET-MR was equivalent to PET-CT ($p<0.001$), confirming that simultaneous hybrid PET-MR is feasible.
When considered in isolation, sensitivity of PET and MR at detecting abnormalities was 0.65 and 0.6, respectively. In contrast, hybrid imaging had improved sensitivity of 0.89 in detecting probable cardiac sarcoidosis with specificity, positive and negative predictive values of 0.42, 0.8 and 0.6, respectively. Sensitivity for detecting confirmed CS using hybrid PET-MR was 100%. Notably, there was poor inter-modality agreement between the location of increased SUV and LGE (k = 0.021). This may reflect the natural history of CS with progression from inflammation to scar and also account for the sensitivity of hybrid imaging. Coefficient of variance analysis of SUV uptake suggested that a COV above 25% predicted CS.
Conclusion: This is the first study to describe the feasibility and improved diagnostic accuracy of novel hybrid cardiac PET-MR imaging in CS. This technique may allow for more accurate and earlier diagnoses and may also allow titration of therapy according to disease activity.

2846 | BEDSIDE
The functional effects of intramyocardial course of coronary arteries and its relation to coronary atherosclerosis

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Purpose: Myocardial bridging (MB) of coronary arteries seen as intramural course is a frequent finding in computed tomography angiography (CTA). We studied the heamodynamic consquences of MB and it's relation to coronary atherosclerosis.
Methods: We prospectively studied 100 patients aged 63±7 years with intermediate likelihood of CAD using CTA, 15-Oxygen (15O) water positron emission tomography (PET) and invasive coronary angiography (ICA). Segments with either superficial ($>$1mm) and deep ($>$2mm) intramural course were identified. Myocardial perfusion (ml/g/min) at rest and at adenosine stress and coronary flow reserve (CFR) were calculated. The systolic collapse of MB segments was recorded in ICA.
Results: MB was detected in 34 (34%) of patients in 48 different vascular segments. Of these 24 (50%) were deep. The MBs were in LAD or diagonal branches (18), LCX (15), intermediate artery (12) and RCA (3). MB was more prevalent in men (29 vs. 5, $p<0.001$), but it was not related to other risk factors of CAD. Systolic constriction on ICA was present in 14 of the 48 (29%) MB in CTA. In the patients without obstructive CAD, stress perfusion distal to MB was comparable with remote control segments (3.3±0.9 vs. 3.3±0.7, n=24, p=0.88). The rest perfusion was higher and, consequently, CFR was lower in the regions supplied by MB vessels but this was explained by the anatomical location since there was no difference between MB segments and control segments from patients without MB (3.1±0.8 vs. 3.4±1.2, p=0.20). The myocardial perfusion was comparable with the superficial and deep MB vessels (3.0±0.9 vs. 2.8±1.2, p=0.47) and in the segments with and without systolic constriction (3.0±0.9 vs. 2.7±1.0, p=0.43). Presence of atherosclerosis and average number of plaques as well as coronary calcium scores were comparable in coronaries with and without MB (73% vs. 60%, p=0.14; 2.0±1.6 vs 1.5±1.7, p=0.06; 260±158 vs. 266±123, p=0.24). Prevalence of obstructive CAD was higher in coronaries with MB (33% vs. 14%, p=0.003). However, this was also explained by the anatomic locations of MB since there was no difference with matched LAD, LCX and RCA control segments. Plaques were more frequently located proximal to MB (21, 72%) than at MB (2, 7%) or distal to a MB (6, 21%).
Conclusions: Intramural course of coronary arteries is common in CTA but only about third of these will have systolic constriction. MB is not associated with abnormal myocardial perfusion during pharmacological stress. Atherosclerotic lesions were located predominantly proximal to intramural coronary arteries.

2847 | BEDSIDE
Non invasive anatomical and functional assessment of coronary artery disease

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Introduction: In suspected coronary artery disease (CAD), invasive coronary angiography (ICA) traditionally emerges as the diagnostic tool of choice. However, patients undergoing ICA often have normal coronary arteries or no significant disease, emphasizing its risks and costs. Moreover, assessment of functional fractional reserve (FFR) in ICA was shown to have prognostic implications on revascularization. In the last decade, Coronary Computed Tomography Angiography (CTA) and Cardiac Magnetic Resonance Perfusion Test (CMR-Perf) have gained their place in CAD management through accurate anatomical and functional assessment, respectively.
Purpose: Our group studied the added value of integrating CTA and CMR-Perf in the diagnostic performance of functional significant CAD by the actual reference standard, FFR.
Methods: 101 patients consecutively referred for outpatient CAD evaluation, submitted to CTA and CMR-Perf one week before ICA, were included. Data was blinded at the time of ICA. FFR was measured if $>$40% stenosis was found in open epicardic coronary arteries with a diameter $>$2 mm. To evaluate the diagnostic potential of integrating non-invasive anatomical and functional assessment (CT+CMR int), lesions were considered positive only if $>$50% at CTA with a

correspondent perfusion defect in CMR-Perf. A follow-up period [mean period of 2.9±0.6 years (0.3 to 3.8 years)] was completed.
Results: All patients completed the study protocol without adverse effects. Forty-four patients were classified as positive for disease. CAD assessment by CTA had an excellent sensitivity and NPV (100%) for detection of functionally significant lesions. As expected, the specificity and PPV were comparatively lower (61 and 67%, respectively). Diagnostic accuracy by FFR was 78% for CTA, 88% for CMR-Perf and 92% for CT+CMR int. When ROC curves were drawn to compare diagnostic accuracy, the integrated protocol showed statistically significant superiority (AUC=0.917, 95% CI 0.845-0.963) compared with CTA (AUC=0.807, 95% CI 0.716-0.879, p=0.0057) or CMR-Perf (AUC=0.882, 95% CI 0.802-0.938, p=0.0398) alone. Considering coronary revascularization prediction during follow-up, the integrated protocol remained with a superior performance.
Conclusions: Our study demonstrates the advantages of integrating anatomical and functional noninvasive evaluation based on CTA and CMR-Perf. Its superior diagnostic accuracy can lead to a considerable reduction in the invasive approach for CAD diagnosis, limiting it to cases with the intention of revascularization, with less risks and greater comfort for patients.

2848 | SPOTLIGHT
Cardiac 18F-FDG PET/MRI for simultaneous quantification of myocardial injury in patients with acute myocardial infarction: initial results and further perspective

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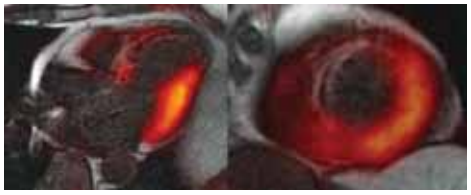
Purpose: To quantify myocardial injury (MI) assessed by hybrid 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/magnetic resonance imaging (MRI) in acute myocardial infarction (AMI).
Methods: Simultaneous PET/MRI was performed in 25 prospectively enrolled patients (23 male; age: 54±14years, event-to-PET/MRI time: 8±5days) with an AMI and early percutaneous reperfusion therapy (pain-to-balloon time: 4±5h). Cine-,T2-weighted and late gadolinium-enhanced (LGE) images were acquired in parallel to volumetric PET data. Short-axis LGE and PET images were mapped as polar plots to quantify infarct transmurality (ITM), the enhanced area in LGE images (LGE%) and the area of reduced FDG uptake in PET images (PET%). Regional wall motion abnormalities (WMA) from Cine-sequences were compared to FDG uptake in each myocardial segment.
Results: Overall, PET% correlated significantly with LGE% ($r=0.57$, $p<0.01$) and ITM ($r=0.44$, $p=0.028$), whereas in 24 (96%) of 25 patients PET% was even larger than LGE% (31±11% vs. 10±10%; $p<0.0001$). In 6 (24%) of 25 patients, MI was confirmed by reduced glucose metabolism (PET%: 32±5%), although no LGE% was detectable. Correlation between PET% and LGE% depended on ITM (ITM<50%: $r=-0.19$, $p=0.50$; ITM50-75%: $r=0.68$, $p=0.14$; ITM>75%: $r=0.99$, $p=0.01$). Categorical inter-method agreement between PET and WMA over all segments was substantial ($\kappa>0.8$).



STEMI: PET/MRI fusion image (LA/SA-view).

Conclusion: MI assessed by cardiac FDG-PET/MRI in patients with reperfused AMI, showed high conformity of PET- and LGE-images in dependence of ITM. Simultaneous assessment of infarct quantification and myocardial viability may improve risk stratification of patients in the setting of acute ischemia.
Comment: Further sub-analyses will be performed till presentation.

2849 | BEDSIDE
Morphological characteristics of culprit coronary lesions according to clinical presentation: insights from a multimodality imaging approach

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Background: Currently there is great interest to characterize vulnerable plaques. New intracoronary diagnostic techniques have the potential to provide important pathophysiological insights of coronary plaques.
Objective: The aim of this prospective study was to assess the morphological characteristics of culprit lesions according to the clinical presentation using several invasive and non-invasive imaging methods (multislice computed tomography [MSCT], angiography, intravascular ultrasound [IVUS] and virtual histology [VH]).
Methods: A total of 46 patients were included in the study. These patients were considered for coronary interventions following acute coronary syndromes or stable coronary artery disease. Before the interventional procedure a MSCT was performed. A study by IVUS and VH was performed in all culprit lesions immediately before interventions.
Results: MSCT detected a lower radiographic density (76.1±50.1 vs. 206.7 ±134.5 Hounsfiel units, $p<0.001$) and a higher remodeling index (RI) (1.18±0.34 vs. 0.98±0.26, $p=0.34$) in unstable patients. Besides, unstable patients had a significantly lower calcium score as measured by the Agatston method (90.9±102.1 vs. 261.3±214, $p=0.022$). IVUS found a larger plaque area (14.48±3.8 mm^2 vs. 9.91±3.05 mm^2, $p<0.001$) and a higher RI (1.15±0.2 vs. 0.89±0.14, $p<0.001$) in the culprit lesions of unstable patients. Furthermore, in unstable patients IVUS-detected calcification was lower whereas the prevalence of soft lesions and lesions with positive remodeling was higher. On VH the composition of culprit plaques in unstable patients had a lower amount of calcium in the area of greatest stenosis severity (4.8±5.8% vs. 10.8±10.1%, $p=0.021$) and a trend towards a lower percentage of calcium volume (6.14±6.3% vs. 9.8±6.1%, $p=0.057$). In addition, unstable patients had a higher prevalence of lesions with vulnerable characteristics by VH (plaque area ≥40% and necrotic core ≥10% without evident overlying fibrous tissue) (19% vs. 0%, $p=0.028$). In the multivariate logistic regression analysis, RI by IVUS and density measurements by MSCT (odds ratio [OR] = 4.97, 95% confidence interval [CI] 1.35 to 18.39, $p=0.016$ and OR = 0.98, 95% CI 0.97 to 0.99, $p=0.041$, respectively) were the only predictors of unstable lesions.
Conclusions: Our study with a multimodality imaging strategy (including invasive and non-invasive techniques) adds further evidence on the best morphological criteria of instability in culprit lesions. RI by IVUS and low radiographic density by MSCT were the only independent predictors of unstable lesions.

2850 | SPOTLIGHT
Three-dimensional fusion of morphological data obtained by coronary computed tomography angiography with quantitative echocardiographic data on regional myocardial function

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Purpose: Three-dimensional (3D) fusion of morphological data obtained by coronary computed tomography angiography (CCTA) with functional data from resting and stress echocardiography could potentially provide additional information compared to examinations results analyzed separately and could increase the diagnostic and prognostic value of non-invasive imaging in patients (pts) with suspected coronary artery disease (CAD). Using software developed in our institution, we aimed to assess the feasibility and reproducibility of 3D fusion of morphological CCTA data with functional echocardiographic data regarding regional myocardial function.
Methods: 30 pts with suspected CAD underwent CCTA and resting transthoracic echocardiography. From CCTA we obtained 3D reconstructions of coronary arteries and left ventricle (LV). Off-line speckle-tracking analysis of the echocardiographic images provided parametric maps depicting systolic longitudinal strain in 17 segments of the LV. Using custom software, three independent investigators fused echocardiographic maps with CCTA reconstructions in all pts. Based on obtained fused models (fig. 1) each segment of the LV was assigned to one of the major coronary artery branches.
Results: The mean time necessary for data fusion was 65±7seconds. Complete agreement between independent investigators in assignment of LV segments to coronary branches was obtained in 94% of segments. The average coefficient of agreement (kappa) between the investigators was 0,950 and the intraclass correlation coefficient was 0,9329 (95% CI 0,9227-0,9420).

Figure 1. Result of data fusion.

Conclusions: 3D fusion of morphological CCTA data with quantitative echocardiographic data on regional myocardial function is feasible and allows for highly reproducible assignment of myocardial segments to coronary artery branches.

BASIC AND TRANSLATIONAL SCIENCE HOT LINE ON VASCULAR DISEASE

2851
Systemic atherosclerotic inflammation following acute myocardial infarction

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Purpose: In murine models, acute myocardial infarction causes atherosclerotic inflammation and progression. Using combined positron emission and computed tomography (PET-CT), we investigated whether this phenomenon occurs in humans. We determined whether aortic atherosclerotic plaque inflammation demonstrated by 18F-FDG uptake would be increased in patients with a recent myocardial infarction in comparison to patients with stable coronary heart disease, and whether this would be most marked in those with larger infarctions. Furthermore, we explored whether infarct size could predict recurrent early myocardial infarction.
Methods: Forty patients with recent myocardial infarction and 40 with stable angina pectoris underwent thoracic 18F-fluorodeoxyglucose (18F-FDG) and 18F-fluoride PET-CT. Radiotracer uptake was measured in aortic atheroma and non-vascular tissue (para-spinal muscle). In 1,003 patients enrolled in the Global Registry of Acute Coronary Events (GRACE), we assessed whether infarct size predicted early (≤30 days) and late (>30 days) recurrent coronary atherothombotic events.
Findings: Compared to patients with stable angina, patients with myocardial infarction had increased aortic 18F-FDG uptake (mean TBRmax 2.15±0.30 versus 1.84±0.18, P<0.0001) despite having similar aortic atherosclerotic burden (aortic Agatston score: 135 [0–805] versus 538 [4–1870] AU, P=0.12; coronary artery calcium score: stable angina 599 [60 -1302] versus myocardial infarction 159 [42–456] AU, P=0.006) and para-spinal muscular 18F-FDG uptake (0.79±0.25 versus 0.75±0.21, P=0.52). Patients with ST-segment elevation myocardial infarction had larger infarcts (peak plasma troponin concentration 32,300 [10,200–50,000] versus 3,800 [1,000–9,200] ng/L, P<0.0001) and greater aortic 18F-FDG uptake (2.24±0.32 versus 2.02±0.21, P=0.03) than those with non-ST elevation myocardial infarction. Aortic 18F-FDG uptake correlated with peak plasma troponin concentration (r=0.42, P=0.01) in all patients with myocardial infarction. There were no differences in aortic 18F-fluoride uptake within the patient groups. On multivariate analysis, peak troponin I concentrations were an independent predictor of early recurrent myocardial infarction (tertile-3 versus tertile-1: relative risk 4.30 [95% CI, 1.85–9.96], p=0.001) but did not predict late re-infarction.

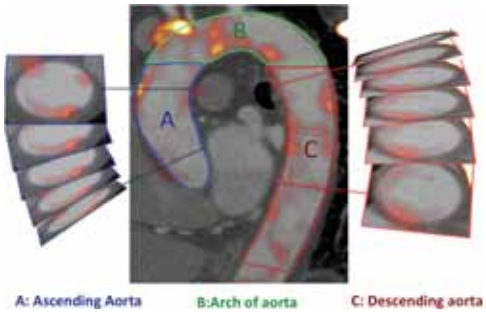


Figure 1. Measurement of 18F-fluorodeoxyglucose (18F-FDG) and 18F-fluoride (18F-fluoride) uptake in the aorta.

Interpretation: Using 18F-FDG PET imaging, we have demonstrated increased metabolic activity in remote atherosclerotic plaques in patients with recent myocardial infarction. This uptake exceeded that observed in patients with stable coronary disease, who had a greater coronary atherosclerotic burden, and correlated with the degree of myocardial necrosis suggesting a causal association. Using the GRACE registry, we explored the validity of our findings from the imaging cohort to assess whether infarct size and the associated increase in atherosclerotic inflammation could predict recurrent coronary atherothombotic events in every day clinical practice. Patients with the largest infarcts had more than a four-fold increase in their risk of early recurrent myocardial infarction with baseline tertiles of plasma troponin concentration emerging as an independent predictor of these events. We therefore provide clinical data to support the hypothesis that myocardial infarction exacerbates systemic atherosclerotic inflammation, destabilizes remote atheromatous plaque and causes an increase in recurrent atherothrombotic events.

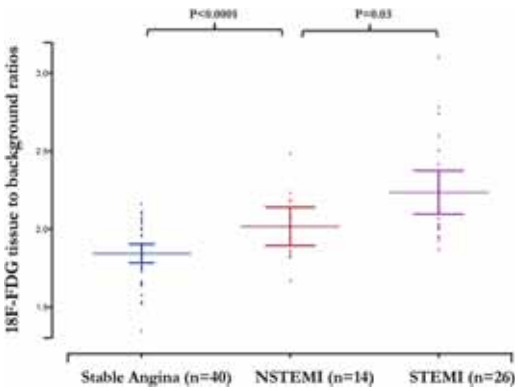
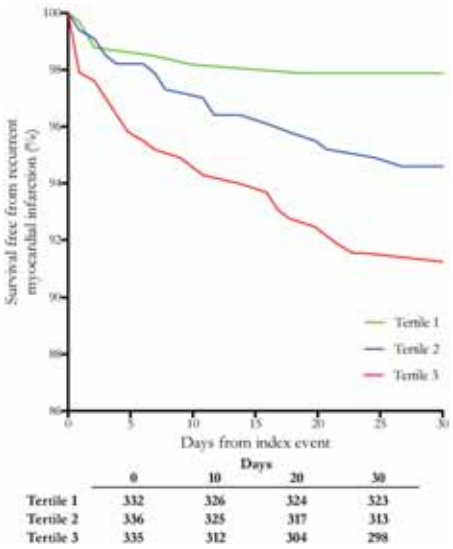


Figure 2. Uptake of 18F-fluorodeoxyglucose by aortic atherosclerosis in patients with stable and unstable coronary heart disease.



Days	0	10	20	30
Tertile 1	332	326	324	323
Tertile 2	336	325	317	313
Tertile 3	335	312	304	298

Figure 3. Kaplan–Meier curves demonstrating survival free from early recurrent myocardial infarction at 30 days.

2852
Simvastatin reverse cerebral microvascular rarefaction and improve endothelial function in a hypertension model

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Purpose: Statins are widely used in the treatment of dyslipidemia, which is usually associated with cardiovascular abnormalities including hypertension. Microvascular rarefaction and endothelial dysfunction are aggravating factors of hypertensive end-organ damage. Thus, this study was designed to investigate the acute effects of simvastatin (SIM) on cerebral microcirculation and endothelial function in spontaneously hypertensive rats (SHR).
Methods: Male Wistar normotensive rats (WKY) and SHR were divided into 3 groups of 6 animals each: WKY-CTL and SHR-CTL treated with 0.9% saline solution, and SHR+SIM treated with SIM 30 mg/kg/day during 3 days by gavage. Systolic blood pressure (SBP) was measured by a tail-cuff plethysmography system. We investigated brain functional capillary density (FCD) and vascular reactivity using intravital fluorescence videomicroscopy after IV injection of FITC labeled dextran. We assessed pial arterioles endothelium-dependent vasodilation responses to acetylcholine (Ach, 10^{-6} M) administration.
Vascular responses were expressed as percentage changes from the baseline arteriolar diameters. Values are means ± S.E.M, compared by ANOVA and Bonferroni's Test, p values <0.05 were considered significant. All protocols were in accordance with the internationally principles for the Care and Use of Laboratory Animals.
Results: SIM administration reduced SBP in SHR (SHR-CTL 203±3 vs. SHR+SIM 172±6 mmHg; p<0.001). Cerebral FCD was reduced in hypertensive rats compared with normotensive rats (SHR-CTL 337±61 vs. WKY-CTL 421±35 capillaries/mm^2; p<0.05). The administration of SIM during 3 days induced a significant increase in cerebral FCD in hypertensive rats (SHR+SIM 530±31 capillaries/mm^2; p<0.05). Ach induced arteriolar vasodilation in WKY rats (WKY-CTL +6.6±1.2%) but arteriolar vasoconstriction in SHR (SHR-CTL −1.4±1.3%; p<0.05); SIM restored Ach-induced arteriolar vasodilation (SHR+SIM +11.5±3.1%; p<0.05). Microvascular endothelial dysfunction in SHR was associated with a down-regulation of endothelial nitric oxide synthase (eNOS) expression in the brain (SHR-CTL 0.76±0.1 vs. WKY-CTL1.25±0.2 eNOS/GAPDH (AU); p<0.05). Treatment of SHR with SIM normalized the brain expression of eNOS (SHR+SIM 2.13±0.7 eNOS/GAPDH (AU); p<0.05).
Conclusions: To date, this is the first study showing that acute treatment with simvastatin reversed cerebral microvascular rarefaction and restored brain microvascular endothelial function of hypertensive rats. In addition to cholesterol-lowering effects, vascular pleiotropic effects of statins could turn out to be a new therapeutic approach for improving microcirculatory function in hypertensive patients.

2853

Increased anti-fibrinolytic proteins characterize elderly individuals with un-healthy ageing due to cardiovascular disease and cognitive decline

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Purpose: The aim of the present study was to identify the proteins potentially involved in healthy longevity by investigating the plasma proteomic profile in a group of octogenarians with healthy ageing in comparison with an age-matched group of patients with un-healthy ageing, including cognitive impairment and previous manifestation of cardiovascular disease.
Background: Ageing is considered as one of the most important risk factors for vascular disease progression, atherosclerosis and clinical event presentation. Moreover, vascular disease is an important contributor to cognitive decline. In this study we sought to investigate the plasma proteomic profile in a group of octogenarians with healthy ageing in comparison with an age-matched group of patients with un-healthy ageing and an atherothrombotic phenotype to identify the proteins potentially involved in healthy longevity.
Methods: Plasma samples were obtained from octogenarian (87±0) subjects (N=100). Healthy ageing octogenarians (preserved performance in activities of daily living and cognitive function) had not had any clinical manifestation of cardiovascular disease (HA-NoCVD) while the unhealthy ageing octogenarians had cognitive and functional decline, malnutrition state and a previous ischemic event (acute myocardial infarction and/or ictus; UHA-CVD). After depletion of the 7 most abundant proteins the plasma proteome was analyzed by 2D-electrophoresis and mass-spectrometry (MALDI-TOF/TOF). Results were validated by ELISA in HA-NoCVD (N=38), in UHA-CVD (N=27) and in an intermediate population without cognitive impairment who had suffered a previous clinical manifestation of cardiovascular disease (HA-CVD; N=35).
Results: Coagulation and haemostasis-related proteins represented 39% of the observed changes between healthy and un-healthy ageing patients. Alpha-2-antiplasmin (A2AP) and coagulation factor XIII B chain (FXIIIB) were significantly decreased in the HA-NoCVD group when compared to UHA-CVD individuals ($P<0.05$ for both). The decrease in both proteins was validated by ELISA. Protein AMBP also showed a decrease in HA-NoCVD together with a change in RBP4 distribution profile ($P<0.05$ for both). Inter-alpha-trypsin inhibitor heavy chain H4 depicted a change in its proteomic distribution between both groups ($P<0.05$).
Conclusions: In healthy octogenarian subjects there is a coordinated decrease in antifibrinolytic proteins, such as alpha-2-antiplasmin and coagulation factor XIII. Increases in anti-fibrinolytic proteins represent an impaired capability for spontaneous microthrombus resolution leading to a higher tendency for cardiovascular disease and cognitive impairment that contribute to un-healthy ageing.

2854

Human validation of genes associated with a murine atherosclerotic phenotype

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Purpose: The genetically modified mouse is the most widely applied animal model for studying the pathogenesis of atherosclerotic disease. However, the validity for extrapolation to human atherosclerotic disease remains unexplored. In this study we assessed the association of genes identified in atherosclerotic murine models with atherosclerotic traits in humans.
Methods: We searched PubMed and Embase and identified 11,209 publications involving atherosclerotic mice that were either genetically modified or received targeted treatment. Of these there were 2,090 relevant papers reporting 651 genes that influence murine atherosclerosis. We mapped these 651 genes to their human homologue and identified 80,581 common single-nucleotide polymorphisms (SNPs) ±50 kb around the genes. Using the Athero-Express Study (AE; N=1,443) we tested these SNPs for association to histological atherosclerotic plaque characteristics. Than we performed targeted gene-based tests using VEGAS on summary level data from the AE association analyses and from CARDIoGRAM (N=143,677). We used Ingenuity to identify canonical biological pathways to which the 651 genes are mapped. The relevance of these biological pathways for human cardiovascular disease was validated using the results from our VEGAS analyses in CARDIoGRAM and the Athero-Express.
Results: Out of 651 genes 87 were nominally ($p<0.05$) associated with the presence of coronary artery disease (CAD) in CARDIOGRAM (binomial $p=1.23 \times 10^{-16}$). In addition, 159 genes were nominally associated with a plaque phenotype (either calcification, macrophages, smooth muscle cells, intraplaque vessel density and/or intraplaque hemorrhage) in the Athero-Express. We analyzed and compared the association results using Ingenuity Pathway Analysis. The 651 genes were mapped to 405 pathways, of these 234 pathways (57.78%) were nominally significant (binomial $p=1.36 \times 10^{-190}$). The 87 genes nominally significantly associated with CAD in humans were mapped to 281 pathways, and 28 out of those (9.96%) were nominally significant (binomial $p=2.57 \times 10^{-5}$). We found significant overlap between pathways involved in mice and men, but also striking discordances. For example, the LXR/RXR activation and PPARα/RXRα activation pathways were significantly associated in mice ($p=1.26 \times 10^{-54}$ and $p=1.26 \times 10^{-26}$, respectively) and in humans with CAD ($p=2.51 \times 10^{-17}$ and $p=7.94 \times 10^{-9}$, respectively) and atherosclerotic plaque phenotypes ($p<7.94 \times 10^{-3}$). In contrast, pathways for T-Helper cell differentiation ($p=3.98 \times 10^{-24}$ in mice) and dendritic cell maturation ($p=1.26 \times 10^{-36}$ in mice) were not associated with CAD in humans ($p=0.281$ and $p=0.569$, for each pathway respectively). However, the latter revealed a strong association ($p=1.63 \times 10^{-5}$) with an inflammatory human plaque phenotype in Athero-Express, supporting a role in plaque stabilization/destabilization.
Conclusions: Using an agnostic in silico gene-based approach we validated genes causal to murine atherosclerosis in humans. Our results suggest that a substantial number of gene candidates are not associated with human atherosclerotic disease or subphenotypes. This challenges the relevance of the atherosclerotic mouse as a model for human atherosclerosis, and has implications for future candidate selection.

2855

Von willebrand factor as a sensor of blood flow: Towards a real time biological assessment of aortic valve interventions

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Background: An acquired deficiency of von Willebrand Factor (VWF) characterized by a quantitative defect of VWF high molecular weight multimers (HMWM) is associated with high shear cardiovascular disorders such as aortic stenosis (AS). It has been shown that HMWM defect is usually corrected after surgical aortic valve replacement. However, the precise time course of recovery of HMWM defect in vivo remains unknown. We hypothesized that recovery of HMWM defect could occur within minutes following correction of the underlying "high shear" condition and as such could be used to monitor acute changes in shear stress induced by transcatheter aortic valve procedures.
Methods: We investigated the time course of recovery of VWF HMWM defect under conditions allowing an almost instantaneous reversion of high shear in a rabbit model of "reversible" AS (n=17). In that model AS was acutely induced and released using a balloon-inflated aortic cuff.
We further investigated the time course of recovery of HMWM defect and it's related bedside whole bood assessment (PFA-100 analyzer) in the WITAVI registry including 18 patients with AS undergoing transcatheter aortic valve procedures: percutaneous valve implantation (TAVI; n=10) or balloon valvuloplasty without valve implant (BAV; n=8). TAVI procedures were used as clinical conditions of acute recovery of"high shear" stress while BAV procedures were used as "negative controls".
Results: In the rabbit model, induction of aortic stenosis was associated with a VWF HMWM defect (normalized ratio = 0.74±0.07; $p<0.01$ versus no stenosis). Partial recovery of HMWM (0.89±0.12 versus AS baseline; $p<0.01$) occurred within 5 minutes of stenosis reversion. Thirty minutes after reversion, a complete recovery of HMWM defect was observed (0.98±0.10). In patients with AS (n=18) a VWF HMWM defect was observed at baseline (0.50±0.18). Among pa-

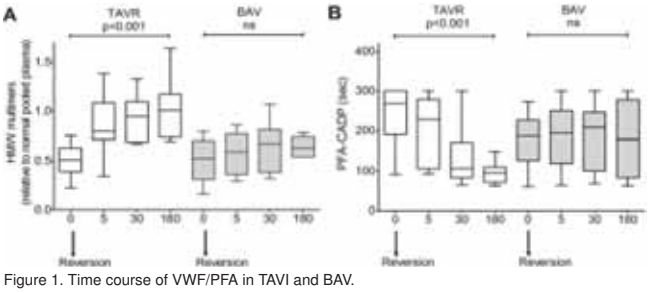

Figure 1. Time course of VWF/PFA in TAVI and BAV.

Abstract 2855 – Table 1. VWF recovery in TAVI and BAV patients

	Transcatheter aortic valve implantion (TAVI, n=10)					Balloon aortic valvuloplasty (BAV, n=8)				
	Baseline	T5	T30	180	p*	Baseline	T5	T30	T180	p*
HMW multimers (ratio versus NP)	0.47 (±0.14)	0.87† (±0.24)	0.93† (±0.17)	0.99† (±0.16)	<0.001	0.52 (±0.21)	0.58 (±0.20)	0.66 (±0.25)	0.63 (±0.10)	ns
PFA-CT ADP (sec)	252 (±68)	193† (±51)	116† (±40)	94† (±26)	<0.001	201 (±46)	212 (±61)	204 (±71)	219 (±76)	ns

Results are expressed as mean ± SD. *P values are for overall time course comparison (repeated Anova), †vs baseline $p<0.05$ (Wilcoxon rank test).

tients with AS, those treated with TAVI experienced an acute decrease in shear stress (4.47±0.41 m s^{-1} to 1.81±0.43 m s^{-1}, p<0.0001, n=10) after treatment while those undergoing BAV alone experienced a modest improvement in shear stress conditions (4.47±0.25m s^{-1} to 3.88±0.65m s^{-1}; p=0.03, n=8). In patients undergoing TAVI (n=10), similar to what was observed in the rabbit model, recovery of VWF HMWM defect was observed within minutes of valve implantation (p<0.001, Table 1 and Fig. 1A). By contrast, in patients undergoing BAV (n=8) no recovery of HMWM defect was observed (p=0.21, Table 1 and Fig. 1A). Interestingly, the time course of PFA-CADP time (sec) mimicked the recovery of HMWM defect both in TAVI in patients, in whom a rapid correction of PFA-CADP was observed (p<0.001, Table 1 and Fig. 1B), and BAV patients, in whom no correction was observed (p=0.69; Table 1 and Fig. 1B).

Conclusion: The recovery of VWF multimeric pattern is highly dynamic after reversion of AS, occurring within minutes of changes in shear stress status. Our findings suggest that VWF multimeric pattern changes, together with their assessment with a PFA-100 point of care assay, could be used in clinical practice to monitor in real time the quality of the result of transcatheter aortic valve procedures.

STRESS, AUTONOMIC REACTIVITY AND HYPERTENSION

2865 | BEDSIDE
Prognostic significance of impaired baroreflex sensitivity in a population-based sample of middle-aged subjects

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Purpose: Depressed baroreflex sensitivity (BRS) is associated with an increased risk of cardiovascular death in patients with a recent cardiovascular event. The prognostic significance of BRS in subjects without history of major cardiovascular complications is unknown. The present study tested the hypothesis that impaired BRS predicts cardiovascular death in a population-based sample of middle-aged subjects.

Methods: The present study is a part of the Oulu Project Elucidating Risk of Atherosclerosis study (OPERA), where middle-aged hypertensive and age- and sex-matched control subjects were randomly selected in the early 1990s from the national registry for reimbursement of medications. Subjects with a history of myocardial infarction or stroke were excluded. Along with clinical and laboratory assessments, BRS was measured by the Valsalva method in 559 subjects (age; 51±6 years; 300 men). The causes of death were registered during a follow-up of up to 19 years. Cardiovascular death (n=23) was defined as the primary endpoint.

Results: Cardiovascular death was predicted by smoking status, alcohol consumption, high-sensitive C-reactive protein, use of diuretics, waist circumference, and fasting glucose. Among measured risk factors, impaired Valsalva BRS (<3 ms/mmHg) was the most potent predictor of cardiovascular death (hazard ratio: 9.1; 95% CI: 3.8–21.7; p<0.001) and remained so after adjustments for the other significant predictors (hazard ratio: 5.3; 95% CI: 2.1–13.3; p<0.001).

Conclusions: Impaired Valsalva BRS is a potent and independent predictor of cardiovascular death in a population-based sample of middle-aged subjects without history of major cardiovascular complications and may have important clinical implications in early risk stratification.

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Sympathetic and metabolic effects of surgical removal of adenomas in acromegalic patients

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Background: It has been previously shown that patients with early stage of acromegaly, not accompanied by organ damage, are characterized by a profound sympathoinhibition coupled with low leptin plasma levels. It has been also shown in animal models that central administration of somatostatin is able to inhibit the adrenergic tone. Whether the surgical removal of the adenoma is able to restore the adrenergic drive and correct the metabolic alterations is unknown.

Methods: Sympathetic tone has been directly recorded to the skeletal muscle through the microneurographic technique (MSNA) in: a) 15 acromegalic patients (3 micro-, 12 macro-adenomas) in the early stage of this pathology (ACRO; age 46.6±10.3.0 years, media±SD) before and after surgery; b) 17 healthy subjects (C; age 49.1±15.6 yrs). The protocol included anthropometric, haemodynamic, echocardiographic, metabolic, humoral, blood pressure, and heart rate values before and after surgical removal of adenomas while in C data were collected only in basal conditions.

Results: Compared to C, ACRO were characterized by insulin resistance (HOMA: 1.57±0.3 vs 4.08±2.2 a.u., p<0.01) and by a significant reduction in plasma leptin (6.42±2.0 vs 1.62±1.0 μg/l, p<0.01) and MSNA (37.8±6. vs 17.7±7.7 bursts/min, p<0.01) values without any organ damage and significant changes on fat and muscle mass or water content assessed via electric impedance. After surgical removal of adenomas ACRO showed a normalization of IGF-1 and this was accompanied by a significant (p<0.01 for all) improvement in HOMA index (2.2±0.6 a.u.), in plasma leptin levels (6.0±2.6 μg/l) and in MSNA (30.1±3.2 bursts/min). No changes were observed in anthropometric, haemodynamic, echocardiographic, and electric impedance parameters. In the population as a whole we osserved a significant direct correlation between MSNA and plasma leptin levels (r=0.38, P<0.01) and an inverse correlation between leptin and IGF-1 (r=0.47, P<0.01).

Conclusions: The study shows for the first time that surgical removal of adenomas is able to almost completely normalize the MSNA and the metabolic alterations associated with the increase in GH and IGF-1 levels. The study provides also additional evidence that in the early stage of the disease plasma leptin levels may have a major role in the sympathoinhibition more than reflex influences induced by changes in water content not present in this phase. Thus surgical treatment is able to restore a condition at a lower impact on morbidity and mortality.

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Different neuroadrenergic activation and baroreflex function in resistant and pseudoresistant hypertension: a microneurographic study

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Introduction: We have recently shown that resistant hypertension (RHT) is characterized by a marked neuroadrenergic activation coupled with metabolic alterations compared to the non-resistant hypertensive state. It is unknown, however, whether these changes are specific for the RHT state or are also detectable in pseudoresistant hypertension (PRHT).

Methods: In 11 treated RHT patients, 14 treated essential hypertensives with controlled blood pressure (HT) and 12 normotensive controls (C), we evaluated sphygmomanometric blood pressure (BP), 24-hour BP (Spacelab), beat-to-beat BP (Finapres), heart rate and sympathetic nerve traffic (MSNA, microneurography). The assessments, which included plasma aldosterone, HOMA index and spontaneous baroreflex control of MSNA using linear regression analysis, were also carried out in 12 treated PRHT (7 white-coat and 5 non-compliant).

Results: The three groups of hypertensive patients had clinic BP and MSNA significantly greater than C. When matched for age, body mass index, clinic and ambulatory pressure, the RHT had a significantly higher MSNA compared to HT (65.4±2.7 vs 43.7±2.4 bs/min, P<0.02) and C (35.8±2.5 bs/min, P<0.01 for both). The PRHT showed clinic BP values similar to RHT but significantly lower values of 24-hour BP and MSNA (44.0±2.7 bs/min, P<0.02). In addition, in the RHT group the plasma aldosterone and HOMA index were significantly greater than in HT and PRHT (aldosterone:13.2±15 vs 8.6±0.6 and 9.2±1.1 ng/dl, P<0.05, HOMA: 2.3±0.3 vs 1.2±0.2 and 1.5±0.3 au). Finally, the modulation of spontaneous baroreflex control of MSNA was reduced in RHT as compared to C and HT (slope:-2.2±0.35 vs -2.9±0.4 and -2.8±0.4, P=NS) and to PRHT (slope:-2.8±0.28).

Conclusions: These data provide evidence that the neuroadrenergic overdrive detected in RHT is specific for this condition and it is not found in PRHT. This specificity might be related to the alterations in the neurohumoral profile as well as to an early impairment of baroreflex-MSNA modulation.

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Sympathetic nervous activity in patients with acute coronary syndromes: a comparative study with inflammatory biomarkers

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Introduction: Previous publications have shown that both sympathetic hyperactivity and enhanced inflammatory response are associated with worse outcomes in acute coronary syndromes (ACS). However, little is known about the correlation between these two pathologic pathways.

Objective: To evaluate sympathetic activity and inflammatory response in patients with ACS, to explore its progress over time and possible correlations.

Methods: Patients hospitalized with uncomplicated ACS were enrolled if they were 18-65 years old and have significant atherosclerosis without any other chronic disease. At fourth day (± 1 day) of hospitalization they were submitted to muscle sympathetic nerve activity (MSNA) analysis and blood sample were collected for ultrasensitive C-reactive protein (usCRP), interleukin-6 (IL-6) and Lipoprotein-associated phospholipase A2 activity (Lp-PLA2) measurements. MSNA was recorded directly from the peroneal nerve using the microneurography technique. Measurements were repeated at 1, 3 and 6 months after hospitalization. Correlations between MSNA and inflammatory markers and baseline characteristics were made using Pearson's test (non-normally distributed variables were logarithmically transformed) and multivariate regression models were performed to assess the independent effects.

Results: Fifty-three patients were included, 81% male, mean age 51.0 (SD 7.4

years). The prevalence of hypertension was 60.4%, diabetes mellitus 11.3%, and previous coronary heart disease 32.1%. The ACS presentation was STEMI in 26 patients (49.1%), NSTEMI in 21 (40.4%) and UA in 06 patients (11.5%). Both MSNA and inflammatory markers were elevated during acute phase of ACS and decreased over time. In the hospitalization phase the mean usCRP was 31.3±40.5 mg/L, IL-6 8.2±6.9 pg/ml, Lp-PLA2 185.8±52.2 nmol/min/mL, and MSNA was 64.2±19.3 bursts/100heart beats. After 6 months, the usCRP was 1.5±1.1 mg/L, IL-6 2.7±2.2, Lp-PLA2 166.9±46.6 nmol/min/mL, and MSNA was 57.9±19.3 bursts/100heart beats. This sympathetic hyperactivity was directly correlated with CKMB on the acute phase of ACS ($p<0.01$) and inversely correlated to left ventricular ejection fraction on 6-month follow-up ($p<0.01$). There was no significant correlation between the sympathetic activity and inflammatory markers in any of the analyzed phases ($p>0.05$).

Conclusion: Despite the increased levels of inflammatory markers and sympathetic activity among patients with ACS, there was no correlation between these assessments in both the acute and the chronic phase, suggesting that they might follow different pathological pathways in those patients.

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Heart rate predicts long-term mortality as well as classical risk factors

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Background: Resting heart rate (RHR) is known as a cardiovascular risk factor (RF), correlated with hypertension, cardiac failure and coronary artery disease. However, while controlling heart rate has become a treatment target, this parameter is rarely included in mortality predictive formulas. The aim of this study was to assess the risk of all-cause mortality in a general population in a prediction algorithm including RHR as an independent parameter.

Methods: Our study population consisted in patients, both women and men, who had consulted from 1995 to 2011 to the Department of Preventive Cardiology (DPC) in a Southwestern University Hospital. We excluded patients whose age was less than 30 years old and all patients with established history of ischemic heart disease. Vital status was obtained for each participant through the national database. Multivariate prediction of total mortality was evaluated with the use a Cox proportional hazards model. An algorithm for prediction of risk of mortality in primary prevention was built using Kaplan-Meier statistic and a Cox proportional hazards model.

Results: 4885 patients were included. 56% were men and the mean age was 53. After a mean follow up of 8.6 years, 129 deaths were recorded. In multivariate analysis, independent RF were age (Hazard Ratio (HR)=1.06, $p<0.001$, 95% CI [1.04-1.08]), gender (HR=5.95, $p<0.001$, 95% CI [3.48-10.19]), diabetes (HR=2.49, $p<0.001$, 95% CI [1.49-4.16]), hypertension (HR=1.44, p=0.05, 95% CI [1.00-2.08]), LDL-cholesterol>4 mmol/L (HR=2.04, $p<0.001$, 95% CI [1.40-2.96]), smoking (HR=2.19, $p<0.001$, 95% CI [1.49-3.20]), lower educational level (HR=1.81, p=0.01, 95% CI [1.18-2.79]) and resting heart rate>65 bpm (HR=1.54, p=0.02, 95% CI [1.06-2.24]). A good calibration was obtained (p value NS for Hosmer-Lemeshow χ^2 test). The median predicted risk of mortality was 6.52% and was not significantly different to the observed risk of all cause mortality (6.60%; 95%CI [5.22%-8.34%]). Considering patients with a predicted risk higher than 5%, the average predicted risk was 12%; 95% CI [5.01%-66.8%] for an observed mortality of 11.18%; 95% CI [8.77%-14.20%]. Considering patients with a predicted risk lower than 5%, the average predicted risk was 2.29% for an observed mortality of 1.85%;95% CI [1.09%-3.14%]. Furthermore, 85% of deceased patients during the following period had a risk higher than 5%.

Conclusions: RHR can be used to predict all-cause mortality in primary prevention and might be evaluated as a simple predictive tool in current practice.

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Enhancing NOS1 adaptor protein levels decreases intracellular calcium handling and neurotransmission in cardiac sympathetic neurons

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Purpose: Genome wide association studies have implicated neuronal nitric oxide synthase adaptor protein (NOS1-AP/CAPON) as a potential molecular marker of both QT abnormalities on the ECG and sudden cardiac death (SCD). SCD is often triggered by cardiac sympathetic stimulation which is also able to modulate the QT interval. Interestingly, NO generated by NOS-1 reduces norepinephrine (NE) release and is down-regulated in animals with hypertension. To establish if this adaptor protein plays a role in sympathetic neurotransmission we investigated whether endogenous NOS1-AP was present in cardiac sympathetic neurons. We also tested the hypothesis that enhancing neuronal NOS1-AP expression via adenoviral gene transfer decreases sympathetic induced NE release by altering regulation of calcium handling.

Methods and results: Immunohistochemistry demonstrated that NOS1-AP resides in cardiac sympathetic neurons in spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) controls, but the expression of NOS1-AP is significantly ($P<0.05$) reduced in the SHR (n=6) compared to the WKY (n=6). The peak [Ca2+]i transient of isolated stellate neurons was significantly enhanced in the SHR (n=12) compared to the WKY (n=11). A novel noradrenergic cell specific vector (Ad.PRSx8-NOS1-AP/mCherry) or its control vector were transfected into sympathetic stellate neurons in vitro. Western blotting showed NOS1-AP expression was up-regulated following gene transfer in the SHR (n=6 v empty virus n=6). The peak [Ca2+]i transient (n=19) was also reduced compared with Ad.PRSx8-mCherry alone (n=16). NOS1 inhibition (AAAN, 10μM) significantly increased the [Ca2+]i transient after Ad.PRSx8-NOS1-AP/mCherry transfection. Electrophysiological studies showed that the peak calcium current (ICa) density in SHR neurons overexpressing NOS1-AP (n=6) was significantly reduced compared with that of the empty vector control in SHR neurons (n=7). Averaged peak current density-voltage relationships revealed significant suppression of peak neuronal ICa density from -20mV to +20mV. Moreover, Ad.PRSx8-NOS1-AP/mCherry reduced 3H-NE release from SHR atria (n=7) compared with empty vector controls (n=6).

Conclusions: Artificial up-regulation of cardiac sympathetic NOS1-AP via targeted gene transfer can directly attenuate intracellular Ca2+ and suppress ICa, resulting in decreased NE release in the SHR. This may provide a novel method for decreasing enhanced cardiac sympathetic neurotransmission in disease states where excessive NE release might trigger sudden cardiac death in patients with QT abnormalities.

CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK POPULATIONS

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Gender differences and early outcome after coronary artery bypass graft surgery: a nationwide study

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Purpose: The outcome of female patients after coronary artery bypass graft (CABG) surgery has been reported to be less favorable compared to the outcome of male patients. Especially, the gender-specific in-hospital mortality risk has been reported to be higher in female patients. The objective of the present study was to compare women with men with respect to baseline characteristics and short-term outcome in a contemporary cohort of patients that underwent CABG surgery.

Methods: All patients (N=41269, 78% males (N=32154)) that underwent CABG surgery (conventional: N=33140, 80.3%; OPCAB: N=6391, 15.5%) in the Netherlands between January 2007 and December 2011 were included in this study. Differences in patient and procedural characteristics, and in-hospital outcome were compared between male en female patients.

Results: Female patients were older (mean age, 69 vs. 66 years, $p<0.001$), had higher logistic EuroSCORE I (median score, 6.7 vs. 4.2, $p<0.001$), presented more often with critical preoperative state (5.0% vs. 4.1%; $p<0.001$), unstable angina (11.9% vs. 8.5%; $p<0.001$) and emergent surgery (8.4% vs. 6.2%; $p<0.001$). Female patients presented less often with history of prior cardiac surgery (2.4% vs. 3.3%; $p<0.001$) or prior PCI (12.6% vs. 13.3%; p=0.0037) and had less often moderate (16.8% vs. 19.6%; $p<0.001$) or poor left ventricular function (3.1% vs. 4.6%; $p<0.001$). Female patients were less likely to receive total arterial grafting (19.2% vs. 23.3%; $p<0.001$) and received more often total venous grafting (5.8% vs. 4.1%; $p<0.001$) or a combination of both arterial and venous grafting (74.9% vs. 72.5%; $p<0.001$). In-hospital mortality was 1.4% (n=562) and higher in female compared to male patients (multivariate OR 1.71, 95%CI 1.38–2.12; $p<0.001$). In males, the AUC for the logistic EuroSCORE I was 0.86 (95%CI 0.85-0.88) versus 0.82 (95%CI 0.79-0.85) in females. The calibration of the logistic EuroSCORE I model resulted in p-values of <0.001 for both males and females.

Conclusions: Female patients undergoing CABG surgery present with higher logistic EuroSCORE I, receive less often total arterial grafting and have a higher risk of 30 day mortality as compared to male patients. There appears to be room for improvement of outcome in female patients by increased utilization of arterial grafts. Discriminative ability of the logistic EuroSCORE I is much better for men than women indicating the need for the development of gender specific risk stratification models. Calibration of the logistic EuroSCORE I model is not appropriate because of systematic overestimation of in-hospital mortality.

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Improved outcomes of total arterial myocardial revascularization in elderly patients at long-term follow-up

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Purpose: Despite the proven advantages of total arterial grafting in patients undergoing coronary artery bypass grafting (CABG), its benefits in the elderly population at long-term follow-up have been widely debated to date.
Methods: Among 1032 consecutive patients scheduled to undergo CABG surgery, we performed a case-match analysis in a population with double and triple vessels disease and older than 70 years of age and compared patients receiving total arterial grafting (Group 1, G1, 150 pts.) with conventional myocardial revascularization (LIMA on LAD plus saphenous vein grafts, Group 2, G2, 125 pts.). Primary end-point was cardiac-related mortality while secondary end-point was the occurrence of MACCEs (defined as cardiac death, myocardial infarction, need for repeated revascularization on grafted vessels, stroke).
Results: Pre-operative and intraoperative patients' characteristics were similar among the groups (mean no. of grafted vessels:G1=2.5±0.5 vs G2=2.6±0.6; p=0.56), as well the incidence of hospital mortality (none in both groups) and early post-operative complications. At a median follow-up time of 120 months, total arterial grafting was associated with significantly improved actuarial survival free from cardiac death (G1= 96.5±2.0% vs G2=82.3±3.9%; $p<0.001$) and occurrence of MACCEs (G1=84.9±3.7% vs G2=70.9±4.6%; p=0.001) Multivariate Cox regression analysis depicted conventional myocardial revascularization (with saphenous vein grafts) as an indipendent predictor for cardiac related mortality (OR=8.2, CI 95%=2.66-25.9; $p<0.001$) and MACCEs (OR=3.48, CI 95%=1.86-6.52; $p<0.001$).
Conclusions: The use of complete arterial myocardial revascularization in elderly patients is associated with a reduced late incidence of cardiac related mortality and major cerebral and cardiovascular events compared with the use of saphenous vein grafts, thereby providing improved long term benefits also in this specific subset of patients.

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Should bilateral internal thoracic artery grafting be used in patients with diabetes?

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Objectives: Bilateral Internal Thoracic Artery (BITA) grafting in diabetics is controversial due to the risk of sternal infection, and the excellent survival benefit obtained with Single Internal Thoracic Artery (SITA). The purpose of this study is to compare outcome of BITA grafting to that of SITA and other conduits, such as saphenous veins (SVG) or radial artery (RA) in patients with diabetes.
Methods: Eight hundreds and eighty seven diabetic patients who underwent BITA grafting between 1996 and 2008 were compared with 734 patients who underwent CABG with SITA and SVG or RA during the same period.
Results: Occurrence of peripheral vascular disease (PVD) (33% versus 27%), age>70 (47% versus 39%), emergency operations (15% versus10%), renal failure (CRF) (16% versus 11%), Insulin Depended Diabetes (IDDM) (19% versus 9%), COPD (11% versus 5%) and female gender (60% versus 42%) was higher in the SITA group.
Operative mortality (3.3% versus 3.2%) and sternal wound infections (1.8% versus 1.1%) were not significantly different between groups
Mean follow up was 9.1±4.5 years. Ten year survival (Kaplan-Meier) of the SITA group was significantly lower (55% versus 65%, p=0.046, log rank test). BITA grafting was associated with improved Kaplan Meier survival in the subsets of patients with NIDDM, age>70, OPCAB, and when more than 3 grafts were used. However, assignment to the BITA group was not associated with improved adjusted survival (p=0.585) in a multivariable Cox model. Independent predictors of decreased survival were: older age, female gender, preoperative MI, EF<30%, COPD, PVD and CRF. To further investigate our results, we performed a propensity matching analysis and could identify 323 well matched pairs of patients. Survival advantage for the use of BITA could not be identified in this group of matched patients as well.
Conclusions: This large cohort study does not support routine use of BITA in all patients with diabetes. Similar long term survival can be achieved with SITA. Further studies of the subsets that had better Kaplan-Meier survival are required

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Coronary revascularization in chronic renal disease and end stage renal disease- a systematic review and meta analysis

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Introduction: Patients with Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD) on dialysis have an increased risk for cardiovascular events secondary to occlusive coronary artery disease. Optimal revascularization strategy is unclear in this high-risk population.
Objective: We performed a meta- analysis to compare Coronary Artery Bypass Graft (CABG) versus Percutaneous Coronary Intervention (PCI) in patients with ESRD and CKD.
Methods: Clinical trials comparing patients with ESRD and CKD undergoing CABG and PCI were considered. We searched PubMed, Ovid, MEDLINE, CINAHL and EMBASE (1980-2013). The relative risk across all study groups was computed using Mantel-Hanszel random effects model. Results were calculated with 95% CI and was considered statistically significant if 2-sided alpha error was <0.05.
Results: 17 trials (N=33,584) in End Stage Renal Disease arm and six studies (n=15,493) in the CKD arm were included in the trial. The mean age in the ESRD group was 62.45 years and in the CKD group was 65.16 years. The weighted average follow up period was 26.7 months in the ESRD group and 34.2 months in the CKD group. In the ESRD and CKD group, we found significantly reduced early mortality with the PCI group with the odds ratio of (2.08 [1.90, 2.26; $p<0.00001$]) and (2.55 [1.45, 4.51; p=0.001]) respectively. Contrary to the early mortality results, we found decreased late mortality with the CABG group when compared to PCI group (0.86 [0.83, 0.89; $p<0.000001$]) and (0.82 [0.76, 0.88; $p<0.00001$]) in the ESRD and CKD arm respectively. When compared to PCI, there was decreased cardiovascular mortality with an odds ratio of (0.61 [0.40, 0.92; p=0.02]) in patients who underwent CABG in ESRD population and a similar trend, albeit insignificant, is observed in CKD population (1.13 [0.34, 3.81; $p<0.84$]). We also observed decreased incidence of myocardial infarction ((ESRD (0.34 [0.32, 0.36; $p<0.00001$])); (CKD (0.89 [0.56, 1.43]; p=0.64))) and repeat revascularization ((ESRD (0.12 [0.08, 0.18]; $p<0.00001$)); (CKD (0.26 [0.18, 0.39]; $p<0.00001$))) in patients undergoing CABG compared to PCI. There is a strong trend for decreased risk of stroke with PCI when compared to CABG in ESRD (3.46 [1.02, 11.78] with p=0.05) and CKD population (0.78 [0.43, 1.41] with p=0.41).
Conclusion: In patients with CKD and ESRD, CABG offers overall mortality benefit compared to PCI. Similar trends are observed in incidence of myocardial infarction and repeat revascularization. We observed decreased risk of stroke with PCI when compared to CABG in ESRD and CKD but more studies are needed to validate this observation.

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Prevention of MACE with modified glucose-insulin-potassium in patients undergoing cardiac surgery with cardiopulmonary bypass: a randomized double-blind placebo-controlled trial

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Objective: Glucose-insulin-potassium (GIK) infusion has been used in cardiac surgery for more than 40 years, but clinical trials have shown no definite beneficial effects, in part because of different doses, timing and protocol of GIK. This study was designed to evaluate the effects of perioperative GIK infusion in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).
Methods and results: We performed a randomized, double-blind, controlled study in 930 patients admitted to our hospital who were receiving CPB. GIK (150 g glucose, 50 IU insulin, 4.5 g KCl; G:I=3:1) or placebo treatment was started at 10 min before anesthesia, running at 60 ml h^{-1} for 12.5 hour. The primary outcome was the incidence of major adverse cardiac events (MACE). GIK therapy significantly reduced the incidence of MACE (OR, 0.57; 95% CI, 0.43-0.75; $P<0.001$) without increasing perioperative blood glucose compared with placebo group. Furthermore, GIK therapy was associated with decreased plasma lactate, improved left ventricular ejection fraction, reduced creatine kinase-MB and cardiac troponin T at 24 h and 48 h after operation. In addition, patients receiving GIK therapy were less likely to require prolonged ventilatory support and extended intensive care although no significant differences in mortality were found at 30-day (1.6% in GIK vs 2.7% in placebo, P=0.37) and 180-day (2.2% in GIK vs 3.0% in placebo, P=0.41) follow-up. The incidence of redooperation, stroke and sepsis did not differ significantly between groups but the need for epinephrine use (48.0% in GIK vs 58.9% in placebo, P=0.001) and the incidence of renal complications (4.9% in GIK vs 8.8% in placebo, P=0.02) were significantly decreased in GIK group.
Conclusion: In patients undergoing cardiac surgery with CPB, perioperative GIK infusion significantly reduced the incidence of MACE but not benefit the mortality at 30-day and 180-day follow-up.

2892 | BEDSIDE
Clinical outcomes of hybrid coronary revascularization versus coronary artery bypass surgery in patients with diabetes mellitus

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Background: Hybrid coronary revascularization (HCR) involves minimally invasive left internal mammary artery to left anterior descending (LAD) coronary

artery grafting combined with percutaneous coronary intervention (PCI) of non-LAD vessels. The safety and efficacy of HCR among diabetic patients is unknown.
Methods: Patients with diabetes were included who underwent HCR at a U.S. academic center between October 2003 and September 2013. These patients were matched 5:1 to similar patients treated with coronary artery bypass grafting (CABG) using a propensity-score matching algorithm. Conditional logistic regression and Cox regression stratified on matched pairs were performed to evaluate the association between HCR and in-hospital complications, a composite measure of 30-day mortality, myocardial infarction (MI) and stroke, and up to 3-year all-cause mortality.
Results: Of 618 patients (HCR=103, CABG=515) in the propensity-score matched cohort, the 30-day composite of death, MI or stroke after HCR and CABG was 4.9% and 3.9% (odds ratio: 1.25, 95%-CI: 0.47-3.33, p=0.66). Compared with CABG, HCR also had similar need for reoperation (7.6% vs. 6.3%, p=0.60) and renal failure (4.2% vs. 4.9%, p=0.76), but required less blood products (31.4% vs. 65.8%, p<0.0001), lower chest-tube drainage (655cc (412-916) vs. 898cc (664-1240), p<0.0001) and shorter length-of-stay (<5 days: 48.3% vs. 25.3%, p<0.0001). Over a 3-year follow-up period, mortality was similar after HCR and CABG (12.3% vs. 14.9%, hazard ratio: 0.94, 95%-CI: 0.47-1.88, p=0.86).
Conclusion: Among diabetic patients the use of HCR appears to be safe and has similar longitudinal outcomes, but is associated with less blood product usage and faster recovery than conventional CABG surgery.

IMMUNE MECHANISMS IN ACUTE MYOCARDIAL INFARCTION

2917 | BEDSIDE
Reduced myocardial infiltration of dendritic cells is associated with impaired reparative fibrosis and development of cardiac rupture

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Purpose: Dendritic cells (DCs) play pivotal roles in regulating the immune system. We previously reported DCs infiltration in the infarcted heart and its protective roles in post-myocardial infarction (MI) healing process with animal models. However, its clinical significance has not been determined.
Methods: We investigated 24 autopsy subjects after MI. Patients were divided into two groups according to presence (n=13) or absence (n=11) of cardiac rupture (CR). The number of infiltrated DCs and macrophages (MΦ) and the extent of reparative fibrosis in the infarcted area were examined via immunohistochemical (IHC) and Masson-trichrome stainings (M-T).
Results: Baseline characteristics of the study patients were comparable between the CR and the non-CR groups including history of prior MI, time from onset to death, and rate of reperfusion therapy. M-T showed decreased % area fraction of reparative fibrosis (%AF) in patients with CR compared to those without (P=0.0008). IHC of the infarcted myocardium showed an increase in the number of infiltrating CD68+ MΦ (P=0.0009), and a decrease in CD209+ DCs (P=0.0007, Fig. 1A), in patients with CR compared to those without. Furthermore, the CD68+/CD209+ cell ratio was higher in patients with CR compared to those without (P=0.026). No significant correlation was noted between the number of CD68+ MΦ and %AF in the infarcted area. However, there was a significant positive correlation between the number of CD209+ DCs and %AF (R=0.88, P<0.0001, Fig. 1B).

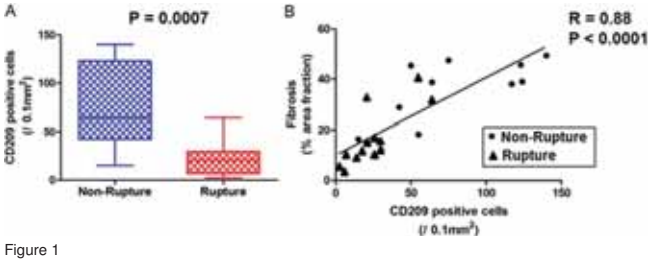

Figure 1

Conclusions: Reduced number of DCs in the human infarcted myocardium was associated with increased MΦ infiltration, impaired reparative fibrosis, and the development of CR after MI. These findings suggest the protective role of DCs in the post-MI inflammation and subsequent healing process.

2918 | BENCH
The anti-inflammatory effects of ly6Clow macrophages on infarcted myocardium at the reparative phase may be modulated through interleukin-1 receptor-associated kinase-M

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Purpose: Two subpopulations of macrophages,defined as Ly6Chigh and Ly6Clow cells, have been found participating in the inflammatory response following myocardial infarction with distinct roles. Ly6Chigh cells exhibit pro-inflammatory properties, while Ly6Clow cells show reparative effects by suppressing inflammation, enhancing angiogenesis and collagen synthesis.However,mechanisms by which Ly6Clow cells affect inflammation remain poorly defined.Toll-Like Receptor (TLR) and Interleukin (IL)-1 signaling have been proved to be critically involved in the post-infarction negative inflammatory response and in the pathogenesis of cardiac remodeling.We hypothesized that the inflammatory suppression of Ly6Clow macrophages may mediated by TLR/IL inhibitory signals.
Methods: Mice lacking expression of Interleukin-1 receptor-associated kinase (IRAK)-M,known as an endogenous inhibitory molecular of TLR/IL pathways,were used to explore the inflammatory actions of Ly6Clow macrophages in an ischemia/reperfusion model.To identify the macrophage subsets,single cell suspension of infarcted hearts were prepared and undergone flow cytometry.
Results: Ly6Clow macrophages appeared on day 3 and peaked on day 7 (174±81 cells/mg vs. 781±81 cells/mg, n=8 for each group, p<0.01).5.52% to 15.40% of these cells expressed high levels of IL1RII, a decoy of TLR/IL signaling pathways, whereas only 0.19% to 0.52% of the Ly6Chi were IL1RII positive (p<0.01).The number of IRAK-M+ Ly6Clow macrophage increased by 9 times 7 days after MI compared to that of 3 days in the infarcted myocardium of wild type mice.The depletion of IRAK-M gene resulted in a 30% reduction of Ly6Clow cell numbers and a 140% increased expression of IL1-beta in these macrophages.
Conclusions: IRAK-M was expressed by Ly6Clow macrophage subset in infarcted hearts with a pattern of late up-regulation at the reparative phase,suggesting that IRAK-M may participate in the cardiac healing through anti-inflammatory and cell-specific actions on macrophages.

2919 | BENCH
Regulation of EMMPRIN (CD147) on monocyte subsets in patients with acute myocardial infarction and aortic stenosis

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Introduction: The role of individual monocyte subsets in cardiovascular inflammatory diseases like myocardial infarction or aortic stenosis is insufficiently understood. The Extracellular Matrix Metalloproteinase Inducer EMMPRIN regulates MMP-release and inflammatory processes on monocytes. To our best of knowledge expression and regulation of EMMPRIN on monocyte subsets have never been characterized. Thus, the aim of the present study was to characterize the expression of EMMPRIN on monocyte subsets in patients with acute myocardial infarction and aortic stenosis.
Methods and results: From 184 patients (80 with Stable Angina pectoris, 49 with acute myocardial infarction, 55 with severe aortic stenosis) blood was drawn and monocytes were divided into 3 subsets accoding to flow cytometry: CD14+CD16- (low), CD14+CD16+ (intermediate), CD14+CD16++ (high). Expression of CD36 (as marker of CD16- monocytes) and EMMPRIN was measured. In patients with SAP EMMPRIN expression was significantly different on all monocyte subsets with the highest expression on CD16- monocytes (MFI CD16- vs. CD16+ vs. CD16++: 223±36 vs. 190±31 vs. 168±29, p<0.01). Whereas EMMPRIN was upregulated on all monocyte subsets in patients with acute myocardial infarction or aortic stenosis, expression of CD36 was not significantly different within the groups. In all patient groups CD16- monocytes revealed the highest EMMPRIN expression.
Conclusion: EMMPRIN is preferentially expressed on CD16- monocytes and is upregulated in patients with acute myocardial infarction and aortic stenosis.

2920 | BENCH
The expansion of CD4+CD28null T cells in patients with coronary atherosclerosis is mediated by proteasomal-dependent defects in apoptosis pathways and apoptosis resistance

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Purpose: Atherosclerosis is now widely recognized as a disease with an underlying immune deregulation. Patients with coronary atherosclerosis that develop myocardial infarction (MI) have an expansion of a unique subset of T lymphocytes, the CD4+CD28null (CD28null) T cells, characterized by the lack of the CD28 co-stimulatory receptor. These cells have a pro-inflammatory and cell-lytic phenotype. Patients harbouring high numbers of CD28null T have increased risk of recurrent severe acute coronary events (i.e. MI) and unfavourable prognosis. Why CD28null T cells accumulate preferentially in patients with MI compared to patients with stable angina (SA) and healthy individuals is currently unknown. T cell homeostasis is maintained by elimination of unwanted T cells via apoptotic cell death. We hypothesized that apoptosis pathways that mediate elimination of T cells are dysregulated in CD28null T cells in patients with MI. Our aim was to investigate molecules involved in apoptosis regulation in CD28null T cells in patients with coronary atherosclerosis (MI and SA).
Methods: Levels of pro-apoptotic (i.e. Fas, FasL, Bim and Bax) and anti-apoptotic (Bcl-2, Bcl-xL) proteins were measured in patients with MI (n=25) and SA patients (n=18) using flow-cytometry. Apoptosis sensitivity of CD28null T cells to the Fas-

ligating antibody CH11 and C2-ceramide was measured with annexin-V and 7-AAD.
Results: Pro-apoptotic molecules Fas, Bim and Bax were dramatically reduced on CD28null T cells in patients with MI, whilst anti-apoptotic molecules Bcl-2 and Bcl-xL were similar in CD28null and CD28+ T cells. Notably, CD28null T cells in patients with MI showed significantly lower Bim and Bax levels compared to CD28null T cells in SA patients. We found that CD28null T cells in MI patients were resistant to apoptosis induction via Fas-ligation or ceramide. Furthermore, we show that proteasomal inhibition restores apoptosis sensitivity of CD28null T cells in patients with MI.
Conclusion: We show that CD28null T cells in patients with MI harbour marked defects in molecules that regulate T cell apoptosis, which tips the balance in favour of anti-apoptotic signals and endows these cells with resistance to apoptosis. Furthermore, we propose a novel mechanism that implicates the proteasome as a key regulator of apoptosis sensitivity of CD28null T cells in patients with MI. A better understanding of the molecular switches that control apoptosis sensitivity of CD28null T cells may reveal novel strategies for targeted elimination of these T cells in patients with coronary atherosclerosis.

2921 | SPOTLIGHT
EN-RAGE: a novel independent inflammatory marker for coronary heart disease

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Purpose: Inflammation is thought to play a key role in atherosclerosis. Several inflammatory proteins have been investigated in association with coronary heart disease (CHD). We aimed to identify additional inflammatory markers of CHD independent of established risk markers as C-reactive protein (CRP), interleukin 6 (IL6) and TNFalpha.
Methods: We prospectively investigated 21 novel inflammatory biomarkers in a random subset of 839 individuals in a population-based cohort study. We tested the age and sex adjusted association between all biomarkers and the incidence of CHD using Cox survival analysis. A Bonferroni corrected p-value of $2.4\times10\text{-}3$ was used to correct for multiple testing. We additionally tested whether the effect of significant novel markers was independent of established CHD risk factors, CRP, IL6 and TNFalpha.
Results: The majority of the individuals were female (58%) and the mean age at baseline was 72.8 years. During a median follow-up of 10.6 years, 99 cases of incidence CHD were observed. Across all novel inflammatory biomarkers, EN-RAGE had the strongest significant association with future CHD events (p-value $1.9\times10\text{-}3$). The age and sex adjusted hazard was 1.31 per standard deviation of the natural log-transformed EN-RAGE (95% CI 1.07 - 1.61) after adjustment for established cardiovascular risk factors. Additional adjusting for CRP, IL6 and TNFalpha did not attenuate the association (1.41, 95% CI 1.11 – 1.77). Excluding individuals with prevalent type 2 diabetes, impaired kidney function or individuals using antihypertensive medication did not change the effect estimates.
Conclusions: Our results support EN-RAGE as a novel inflammatory marker for CHD independent of established CHD risk factors and inflammatory markers, suggesting a distinct inflammatory risk pathway for CHD that requires further validation and explorative evaluation.

2922 | BEDSIDE
Increased risk of major adverse cardiovascular events during flares after first-time myocardial infarction in inflammatory bowel disease – a nationwide cohort study

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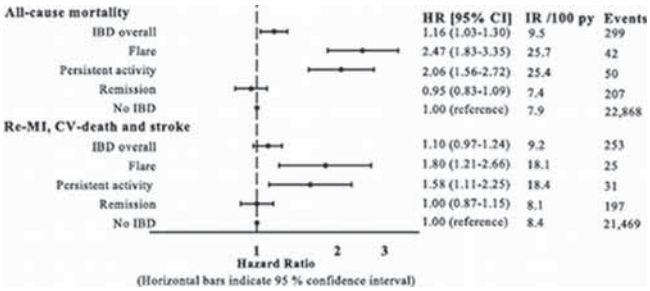
Background: Inflammatory bowel disease (IBD) is associated with an increased cardiovascular risk. We examined the effect of active IBD on major adverse cardiovascular outcomes after myocardial infarction (MI).
Methods: Between 2002 and 2011, we identified 86,790 patients with first-time MI, including 1,030 with IBD from nationwide registries. IBD activity was categorized in stages of flare, persistent activity or remission. Hazard ratios (HRs) of recurrent MI and all-cause mortality, and a composite of recurrent MI, cardiovascular (CV) death, and stroke were estimated in patients alive seven days after discharge, whereas short-term mortality defined as death during hospitalization or within seven days of discharge was assessed using logistic regression.
Results: Among 75,288 patients alive seven days after discharge, IBD-associated HRs were 1.12 (95% confidence interval [CI] 0.95-1.38) for recurrent MI, 1.16 (95% CI 1.03-1.30) for all-cause mortality, and 1.10 (95% CI 0.97-1.24) for the composite endpoint. IBD flares were associated with a markedly increased risks of recurrent MI (HR 2.70 [95% CI 1.63-4.48]), all-cause mortality (HR 2.47 [95% CI 1.83-3.35]) and the composite endpoint (HR 1.80 [95% CI 1.21-2.66]). HRs for these adverse endpoints were somewhat lower during persistent activity, whereas no increased risk was identified in quiescent stages (Figure). Odds ratios for short-term mortality (n=11,502 including 138 with IBD) corresponded to 1.74 (95% CI 1.09-2.77) for patients with flares of IBD, 1.25 (95% CI 0.71-2.20) for persistent activity, and 0.92 (95% CI 0.74-1.14) for those in remission.
Conclusion: Active inflammatory bowel disease worsens the prognosis after myocardial infarction, in particular in relation to flares.



Risk of major adverse events after MI.

PREVENTING CARDIOVASCULAR EVENTS IN VULNERABLE POPULATIONS

2931 | BENCH
Coronary heart disease and hospital admission rate in patients with schizophrenia

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Background: Coronary heart disease (CHD) is increased in patients with Schizophrenia. However the exact proportion of CHD mortality and hospital admission rate for CHD are not known.
Objective: The aim of this study was to evaluate mortality from CHD with acute myocardial infarction (AMI) as its most important component, and also CHD hospitals admissions, in persons with schizophrenia in Sweden between 1987 and 2010 compared to the general population
Material and methods: The cohort includes all persons who resided in Sweden between the 1st of January 1987 and the 31st of December 2010 (n=10 631817) of these 46 911 were people diagnosed with schizophrenia. We used the Swedish Total Population Register (TPR) to identify each individual and by linking to national Swedish Cause-of-Death Register and the National Patient Register (NPR) we could follow mortality for each person during 24 year. Information on hospital admission, medical diagnosis, and cause of death was obtained by linking the TPR with the national Swedish Cause-of-Death Register and the National Patient Register (NPR) using each resident's unique personal identification number. Hospital admission rate ratios (ARR) for CHD were calculated for persons with schizophrenia relative to the population during 1990 to 2010 with a previous three year run-in period (1987 to 1989).
Results: During the period 1987 to 2010, there were 13,895 deaths among persons with schizophrenia in Sweden, with a mortality rate ratio (MRR) of 3.13 (95% CI: 3.08-3.19) compared to the general population. In CHD, there were 2,671 deaths, with a MRR of 2.83 (95% CI: 2.73-2.95). However, the ARR for CHD, was reduced in patients with schizophrenia 0.88 (95% CI: 0.83-0.94). The MRR for Acute myocardial infarction (AMI) was 2.62 (95% CI: 2.49-2.75).
For AMI and CHD the increased risk was most apparent in the age group below 65.
Conclusion: The increased CHD mortality and low admission rate for CHD in patients with schizophrenia are alarming and call for intensified efforts to prevent and treat heart disease in this high risk group.

2932 | BEDSIDE
Low bone mineral density predicts incident heart failure in men and women in EPIC-Norfolk prospective study

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Aims: Recent evidence suggests shared risk factors between heart failure and osteoporosis. It is unknown whether bone mineral density as a measure of osteoporosis is associated with development of heart failure.
Methods and results: We examined the prospective association of bone mineral density measured as broadband ultrasound attenuation by quantitative ultrasound of the heel with incident heart failure events in 13,666 apparently healthy persons aged 42-82 participating in the EPIC-study in Norfolk.
During a mean follow-up of 9.3 years 380 incident cases of heart failure occurred.

The risk of heart failure decreased with increasing bone mineral density. The hazard ratios comparing each quartile with the lowest were 0.40 (95% CI 0.27-0.59), 0.54 (95% CI 0.37-0.79) and 0.46 (95% CI 0.32-0.68) in analysis adjusting for age, sex, smoking, alcohol consumption, physical activity, occupational social class, educational level, systolic blood pressure, diabetes, cholesterol concentration and body-mass index (p for trend =0.002), with a 23% risk decrease associated with every increase in 1 SD of bone mineral density (HR 0.77, 95% CI 0.66-0.89). The association was stronger with heart failure without (HR 0.75, 95% CI 0.63-0.89) than with antecedent myocardial infarction (HR 0.82, 95% CI 0.62-1.09).
Conclusion: We observed an inverse association between bone mineral density and the risk of heart failure in apparently healthy individuals. Our findings give support for cardiac assessment in people with reduced bone mineral density and warrant further exploration of underlying biological mechanisms linking osteoporosis and heart failure.

2933 | BENCH
The effect of family stress on 16-th years risk of cardiovascular diseases in female population 25-64 years in Russia: MONICA-psychosocial epidemiological study

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Purpose: To explore the influence of family stress on risk (HR) of an arterial hypertension (AH), myocardial infarction (MI) and stroke in female population aged of 25-64 years in Russia over 16 years of follow-up.
Methods: Under the third screening of the WHO "MONICA-psychosocial" (MOPSY) program random representative sample of women aged 25-64 years (n=870) were surveyed in our city. Questionnaire MOPSY "Awareness and attitude towards the health" was used to estimate levels of family stress. From 1995 to 2010 women were followed for the incidence of AH, MI and stroke with using "Acute Myocardial Infarction Registry" data (an ongoing WHO program), medical records. Cox regression model was used for relative risk assessment (HR).
Results: The prevalence of high family stress level in women aged 25-64 years was 20.9%.
HR of AH over 16 years of follow-up in women with high family stress was 1.39-fold higher (95.0%CI: 1.08-1.78, p=0.001) compared to those with lower levels of family stress. HR of MI over 16 years was 5.59-fold higher (95.0%CI: 1.99-15.70, p=0.001) and for stroke it was 3.53-fold higher (95.0%CI: 1.82-6.84, $p<0.001$) for high stress level.
There were increasing AH, MI and stroke rates in married women experienced stress in family. AH developed significantly higher in women with university and vocational education compared to those having elementary school with (χ^2=5.63 df=1 $p<0.05$; χ^2=4.01 df=1 $p<0.05$, for university and specialized secondary, respectively) or without stress at home (χ^2=5.45 df=1 $p<0.05$; χ^2=4.39 df=1 $p<0.05$, respectively). In relation to occupational class AH rates were higher in groups "first-line manager" (χ^2=5.94 df=1 $p<0.05$) and "physical worker" (χ^2=8.14 df=1 $p<0.01$) experienced stress in family. Higher stroke rates were more likely in "physical workers" with family stress compared to those without it (χ^2=3.69 df=1 p=0.055) and MI rates were tend to be higher in "managers" and "engineers" experienced stress in family.
Conclusions: There is high prevalence of family stress in female population aged 25-64 in Russia. Women with high family stress had significantly higher HR of cardiovascular diseases over 16-th years of follow-up. Rates of AH, MI, stroke development were more likely in married women with higher educational level and high family stress in professional class "managers" and "physical workers".

2934 | SPOTLIGHT
Association between pre-existing dementia and poorer quality of care in older patients with ST-elevation myocardial infarction

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Purpose: ST-elevation myocardial infarction (STEMI) patients with comorbid mental disorders, such as schizophrenia, substance abuse and depression, were less likely to receive reperfusion procedures than those without mental disorders. We supposed presence of dementia in STEMI patients would also influence the physician's decision to provide aggressive strategy, such as reperfusion therapy. In this study, we examined the association between presence of dementia and non-use of standard care in an incident STEMI cohort from a population-based database.
Methods: Our National Health Insurance claims data from 2002 through 2010 was used. Incident cases of STEMI with age over 65 years were included. The complete claims records of each patient as far as 1 year prior to the index hospitalization were retrieved to constitute baseline information. According to the treatment guidelines of STEMI, we defined 6 measures of quality of care including use of anti-platelet agents at discharge, use of beta-blockers at discharge, use of statins at discharge, evaluation of left ventricular systolic function during hospitalization, receiving reperfusion therapy during hospitalization, and receiving rehabilitation program after discharge. The sum of the 6 measures constituted a 0-6 composite quality score. We used the ordinal logistic regression model to model the effect of dementia on the composite quality score with adjustment of demographics, comorbidities and socioeconomic status.
Results: We identified 21843 eligible patients, 1119 (5.1%) had a diagnosis of dementia and 20724 (94.9%) had no diagnosis of dementia prior to the index STEMI. Among patients with dementia, 86 (7.7%) had a composite quality score of 0 and only 107 (9.6%) had a composite quality score of more than or equal to 5. On the contrary, among patients without dementia, 623 (3.0%) had a composite quality score of 0 and 3525 (17.0%) had a composite quality score of more than or equal to 5.($p<0.0001$) By ordinal logistic regression model, presence of dementia was associated with a lower composite quality score (adjusted odds ratio, 1.44; 95% confidence interval, 1.28-1.61).
Conclusions: Our study showed that patients with dementia received poorer quality of care while suffering from STEMI. Further studies are needed to determine the effect between quality of care and outcome in STEMI patients with pre-existing dementia.

2935 | BEDSIDE
Female gender may not be a risk of stroke in Japanese patients with atrial fibrillation: from the Fushimi AF Registry

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Purpose: 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). Female gender is considered a risk factor for thromboembolism in patients with AF, and is included in the risk stratification scheme, CHA2DS2-VASc score as Sc (sex category) factor. We previously reported that female gender was not associated with the history of thromboembolism in Japanese AF patients. The purpose of the present study is to investigate the one-year outcomes of female AF patients in the Fushimi AF Registry.
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 3,821 Japanese AF patients (1.2% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013.
Results: Female AF patients (n=1,200, 40.5%) were older than male (77.0 vs. 71.8 years of age; $p<0.01$), had lower body weight (50.8 vs. 64.5 kg; $p<0.01$), and lower body mass index (22.4 vs. 23.4 kg/m^2; $p<0.01$). CHADS2 score, and CHA2DS2-VASc score excluding Sc factor were greater in female patients (2.16 vs. 1.99; $p<0.01$: 3.14 vs. 2.90; $p<0.01$). Female AF patients were more likely to have heart failure (31.2% vs. 24.1%; $p<0.01$), less likely to have diabetes (20.2% vs. 25.8%; $p<0.01$). Hypertension was comparable between female and male (61.6% vs. 61.1%; p=0.79). Despite that the prescription of oral anticoagulants (OAC) was less in female (48.6% vs. 55.7%; $p<0.01$), the history of stroke or systemic embolism was not different (20.4% vs. 22.5%; p=0.18). During one-year follow-up period, stroke or systemic embolism occurred in 35 female patients (2.9%) and 46 male patients (2.6%), with an odds ratio for female patients of 1.12 (95% confidence interval [CI], 0.71 to 1.75; p=0.61). Furthermore, we investigated patients with or without OAC; stroke or systemic embolism occurred in 19 female patients (3.1%) and 20 male patients (2.6%) without OAC, with an odds ratio for female patients of 1.21 (95% CI, 0.63 to 2.30; p=0.55) and in 16 female patients (2.7%) and 26 male patients (2.6%) with OAC, with an odds ratio for female patients of 1.04 (95% CI, 0.54 to 1.94; p=0.90).
Conclusion: The Fushimi AF Registry provides a unique snapshot of current real-world AF patients in an urban community in Japan. Female gender may not be a risk of stroke, at least in Japanese AF patients.

2936 | BEDSIDE
Long term survival after acute myocardial infarction according to attained education level in the Chilean AMI Register, GEMI 2009-2012

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Background: A low socioeconomic status (income and attained education level) is associated with higher long term mortality rates after an acute myocardial infarction (MI). Chile is considered a high-income country according to the OECD, however social inequalities in the country are marked.
Purpose: To evaluate the effect of socioeconomic status, measured as attained education level (AEL), on the prognosis of patients admitted in the Chilean Registry of Myocardial Infarction GEMI, which allows studying this relationship in a developing country with persistent social inequities.

Methods: Patients with a first MI admitted at 17 centers in the GEMI Registry between 2009 and 2012. Baseline characteristics, in-hospital treatment and in-hospital mortality were obtained from the GEMI records; vital status until June 2013 was collected from the National Mortality Database of the Ministry of Health. AEL was stratified as: none, primary (<8 years), secondary (8-12 years) and tertiary (>12 years). Survival was estimated using Kaplan -Meier method and the effect of AEL crude and adjusted for demographic and clinical characteristics, in-hospital treatment and type of hospital (public or private) was assessed with Cox regression (HR and 95% CIs). The upper AEL was used as reference (HR = 1. 00).
Results: 4315 patients were admitted, 663 patients (15. 4%) were excluded due to missing data in AEL. The average follow-up was 24±15 months. Mean age of patients was 63±13 years and 27% were women. Distribution by AEL was 3.2% none (N=115), 31.9% primary (N=1166), 42.9% secondary (N=1568) and 22% tertiary (N=803). Patients in the lower AEL were older and had more prevalence of females, hypertension and diabetes ($p<0.0001$ for trend). In addition they consulted later and with more evidence of heart failure on admission. Case-fatality for the entire follow-up was 17.3% and it was higher in the lower education groups: 46.1% none, 26.4% primary, 13.4% secondary and 7.7% tertiary ($p<0.001$ for trend). Educational attainment was inversely associated with all cause-mortality; adjusted HRs compared with the highest AEL was 2.98 (IC 1.98-4.48) for none, 1.83 (IC1.36-2.48) for primary and 1.53 (IC 1.15 - 2.05) for secondary.
Conclusions: In a developing country as Chile, lower AEL is independently related with higher long-term case-fatality after AMI.

SUDDEN CARDIAC DEATH: FROM PREVENTION TO RESUSCITATION

P2949 | BEDSIDE
Analysis of asystole in out-of-hospital cardiac arrest

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Purpose: In the current European resuscitation guidelines, little emphasis is placed upon transcutaneous pacing in advanced life support (ALS). The guidelines are based on few studies, the most recent published in 1993. Pacing for asystole in out-of-hospital cardiac arrest (OHCA) is considered useless but differences between various origins of asystole have not been appreciated. Treatment in asystole may depend on different causes of asystole, and further classification of asystolic rhythms is needed.
Methods: Data from the ARREST-study, an OHCA registry in the Netherlands, were used. A random selection of 533 patients (pts) out of 1644 OHCA pts with asystole as initially recorded rhythm between 2006-2012 were subdivided in 4 categories: baseline deviations <1mm, flat line, p-waves without QRS-complex and QRS complexes <12/min. We noted defibrillation for VF/VT (if present later in the efforts), return of organized rhythm (ROOR), return of spontaneous circulation (ROSC) and survival to discharge. We determined the use of transcutaneous pacing by paramedics. All defibrillators in the system could use pacing.
Results: Figure 1 shows the subdivision of asystole. Initial conduction disorders were observed in 20% (108/533) of pts. In only 5 of 108 pts (5%) pacing was attempted, starting 12-30 min after initial rhythm analysis. In all pts electrical capture was noted, however without sustained output. One pt died at the emergency department, all other pts died before transportation. Overall survival from asystole was 1%.

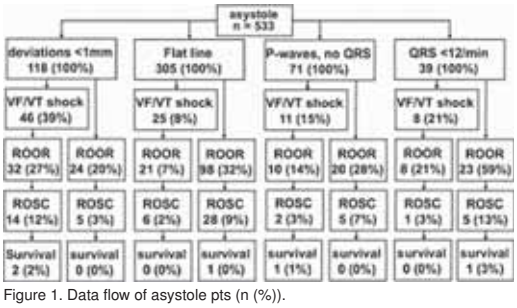

Figure 1. Data flow of asystole pts (n (%)).

Conclusions: Although most asystole can be classified as flat line, 20% of pts show conduction disorders. Pacing is rarely and very late initiated, and these 5 pts did not survive. Very low survival in asystole warrants more pacing attempts in properly selected patients.

P2950 | BEDSIDE
Risk of malignant outcome in patients with wolff-parkinson-white syndrome: results of 28-years prospective electrophysiological follow-up study

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Purpose: The Wolff-Parkinson-White (WPW) syndrome can be associated with sudden death (SD), thus risk assessment (RA) with electrophysiological (EP) testing (EPT) is a mandatory to identify patients (pts) requiring catheter ablation (CA). Our prospective study aimed to identify and treat WPW pts at high arrhythmogenic risk (HAR), and to evaluate the predictive value of transesophageal EPT (TEEPT) for RA, evaluation of treatment efficacy, and longitudinal EP follow up (F-up) of untreated athletes/pts.
Methods: 318 WPW pts referred to us between 1985 and 2013. Antegrade effective refractory period (ERP) of accessory pathway (AP) and of the atrioventricular node (AVN), Wenckebach point (WP), shortest preexcited RR intervals (SPERRI) during atrial fibrillation (AF) and/or atrial pacing, and inducibility of supraventricular arrhythmias (SVTA) were assessed, at rest (in supine and upright position) and during effort.
Results: Out of 318 pts, 275 untreated pts (53.8% athletes) were enrolled. AP's/AVN's ERP and SPERRIs varied as a function of autonomic modulation and were shorter in the 128 symptomatic (S) compared with 147 asymptomatic (AS) pts, ($p<0.05$). One or more sustained SVTA were inducible in 128/275 pts (46.54%), and AF in 70 pts. During the F-up (12.3±5.2 pts years), out of 57 pts classified at HAR, 37 were ablated. Before CA availability, two S pts, with inducible antidromic AVRT and AF (SPERRI <180 msec at rest), refused surgery and died suddenly (at rest). Both had self-discontinued antiarrhythmic therapy (AAD). Other 18 HAR pts were treated with AAD, without complications. Overall mortality was (0.06%/year of F-up). Among 218 pts classified at low (198) or medium (20) risk, 21 pts underwent elective CA for fit-for-duty requirements. Periodical reevaluation was performed, if clinically or legally required (overall 922 F-up TEEPTs). 56 refused a second study (TEEPT2), which was performed in 161 pts. Compared to TEEPT1, EP data of untreated pts who underwent TEEPT2 were highly reproducible. Clinical F-up data of untreated pts remained unchanged in 79.4%. Only 5.3% of initially AS became S, whereas 41.8% of S became AS.
Conclusions: This study confirms good long-term prognosis in WPW pts. Our two casualties were avoidable, given the correct HAR identification provided by TEEPT, if surgery was accepted or CA available. No other patient had complications during the F-up, even though 72.2% of athletes were allowed to continue competitive sports activity. TEEPT is an efficient method which can minimize invasivity for EP RA of WPW pts and for longitudinal F-up of professional athletes.

P2951 | BEDSIDE
Significance of electrocardiogram recording in high intercostal spaces in patients with early repolarization syndrome

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Purpose: Before publication of the new Expert Consensus Statement in 2013, electrocardiogram (ECG) recording in the right precordial leads positioned in the high intercostal (2nd and 3rd) spaces was not essential for diagnosing Brugada syndrome (BrS). Therefore, there is a possibility that previously reported cases of inferolateral early repolarization syndrome (ERS) might have included patients with Brugada-pattern ECG (Br-ECG) in high intercostal spaces only. We investigated the prevalence of Br-ECG in the high intercostal recording in patients with ERS and the outcome in patients with and without Br-ECG.
Methods: Sixty-three patients with inferolateral early repolarization and spontaneous ventricular fibrillation (VF) unlinked to structural heart disease underwent drug provocation tests with right precordial ECG (V1-V3) recording in the 2nd -4th intercostal spaces. After 25 patients showing type 1 Br-ECG in the standard ECG were excluded, 38 patients (34 males, mean age; 40.1±13.4 years) were classified into 3 groups based on ST-T morphology (group A: ERS with type 1 Br-ECG only in the high intercostal recording, group B: ERS with non-type 1 Br-ECG in any of precordial leads in control and/or after drug provocation test, and group C: ERS only). Clinical characteristics and outcomes during follow-up periods of 86±52 months were compared among the three groups.
Results: ECG screening identified 6 patients (16%) as group A, 13 patients (34%) as group B, and 19 patients (50%) as group C. VF was observed during sleep or near sleep in 3 patients (50%) in group A and 11 patients (85%) in group B, but in 2 patients (11%) in group C (A and B vs. C, $p<0.05$). VF recurrence including electrical storm was significantly higher in group A (67%) and group B (62%), compared with group C (11%) (A and B vs. C, $p<0.05$). Five patients (13%) in group B showed non-type 1 Br-ECG only in high intercostal spaces before (n=4) and after (n=1) drug provocation tests, and 4 of these had recurrences of VF.
Conclusions: Approximately 30% of ERS patients showed type 1 or non-type 1 Br-ECG only in high intercostal spaces and 50% of ERS combining atypical Br-ECG showed grim prognosis, although the remaining 50% without Br-ECG exhibited favorable outcome and clinical profiles dissimilar to BrS. High intercostal ECG recording was considered essential not only in BrS but also in ERS.

P2952 | BEDSIDE
Brugada syndrome in women

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Introduction: Brugada syndrome (BrS) is an inherited arrhythmia syndrome with an increased risk of syncope and sudden death. Disease manifestation is clearly predominant in males and up to now the studied population mainly consisted in men. The aim of this study is to describe the clinical characteristics of BrS in women.
Methods: Women with BrS were recruited from 12 tertiary centers. Clinical data investigation of family history, 12-lead ECG and results for pharmacological challenge were collected. The average follow-up was 79±52 months.
Results: In this study, 202 women were recruited (mean age 46±16 years). The circumstances of diagnoses were as follows: familial screening (n=94, 47%), systematic ECG (n=61, 30%) and symptoms (n=47, 23%). Sixty-nine patients (34%) were symptomatic: resuscitated sudden cardiac death (SCD) in 11 women (5%), 42 syncope (21%), 8 supraventricular tachycardia (4%), 21 palpitations (10%), 24 lipothymia (12%) and 7 pain (3%). Moreover, 20 women (10%) have a history of familial SCD. Implantable cardiac defibrillator (ICD) was implanted in 44 of 202 patients (22%).
At baseline, mean heart rate was 71±12 bpm, PR 174±32 mm, QRS 99±17 mm and QTc 419±29 mm. Fifty-nine women (29%) have a spontaneous type-1 ECG. Mean ST elevation were 3.3±1.1 mm. In the remaining individuals, a type 1 ECG was present only after ajmaline or flecainide challenge.
During follow-up, 7 of 202 patients (3.5%) have an arrhythmic event: resuscitated SCD (n=1), syncope (n=3), ventricular arrhythmia (n=1) and appropriate ICD shock (n=2). Among them, 5 women were symptomatic (syncope) and 2 were asymptomatic. Asymptomatic women don't have a spontaneous type-1 ECG at baseline whereas 3/5 symptomatic women have a type-1 ECG at baseline.
We compared our results in women to the men of the FINGER BrS Registry (n=745 men). The number of ICD implanted patients was higher in FINGER cohort (22 vs 47%). Men of the FINGER cohort presented more arrhythmic events than women in this study (5.7 vs 3.5%).
Conclusion: In this study, women seem to represent a lower-risk group than men. A spontaneous type-1 ECG at baseline doesn't seem to be a risk factor for arrhythmic event in women. Further studies are needed in larger women population in order to identify risk factor in Brugada women.

P2953 | BEDSIDE
Circadian variation of ventricular arrhythmias does not affect survival in patients using the wearable cardioverter defibrillator

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Purpose: The wearable cardioverter defibrillator (WCD) is an external, ambulatory device that protects patients from tachyarrhythmic sudden cardiac death (SCD). Previous epidemiological studies report increased frequency of ventricular arrhythmias and SCD in the morning and evening hours. We examined the circadian variation of sustained VT and VF in patients wearing the WCD, and hypothesized that the circadian VT/VF variation would not affect WCD patient survival.
Methods: The manufacturer-maintained registry was searched for patients treated for VT/VF between July 2001 and November 2013. Each day of wear was segmented into one-hour intervals and harmonic regression was used to curve-fit VT/VF events. Data were reviewed for 24-hour patient survival. Multiple treatments on the same day were assessed as a single episode for analysis of survival and grouped in four-hour intervals. T-test and chi-square analyses were used to determine significance for the distribution of VT/VF events and survival, respectively.
Results: A total of 2950 treated VT/VF events (43% VF events) occurred in 1428 patients (Gender: 75.3% male; Age: 62.7±12.9 years; Ejection fraction: 25.3±10.3%; Duration of use: 43.3±77.9 days). Harmonic regression showed that the VT/VF circadian variation exhibited a bimodal distribution, with a peak between 9 AM and 11 AM and a second between 6 PM and 8 PM (Fig. 1). The peaks were significantly different ($p<0.001$) from the rest of the distribution. Survival was 92% with no significant difference (p=0.203) among the specified time intervals (Fig. 1).
Conclusions: WCD treatment for VT/VF events followed a bimodal distribution, with increased frequency in the morning and evening hours. WCD treatment survival was high with no evident circadian variation.

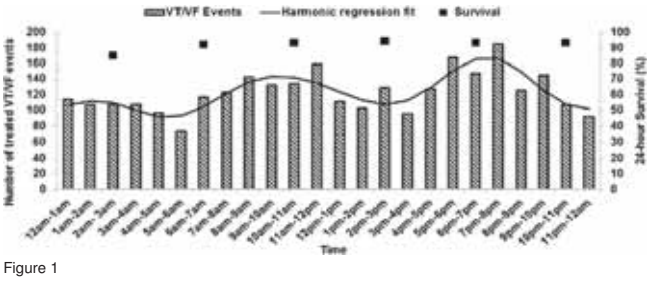

Figure 1

P2954 | BEDSIDE
Non-steroidal antiinflammatory drug use is associated with risk of out-of-hospital cardiac arrest - A nationwide case-time-control study

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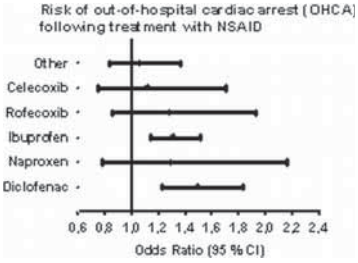
Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used and have been found to pose a risk to cardiovascular safety. Whether use of NSAIDs is associated with out-of-hospital cardiac arrest (OHCA) is unknown.
Methods: We used data from the nationwide Danish Cardiac Arrest Registry and identified all persons with OHCA from 2001-2010. In The Danish Registry for Medical Product Statistics we identified all collected prescriptions of NSAIDs 30 days prior to OHCA divided into diclofenac, naproxen, ibuprofen, rofecoxib, celecoxib, and other. Risk of OHCA associated with use of NSAIDs was analyzed in case-time-control models matching four controls on sex and age per case to account for variation in drug utilization over time.
Results: A total of 28 977 persons with OHCA were identified; 3369 of these were treated with a NSAID up to 30 days prior to OHCA. NSAID users had a mean age of 67.7 years (SD ± 14.5) and 41.1% were women. Among non-users 33.8% were women and the mean age was 68.1 years (SD ± 16.0). Ibuprofen and diclofenac were the most commonly used drugs and represented 51.0% and 21.9% of total NSAID use, respectively. Compared with nonusers, use of diclofenac was associated with an increased risk of OHCA (OR, 1.50; 95% CI, 1.23-1.82) as was ibuprofen (OR, 1.31; 95% CI, 1.14-1.51). Naproxen, celecoxib, and rofecoxib were not significantly associated with OHCA (OR, 1.29; 95% CI, 0.77-2.16; OR, 1.13; 95% CI, 0.74-1.70; OR, 1.28; 95% CI, 0.74-1.70), respectively.



Conclusion: Use of ibuprofen and diclofenac was associated with an increased risk of out-of-hospital cardiac arrest. Careful consideration is warranted when treating people with NSAID.

P2955 | BEDSIDE
Optimal defibrillation energy for out of hospital cardiac arrest - 150 vs. 200 Joule

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Purpose: The optimal initial defibrillation energy for out of hospital cardiac arrest is unknown. We thought to investigate whether there is a difference in Return Of Spontaneous Circulation (ROSC) after initial shocks with 150 or 200 Joule in out of hospital cardiac arrest.
Methods: Automated external biphasic defibrillators from ambulances staffed with emergency medical technicians (EMT-d) were randomized to a fixed energy of either 150 or 200 Joule. All attempts of out of hospital resuscitation by EMT-d from 01/2010 until 07/2012 for which data were available were analyzed. ROSC at time of admission to the hospital served as the primary endpoint.
Results: 1490 attempts were evaluated. 498 cases showed ventricular fibrillation. In 277 cases of ventricular fibrillation shocks were applied with 150 Joule (group A) and in 221 cases with 200 Joule (group B). The two groups had similar characteristics concerning age (group A: 65.03±17.1 years; group B: 63.24±15.3

years, p>0.05) and gender (males group A: 77.6%; group B: 80.5%) as well as witnessed cardiac arrest (group A: 61%, group B: 59.3%) and bystander resuscitation (group A: 45.1%, group B: 45.7%). With regard to ROSC as the primary endpoint of the study we did not find a difference between the two groups (group A: 49.5% vs. group B: 52%, p>0.05).
Conclusion: There was no difference in ROSC at admission to hospital for defibrillation with 150 vs. 200 Joule.

RIGHT VENTRICULAR FUNCTION: COMING OF AGE

P2956 | BEDSIDE
Age and sex related changes in left and right ventricular function

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There are limited data regarding performance of RV and LV with age and sex.
Methods: We assessed these changes in 131 normal subjects (19-78 yrs, 89 women) by conventional, tissue Doppler, and speckle tracking echocardiography. They were divided in 4 groups (table). LV systolic function was assessed from ejection fraction (EF), global longitudinal strain and strain rate (LVSRs), radial and circumferential strain, torsion, and basal rotation; LV diastolic function from E/E', and early and late global longitudinal strain rate (LVSRe, LVSRl). RV systolic function was assessed from TAPSE, FAC, tricuspid annular velocity, global systolic strain and strain rate; diastolic function from early and late global strain rate (RVSRe and RVSRl).
Results: LV global systolic function (EF), radial and circumferential strain, and torsion were not affected by age, whereas longitudinal strain rate decreased with age (r=0.33) and basal rotation increased compensatory (r=-0.27). LV estimated filling pressure (E/E') increased with age (r=0.33); early longitudinal strain rate was impaired with age (r=-0.52), whereas late longitudinal strain rate increased compensatory (r=0.24). RV systolic function was not affected by age, whereas early and late strain rate had similar changes as in the LV (r=-0.38 and r=0.27) (all p<0.001). RV and LV early diastolic changes were correlated (r=0.48). All these changes of diastolic function in both ventricles became significant after 50 years (table). Women had better systolic and diastolic LV function (LVSRs, LVSRe), and also diastolic RV function (RVSRe) (p<0.01), but only for the group <40 years. Changes of LV or RV function with age where similar for men and women.

Age changes of LV and RV function

AGE	LVSRs (1/s)	E/E'	LVSRe (1/s)	LVSRl (1/s)	RVSRe (1/s)	RVSRl (1/s)
<40 yrs (n=37)	–1.2±0.2	6.5±2	1.6±0.4	0.94±0.2	1.47±0.38	1±0.2
41–50 yrs (n=33)	–1±0.2	7±1.8	1.44±0.3	1±0.2	1.35±0.4	1±0.3
51–60 (n=37)	–1±0.2	8.2±2.6	1.27±0.3	1±0.3	1.36±0.4	1.1±0.3
>61 yrs (n=24)	–1.±0.1	9±2	1.1±0.2	1.1±0.2	1.1±0.4	1.3±0.3
P value (ANOVA)	0.001	0.006	<0.001	0.008	0.002	0.009

Conclusion: LV global, radial and circumferential systolic function, and RV systolic function are not affected by age, whereas both LV longitudinal and RV diastolic functions are impaired by age. Changes are significant after 50 years, and similar between men and women.
Acknowledgements: Grant 112/2011.

P2957 | BEDSIDE
Independent role of the right ventricle systolic and diastolic function in predicting the long-term survival of outpatients with systolic heart failure. 3 years follow-up

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Objective: To determine in outpatients with systolic heart failure (SHF) the best echocardiographic parameter of the right ventricle (RV) function to evaluate the long-term survival.
Methods: 142 outpatients with SHF (LV ejection fraction – 29.8 +8.9%) followed-up in a single heart failure unit. A complete echocardiographic study and the RV function was characterized with the RV diastolic dimension at PLAX (RVd), TAPSE, RVFAC, tricuspid annulus TDI (S, E and A) and RV global strain (RV-GS), strain-rate S (RV-GSRs), E (RV-GSRe) and A (RV-GSRa). Clinical follow-up was 3 years. Events: Cardiovascular death. Statistics: Group t-Test, ROC curve (AUC), Survival curve (KM-Log-Rank test), Univariate and multivariate Cox regression.
Results: (1) Mortality rate was 35.2% (2)The ROC curve for death was associated with RV-d (AUC=0.619 p=0.034), TAPSE (AUC=0.659; p=0.002), STr (AUC=0.7; p=0.002), ATr (AUC=0.664; p=0.029), RV-GS (AUC=0.725; p<0.001), RV-GSRs (AUC=0.7; p<0.001) RV-GSRa (AUC=0.672; p=0.002). (3) All these parameters were predictors of the survival by univariate Cox regression (see table); (5) the independent predictors of survival with the multivariate Cox regression were: systolic- STr (HR2.25; p=0.032) and RV-GS (HR=4.9; p=0.001); diastolic – ATr (HR=2.6; p=0.036) and RV-GSRa (HR=2.4; p=0.069. The multivariate Cox regression model combining these significant parameters showed the RV-GS>-11.2 (HR=4.6; p=0.014) and ATr <108.33 (HR= 2.5; p=0.09) were independent predictors of survival.
Conclusion: RV functional parameters are important predictors of the long-term survival of outpatients with SHF.

P2958 | BEDSIDE
Right atrial volumes and function by three-dimensional (3D) echocardiography and left ventricular 3D Speckle tracking in dilated cardiomyopathy

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Background: Right atrial (RA) size and function have clinical and prognostic value in dilated cardiomyopathy (DCM). 3D echo (E) and speckle tracking provide robust and reproducible data to measure RA volumes and RA and left ventricular (LV) function.
Purpose: To obtain RA volumes and ejection fraction (EF) by 3DE and RA deformation properties by 2D speckle tracking and LV function by 3D Speckle tracking in DCM, and to look for their clinical importance in management and prognosis.
Methods: By 3DE (software Auto LVQ GE Healthcare and Tomtec 4D) and by speckle tracking echocardiography we studied 80 subjects: 50 (mean age: 62 yrs) patients (pts) with DCM and 30 healthy controls. All pts underwent coronary angiography except controls and all had LV ejection fraction (EF) <35%. By E9GE we measured RA maximum and minimum volumes by tracing RA endocardial borders at ventricular end-systole and end-diastole, both by biplane method, 3D and 4D methods; all volumes were indexed for body surface. By Speckle tracking, in apical 4-chambers view, we measured 2D longitudinal systolic RA Strain (S) and Strain rate (SR), at level of RA free wall (basal, medium and apical segments) and 3D LV deformation properties (peak of global longitudinal, circumferential, radial and area S). We measured LV volumes and EF by 2DE and 3DE; and propagation velocity (Vp) by color M-mode; we calculated wedge pressure (PCWP) by E/Ea ratio.
Results: RA maximum volumes were significantly higher in DCM pts (90,5±28,2 ml by Auto LVQ, 85,4±23,6 ml by Tomtec4D) than in controls (43,09±11,21 ml by Auto LVQ, 41,68±12,22 by Tomtec4D; p<0,01). In DCM pts we found significantly lower values of longitudinal systolic RA S for all segments (35±15% basal; 24±11% medium; 15±4,5% apical) than in controls (>80% basal; 62,5±9,6% medium; 26,5±3,5% apical; p<0,01); lower values of longitudinal RA SR for all segments (2,5±0,8 s^{-1} basal; 1,8±0,7 s^{-1} medium; 1,2±0,5 s^{-1} apical) than in controls(basal 5,1±0,71S-1; medium 3,33±0,61 s^{-1}; apical 2,1±0,26 s^{-1}; p<0,01); lower 3D LV deformation properties than in controls (3D longitudinal S: -7,6±3,3% vs -19±3,1%, 3D circumferential S: -8,7±2,8% vs -15,3±2,6%, 3D radial S: 19±7,9% vs 48±9%, 3D area S: -14±5,1% vs -30,1±3,6%; p<0,001). Pts with higher RA volumes and lower RA S and SR had higher E/Vp values and higher PCWP by E/E', and had more symptomatic illness independently from LVEF and 3D LV S.
Conclusions: In DCM 3DE and speckle tracking provide simple and reliable values of RA volumes and function. RA volumes and deformation properties are expression of illness clinical severity, and may be predictive of adverse clinical events.

P2959 | BEDSIDE
Speckle tracking echocardiography with a 12-segments model approach of the right ventricle might identify better right ventricular dysfunction

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Background: Right ventricular (RV) dysfunction is associated with increased mortality in patients with acute or chronic coronary artery disease (CAD). Con-

Abstract P2957 – Table 1

	KM	Univariate Cox (HR; p)	Multivariate Cox regression (HR; p)		
			RV-Systolic	RV-Diastolic	Syst vs Diast
RV-d >26.95mm	0.003	2.5 (1.3–4.8); p=0.004	–	NS	–
TAPSE <20	0.001	2.7 (1.5–4.7); p=0.001	NS	–	–
S-Tr <9.5	0.001	3.2 (1.6–6.4); p<0.001	2.2 (1.1–4.8) ; p=0.03)	–	NS
A-Tr <108.33	0.005	3.0 (1.3–6.9); p=0.008	–	2.6 (1.1–6.6); p=0.03	2.5 (0.9–7.4); p=0.09
RV-GS >-11.2	<0.001	3.7 (1.8–7.5); p<0.001	4.9 (1.9–12.2); p=0.001	—	1.7 (1.4–16); p=0.014
RV-GSRs >-0.7	<0.001	3.3 (1.-6.3); p<0.001	NS	–	–
RV-GSRa < 0.5	0.002	3.2 (1.5–6.8); p=0.003	–	2.4 (0.9–6.4); p=0.07	NS

ventional echo parameters may not identify always RV dysfunction, since they ignore the contribution of some RV walls to ejection. MRI studies suggested that tricuspid annular systolic velocity (S') might be a better marker of RV dysfunction, but they included only the 4C view evaluation. Speckle tracking echocardiography (STE), by assessing the RV as a whole, might be a better technique for the diagnosis of RV dysfunction. Thus, we investigated the role of a 12-segments model of the RV in the detection of the RV dysfunction by STE, in patients with acute or chronic CAD.

Method: We studied 95 subjects: 45 with acute myocardial infarction (AMI) and right coronary artery occlusion, 25 with severe, surgical CAD, and 25 normals (with similar age and sex). RV dysfunction was diagnosed by conventional echo, from tricuspid annular systolic excursion (TAPSE) and fractional area change (FAC), being defined by TAPSE<16mm and FAC<32%; by tissue Doppler from S', being defined by a S'<11 cm/s; and by STE, from lateral (LS) and septal (SS) strain (4C view), and from anterior (AS) and inferior (IS) strain (2C view), global RV strain (RVGS) being calculated.

Results: RV dysfunction was diagnosed by conventional echo in 34%, by tissue Doppler in 54%, and by all 3 parameters in 57% of CAD patients. However, in the remained 43% of CAD patients, labeled with "no RV dysfunction", we found decreased all deformation parameters by comparison with normal subjects (table), with no differences between acute and chronic CAD.

Comparison between CAD and normals

	LS	SS	4C GS	AS	IS	2C GS	RVGS
Acute CAD (n=19)	−19±7	−14±6	−16±5	−19±7	−21±8	−20±6	−18±5
Chronic CAD (n=11)	−22±6	−12±6	−17±4	−20±7	−23±7	−21±6	−19±4
Normals (n=25)	−28±5	−20±3	−24±3	−28±4	−30±3	−29±3	−26±2
p value (CAD vs. N)	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001

Conclusion: Speckle tracking echocardiography with a 12-segments model approach of the right ventricle might identify better right ventricular dysfunction in patients with acute or chronic CAD. Further studies are needed to establish cut-off values, and provide accuracy and prognostic value of this new approach.

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P2960 | BEDSIDE
The right heart in HFpEF, insights from a cardiac magnetic resonance study

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Purpose: Cardiovascular magnetic resonance imaging (CMR) is the gold-standard technique for the assessment of right ventricular function. Recent data indicate that right ventricular ejection fraction (RVEF) <45% by CMR is a strong predictor of outcome in patients with dilated cardiomyopathy. However, the prognostic significance of RVEF in heart failure with preserved ejection fraction (HFpEF) is unknown.

Methods and results: Between December 2010 and September 2013 we prospectively enrolled 105 HFpEF patients. At baseline, all patients underwent CMR imaging in addition to invasive and non-invasive testing. Right ventricular systolic dysfunction (RVSD), defined by RV ejection fraction <45%, was present in 27 (25.71%) patients.

Patients were followed for 434±325 days, during which 31 had a cardiac event (hospitalization for heart failure and/or death for cardiac reason).

By univariate Cox analysis RVSD (p=0.007), NYHA functional class (p=0.006), 6-minute-walking-distance (p<0.001), diabetes (p<0.001), and invasively measured systolic (p<0.001) and mean pulmonary artery pressures (p<0.001) were significantly associated with outcome. By multivariable analysis only RVSD (HR 4.852, CI 1.97 - 11.92, p=0.001) and diabetes (HR 3.99, CI 1.65 - 9.65 p=0.002) remained significant predictors of cardiac events. In addition, patients with RVSD presented with significantly higher resting heart rate (p=0.022), more advanced NYHA functional class (p=0.016) and shorter 6-minute-walking-distance (t-test p=0.016). By Kaplan Meier analysis, outcome was significantly worse in patients with RVSD (log rank, p=0.0052).

Conclusions: Although HFpEF is considered a disease of the left ventricle, respective parameters are not related with outcome. In contrast, RVSD has a significant impact on outcome and clinical status in HFpEF patients. Assessment of RVSD by CMR is important for risk-stratification in this patient population.

P2961 | BEDSIDE
Evolution of right ventricular function after cardiac transplantation

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Right ventricular (RV) dysfunction is involved in many of the early cardiac complications in heart transplantation (HT).However, limited data on changes in RV post-HT time course have been published.We sought to describe the evolution of parameters of RV function during the first two years after HT.

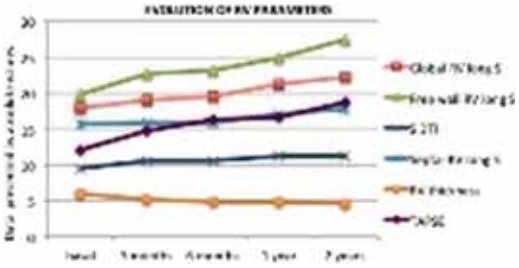
Methods: We include 29 recipients followed during 1 year, 20 of these during 2 years. For RV systolic functional assessment, TAPSE, RV fractional area change (FAC), DTI systolic (S) velocity and Tei index were measured. RV longitudinal strain was measured in 4 chamber view. Studies with ≥2R rejection were excluded.

Results: Evolution of echo parameters is shown in the table.

Evolution of RV parameters after HT

Parameter	Basal echo	3 months	6 months	1 year	2 years
TAPSE (mm)	12.1±2.7	14.8±3.5*	16.3±3.7*	16.6±4.1*	18.7±4.1*
FAC (%)	44.8±10.3	44.4±8.0	43.5±9.4	43.8±8.3	44.6±9.5
TEI index	0.83±0.4	0.71±0.3	0.69±0.3	0.72±0.3	0.72±0.3
S DTI (cm/s)	9.5±2.1	10.6±2.8	10.6±2.0	11.3±3.1	11.2±2.3
Global RV long S	−17.9±3.6	−19.1±4.4	−19.5±3.6	−21.2±4.2#	−22.3±4.0#

#p<0.05, *p<0.01 compared to basal parameters.



Evolution of echocardiographic measures.

Conclusion: In our cohort of HT patients measures of RV longitudinal function like TAPSE and RVGLS were markedly reduced in the early postHT period. TAPSE improves at 3 months while RVGLS does not normalise until 1 year. RV-FAC is normal in early postHT and remains unchanged. At 2 year follow-up longitudinal and transversal function of RV are completely normalized. This information should be useful to monitorise the normal evolution of RV after HT.

P2962 | BEDSIDE
The relationship between RV-LV delay and left ventricular reverse remodeling with Cardiac Resynchronization Therapy

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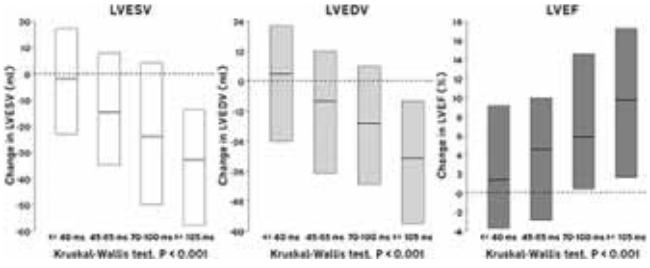
Purpose: Placing leads at sites of increased electrical dyssynchrony, as measured by QLV, provided incremental predictive value for left ventricular (LV) reverse remodeling independent of QRS duration and morphology during Cardiac Resynchronization Therapy (CRT). The RV-LV interval is another measure of electrical delay that can be easily measured by CRT devices. Accordingly, the goal of this analysis was to evaluate RV-LV interval to predict echocardiographic outcomes.

Methods: A total of 419 patients (66% male, mean age 66±11 years, LV ejection fraction (EF): 28% ± 9%, QRS duration 150±25 ms, LVESV 129±63 ml) were analyzed. The RV-LV was defined as the time from the peaks of the RV to the LV electrograms, as measured by a blinded core lab. The prespecified primary endpoint (CRT response) was a >15 ml reduction in LVESV from implant to 6 months, as assessed by the core lab. Multivariate logistic regression models were used to adjust for baseline covariates.

Results: Patients were grouped by RV-LV quartiles with cutoffs of 40, 65 and 100 ms. The changes in LVESV and other remodeling endpoints with CRT (median ± inter-quartile range) were strongly affected by electrical delay. The response rates for the RV-LV quartiles were 30%, 49%, 59%, 75%, respectively (P<0.001). RV-LV added significant predictive value for CRT response after adjusting for baseline covariates. Patients in the longest RV-LV quartile had a greater than 6 fold increase in their odds of response vs. the shortest quartile.



Conclusions: Baseline electrical dyssynchrony, as assessed by RV-LV, predicted the magnitude of structural responses to CRT. This measure can easily performed

and may provide a simple means of selecting/optimizing LV stimulation site and possibly maximizing CRT response.

DIAGNOSTIC ADVANCES IN CARDIOMYOPATHIES

P2963 | BEDSIDE
HIV infection is associated with diastolic dysfunction independently of antiretroviral therapy

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Background: Patients (pts) with HIV infection have a substantially increased risk of cardiovascular disease.Different pathophysiological mechanisms can be responsible for this association, such as the high prevalence of cardiovascular risk factors in HIV infected pts, the metabolic changes induced by antiretroviral therapy (ART), the systemic inflammatory response associated with HIV infection, and the direct action of HIV on cardiac cells.
Aims: To evaluate the impact of HIV infection on cardiac structure and function, and to determine if these changes are dependent on the ART.
Methods: Between January 2012 and May 2013, 206 consecutive pts with type 1 HIV infection and 30 age and gender-matched healthy control subjects were prospectively enrolled.Clinical evaluation, blood sample analysis and detailed transthoracic echocardiography were performed. Pts with HIV were divided in two subgroups:ART-naïve group (n=88) and ART group.Cardiac morphology and function were assessed according to the European Echocardiography Association and American Society of Echocardiography Consensus criteria.
Results: Among the HIV-infected pts the mean age was 41±9 year-old and 70% was male.The prevalence of diastolic dysfunction (DD) in the HIV group was 23%; the majority was grade 1 DD (73%), and only 9 (6%) of ART and 4 (5%) of ART-naïve groups had grade 2 DD.Compared to controls, ART-naïve and ART pts had lower early diastolic tissue Doppler velocities (decreased E' septal and E' mean velocities), and higher LV filling pressures (increased E/E' septal and E/E' mean ratios).No significant differences in diastolic function parameters were found between ART-naïve and ART groups.In a multivariable logistic regression model, higher age and BMI were demonstrated to predict DD in HIV pts.After adjustment for age and BMI, the odds of having DD was 10.4-fold (95% CI of 1.3 to 84.3) higher in the population with HIV than in healthy controls.There was no significant difference in any systolic function parameter comparing controls with ART-naïve or ART groups, or between HIV pts.After adjusting for age and BMI, the population with HIV had a higher mean LV mass index (15.0 g/m^2, 95% CI of 6.2 to 24.7, P=0.001) and larger mean LV telediastolic volume (8.7 mL/m^2, 95% CI of 1.0 to 16.4, P=0.026) than controls.LV mass and LV telediastolic volume did not differ between ART-naïve and ART groups (P=0.331 and P=0.584, respectively).
Conclusions: HIV infection was independently associated with DD, higher left ventricular mass and telediastolic volume compared with healthy controls. These differences were not dependent on antiretroviral therapy.

P2964 | BEDSIDE
Consequences of Interleukin-1 signaling in virus-induced and autoimmune myocarditis

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Purpose: The etiology of acute and chronic myocarditis is highly variable. It comprises infectious agents such as viruses (enteroviruses, parvovirus B19, EBV, HHV6) but also non-infectious causes, including systemic diseases or autoimmune processes. Importantly, in all types of myocarditis cytokines are known to play a decisive role in the induction and maintenance of inflammation.
Methods and results: In order to evaluate the role of IL-1ß in patients with virus-associated and virus-negative, immune-mediated myocarditis we performed quantitative RT-PCR and radioactive in situ hybridization (ISH) experiments. We found in patients with viral myocarditis 6 times more and in patients with virus-negative myocarditis 2,5 times more IL-1ß mRNA than in those with dilated cardiomyopathy (DCM) and ischemic cardiomyopathy (ICM). In acute and chronic viral as well as autoimmune myocarditis we found high amounts of IL-1ß positive cells within areas of inflammation and necrosis by ISH compared to DCM patients.
As IL-1ß is involved in the IL-6 signalling pathways we determined the cardiac IL-6 mRNA expression by qRT-PCR. Patients with viral and non-viral myocarditis express significantly more cardiac IL-6 mRNA than DCM patients. Interestingly, patients with ICM express more cardiac IL-6 than patients with DCM. This is probably due to the fact that IL-6 represents a crucial checkpoint regulator of neutrophil trafficking by orchestrating chemokine production and leukocyte apoptosis, which are present in hearts with ICM but not with DCM. Previously, we observed in experimental myocarditis that IL-1 expression influences ERK pathways as well as the expression of osteopontin with severe consequences for the evolvement of cardiac fibrosis. Also, in patients with both types of acute myocarditis we found by immunohistochemistry numerous osteopontin and ERK protein expressing immune cells in the damaged myocardium. During chronic myocarditis the number of these immunohistochemically positive cells are still significantly enhanced compared to DCM or normal hearts.
Conclusions: In this study we demonstrate that in human infectious as well as non-infectious acute and chronic myocarditis IL-1ß is significantly upregulated in interstitial immune cells in the inflamed myocardium, which has severe consequences on the activation of further inflammatory pathways and molecules including IL-6, ERK, and osteopontin, finally resulting in cardiac fibrosis and heart failure. It is hoped that of blocking IL-1ß will allow to interrupt inflammatory processes in myocarditis, thus preventing DCM.

P2965 | BEDSIDE
Predictors of atrial arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia

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Purpose: Data about risk factors predicting atrial fibrillation/flutter (Afib/Aflu) in arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC) are scarce. The purpose of the present study was to identify electrocardiographic (ECG) and echocardiographic (TTE) variables that predict Afib/Aflu in patients with ARVC.
Methods: 12-lead ECGs and TTE of 90 patients from three centers diagnosed with definite or borderline ARVC according to the 2010 TFC were analyzed. Data were compared in two patient groups: (1) patients with Afib/Aflu and (2) all other patients.
Results: 18 (20%) patients experienced Afib/Aflu during a follow-up period with median of 5.8 years (interquartile range 2.0-10.4 years). Kaplan-Meier and Cox regression (Table) revealed reduced times to atrial arrhythmia among patients with a right ventricular fractional area change (FAC) <27% (p<0.001), left atrial diameter (parasternal long axis) ≥24.4 mm/m^2 (p=0.001), and right atrial short axis diameter (4-chamber view) ≥22.1 mm/m^2 (p=0.05). P sinistroatriale conferred a HR of 3.37 (95% CI 0.92-12.36, p=0.067). Five (28%) patients with Afib/Aflu experienced inappropriate ICD shocks. Presence of Afib/Aflu was more frequent in patients with heart transplantation and cardiac death during follow-up (38% vs. 6%, p=0.014).

Table 1. Univariable Cox regression: electrocardiographic and echocardiographic variables associated with atrial fibrillation/atrial flutter

Variable	Univariable Analysis	
	Hazard ratio (95% CI)	p-value
FAC (%) per unit decrease	1.09 (1.03–1.14)	0.003
LA (mm/m^2) per unit increase	1.15 (1.01–1.31)	0.031
RA (mm/m^2) per unit increase	1.08 (1.02–1.15)	0.013
P sinistroatriale	3.37 (0.92–12.4)	0.067
Age at inclusion (per year increase)	1.02 (0.99–1.06)	0.13
Moderate/severe tricuspid regurgitation	2.07 (0.72–5.97)	0.18
Left ventricular involvement	1.95 (0.63–6.02)	0.25

Conclusions: In this multicenter long-term study we demonstrate that Afib/Aflu are common in patients with ARVC, and associated with inappropriate ICD shocks, heart transplantation, and cardiac death. Echocardiographic evidence of reduced RV function and atrial dilation may help to identify those patients being at increased risk for the development of Afib/Aflu.

P2966 | BEDSIDE
Ventricular arrhythmias in subjects with ARVC are associated with increased cardiac volumes but not with ejection fraction by cardiac magnetic resonance imag

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Purpose: Ventricular arrhythmias are frequent in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC), but risk stratification is still challenging. We investigated the relation between ventricular arrhythmias and cardiac volumes and function by cardiac magnetic resonance imaging (MRI).
Methods: In total, 56 ARVC subjects (mean age 43±16 years, 57% male) were studied by cardiac MRI. We assessed end-diastolic volume indexed by body surface area (EDVI) and ejection fraction (EF) in the right (RV) and in the left ventricle (LV). Ventricular arrhythmias were defined as documented ventricular tachycardia or fibrillation or aborted cardiac arrest.
Results: Of the 56 included, 33 (59%) were index patients fulfilling 2010 Task Force Criteria for ARVC diagnosis and 23 (41%) were mutation positive family members. Ventricular arrhythmias had occurred in 29 (52%). Indexed LV and RV volumes were increased in patients with ventricular arrhythmias compared to those without (LVEDVI: 80±16 ml/m^2 vs. 67±18ml/m^2, p=0.01 and RVEDVI 104±36 ml/m^2 vs. 69±25 ml/m^2, p<0.01) (Fig. 1). LV and RV function by EF did not differ in ARVC subjects with and without arrhythmic events (LVEF: 51±8% vs. 50±9%, p=0.66 and RVEF: 39±14% vs. 40±11%, p=0.77). Body surface area was similar in both groups (1.92±0.18 m^2 vs. 1.89±0.24 m^2, p=0.64).
Conclusions: ARVC subjects with ventricular arrhythmias had increased indexed

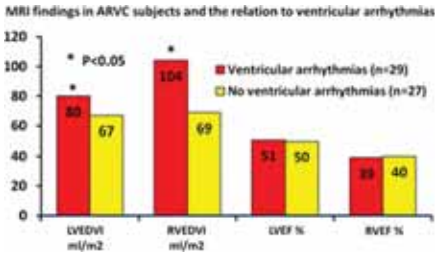

Figure 1

RV and LV end-diastolic volumes compared those without, while myocardial function by EF did not differ in RV nor in LV. Risk stratification of ventricular arrhythmias in ARVC subjects by MRI should not rely on EF, but focus on increased volumes in RV and LV.

P2967 | BEDSIDE
High-throughput sequencing in italian patients with hereditary cardiomiopathies

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Purpose: While current clinical guidelines recommend routine genetic testing in patients (pts) with hereditary cardiomyopathies (CMs), its use has been limited by the cost and the complexity of conventional sequencing technologies. Next Generation Sequencing (NGS) is rapidly changing the landscape of genetic testing enabling simultaneous screening of multiple genes for multiple patients in a single sequencing run. The aim of this study was to explore a NGS based genetic test as replacement for Sanger sequencing.
Methods: We designed a 111 monogenic cardiovascular disease causative gene panel and we studied 94 unrelated patients (pts) including 80 with Hypertrophic Cardiomyopathy (HCM), 18 pts with Dilatative Cardiomyopathy (DCM) and 6 pts with Arrhythmogenic Cardiomyopathy (AC). Targeted resequencing was performed on HiScan SQ platform.
Results: 98,13% of the target region was covered to a depth of 20 or more with a mean coverage on target of 530X. A total of approximately 1016 variants were found for each patient. Rare (frequency <0.05), non-synonymous, loss- of- function and splice-site variants were defined as candidates. Pathogenic or likely-patogenic variants were all confirmed by Sanger Sequencing and cosegregation was tested when possible. Excluding titin missense variants, we identified 48 candidate variants in sarcomeric or associated genes (27 novel) in 48 of the 70 HCM patients (68%) with 14% of complex genotype. MYH7, MYBPC3 and TNNI3 resulted the high-yield genes; 19 additional candidate variants (13 novel) in desmosomal and ion-channel genes in 14 patients (20%) were identified in this group. We also identified 10 candidate variants (7 novel) in 7 of the 18 patients (39%) with DCM and 5 variants in 3 of the 6 patients (50%) with AC.
Conclusions: A targeted protocol allowed the identification of a likely pathogenic variants in a large proportion of patients with hereditary cardiomyopathies, irrespective of phenotype, with marked increase compared to standard Sanger sequencing. The unexpected finding on rare non synonymous variants in desmosomal and ion-channel genes among HCM pts raises important issues regarding their role as previously unappreciated modifiers of the disease, potentially relevant to risk prediction and counseling.

P2968 | BEDSIDE
Relationship between time course of morphometric improvement and extent of cardiac fibrosis in patients with idiopathic dilated cardiomyopathy

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Purpose: Left ventricular reverse remodeling (LVRR) is a morphometric surrogate marker of favorable prognosis in dilated cardiomyopathy (DCM), and a prediction of those is an urgent issue for therapeutic strategy. However, prediction of LVRR is difficult because its time course is significantly varied.
Methods: We reviewed 207 consecutive idiopathic DCM patients treated by optimal pharmacotherapies whose echocardiographic data for the first 3 years were available. LVRR was defined as ≥+10% increase in LV ejection fraction to a final value of ≥35%, along with ≤-10% decrease in LV end-diastolic dimension. Cardiac events (CEs) such as cardiovascular death, readmission for heart failure, or detection of major ventricular arrhythmia were recorded, and patients were observed until death.
Results: LVRR was detected within 6 months in 56 patients (27%, E: early responders), after 1 year in 52 patients (25%, L: late responders), and not detected in 99 patients (48%, N: no responders). Kaplan-Meier analysis revealed that the survival rate for CEs was lower in N group than in E or L group ($p<0.05$, Fig. 1A).

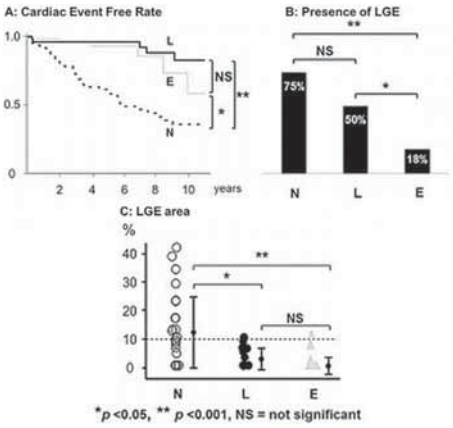

Figure 1

Among 60 patients (23%) evaluated using cardiac magnetic resonance imaging, late gadolinium enhancement (LGE) was detected more often in L than E (50% vs. 18%, $p<0.05$), whereas percentage area of LGE (LGE area) was equal and below 10% in both groups (3±3% vs. 1±3%, NS) (Fig. 1B, C). Multivariate analysis showed LGE area was an independent predictor of L group in patients without LVRR at 6 months (adjusted odds ratio = 0.87; 95% confidence interval, 0.72-0.98; $p<0.05$).
Conclusions: Late response to pharmacotherapies has a favorable prognostic value in IDCM patients, with an equivalent impact to the early one. The extent of LGE together with its existence is useful to predict clinical course.

P2969 | BEDSIDE
Genetic spectrum of idiopathic restrictive cardiomyopathy uncovered by NGS

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Background: Cardiomyopathies represent a rare group of disorders often of genetic origin. The genetic spectrum of cardiomyopathies include more then 50 genes. While approximately 50% of genetic causes is known for hypertrophic and arrhythmogenic cardiomyopathy, the genetic spectrum of restrictive cardiomyopathy (RCMP) is widely unknown. Sanger sequencing approach revealed that sarcomeric protein gene mutations and mutations in structural proteins can be associated with idiopathic restrictive cardiomyopathy. The aim of the present study was to identify genetic background of idiopathic RCMP using new generation sequencing.
Patients and methods: We applied new generation sequencing approach (Ion Torrent) to perform a genetic screening for 62 cardiomyopathy-associated genes in 19 patients with idiopathic RCMP.
Results: In 70% of patients more then 1 pathogenic variant was identified. Among all identified pathogenic substitutions only 27% represented variants in sarcomeric protein genes being the only pathogenic variant only in 21% of patients. Pathogenic variants in cytoplasmic and intrasarcomeric cytoskeletal protein genes represented 43%, the rest 30% of the variants were detected in membrane-associated cytoskeletal and matrix-interacting proteins.
Conclusions: We identified more then one pathogenic variant in most of patients with RCMP. Most of the variants were identified not in sarcomeric, but in cytoskeletal and matrix-associated protein genes.

ADVANCED TECHNIQUES TO IMPROVE OUTCOME IN CARDIAC ARREST

P2970 | BEDSIDE
Is urgent invasive strategy for out-of-hospital cardiac arrest survivors associated with better survival?

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Purpose: Out of hospital cardiac arrest (OHCA) is a leading cause of adult death in Europe. Hospital survival rate is low and have not improved in recent years. Acute coronary occlusion is the leading cause of cardiac arrest, however, because of limited data, the indications and timing of coronary angiography (CA) and angioplasty (PCI) in this setting are controversial except for ST-elevation in 12-lead electrocardiogram (EKG). The aim of our study was to understand etiology and survival of patients (Pts) admitted to our hospital with return of spontaneous circulation (ROSC) after OCHA and whether a strategy that leads to an urgent CA and PCI, if required, can improve the outcome.

Methods: Observational retrospective study from January 2006 to December 2009.
Results: In the study period 70 Pts with ROSC after OHCA were referred to our hospital. Mean age was 69,5±13,9; 63% male gender; 11% previous coronary artery disease (CAD), first rhythm was ventricular tachycardia/ventricular fibrillation (VT/VF) in 62%; in 41% diagnosis was acute coronary syndrome (ACS) based upon EKG and enzyme. Hospital survival rates was 48,5%. One year survival rates was 76% of dismissed. Postresuscitation neurologic injury (PNI): 32,8%. According to the presence of ACS: Pt with ACS are mostly male, without differences in age or previous CAD versus no ACS Pt. VT/VF is the most frequent presentation rhythm in ACS Pt (89% vs 40%; p<0,01). Only in 34% of ACS Pt first EKG showed clear sign of myocardial infarction/ischemia. VT/VF is the first recorded rhythm equally in both STEMI and nSTEMI. Early sign of PNI generally are associated with underuse of CA and PCI and worst prognosis. Successful urgent CA and PCI are associated with improved hospital survival in Patient with ACS (equally in STEMI 83% vs 51% p=0,003 and NSTEMI 81% vs 55% p=0,004); and in FV/TV as first rhythm (90% vs 38% p>0,001).
Conclusions: In patients survived from OHCA successful urgent PCI is associated with improved in hospital survival for STEMI, NSTEMI and VT/VF as first rhythm.

P2971 | BEDSIDE
Emergency coronary angiography and revascularization in patients with out-of hospital cardiac arrest, relation to post ROSC ECG, a prospective observational study

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Purpose: The aim of this prospective cohort study was to evaluate the use of post-ROSC ECG to select patients with out-of-hospital-cardiac-arrest (OHCA) in need of immediate coronary angiography (ICA) and acute revascularization.
Methods: All patients with stable ROSC after OHCA were directly transferred to ICA, irrespective of ECG findings. Patients with a clear non-cardiac aetiology were excluded. Patients were classified into three groups according to post-ROSC ECG by two cardiologists blinded to the ICA results: 1) ST-elevation or new LBBB, 2) other signs suspected of coronary ischemia, or 3) no signs of coronary ischemia. In order to identify patients with an indication for ICA, based on either an acute occluded infarct related coronary artery (IRA) or a flow-limiting coronary stenosis, the coronary angiography were re-evaluated in all patients by an interventional cardiologist blinded to the post-ROSC ECG.
Results: A total of 124 patients were admitted to our hospital with ROSC after OHCA. The median age was 62 (IQR 54-69) years, 84% were males, 82% had an initial shockable rhythm. Of the 124 patients 88 (71%) were classified with an indication for ICA according to the ECG (Table). Post-ROSC ECG had a sensitivity of 88% in detecting patients with an indication for ICA. ST-elevation and LBBB alone had a sensitivity of 72%. Acute PCI was performed in 63 (51%) patients. If post-ROSC ST-elevation or new LBBB alone had been used to select patients for ICA, 19 (11+8) out of 124 (15%) patients would have missed a successful PCI.

ECG groups and angiography evaluation (n=124)

	Classification based on post-ROSC ECG evaluation		
	Group 1* (n=68)	Group 2* (n=20)	Group 3* (n=36)
Classification based on coronary angiography evaluation			
Indication for ICA	47 (69%)	11 (55%)	8 (22%)
Occluded IRA or thrombus	33	6	2
Flow limiting stenosis	14	5	6

*Group 1: ST-elevation or new LBBB. Group 2: Other signs of coronary ischemia. Group 3: No signs of coronary ischemia.

Conclusion: ECG findings early after OHCA are difficult to interpret and should not be used as strict selection criteria for referral to hospitals with acute PCI service. Even in the absence of ST-segment deviation or LBBB on post-ROSC ECG, flow limiting coronary lesions may be present and patients may benefit from acute revascularization.

P2972 | BEDSIDE
Experience of using venoarterial extracorporeal membrane oxygenation as emergency cardiac support

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Background: There is no substantial argument about the prognostic factors of patients in cardiac arrest who are treated with venoarterial extracorporeal membrane oxygenation (V-A ECMO) because only a few comparative data are available. Use of V-A ECMO for patients with out-of-hospital cardiac arrest is still controversial.
Methods: We studied 107 consecutive patients (mean age=62.5±15.8 years, 53 patients with out-of-hospital cardiac arrest and 54 patients with in-hospital cardiac arrest) who underwent V-A ECMO due to refractory circulatory collapse between January 2008 and September 2013 in our hospital.
Results: V-A ECMO was safely initiated in 105 patients. Meanwhile, vessel perforation occurred in 2 patients during cannulation. The median time from cardiac arrest to V-A ECMO initiation was 59.3±29.2 minutes. V-A ECMO was initiated due to the following causes: acute coronary syndrome, n=57; myocarditis, n=1; pulmonary embolism, n=4; idiopathic ventricular fibrillation n=10; others, n=32. Mean duration of V-A ECMO was 2.1±2.1 days and 32 (29.9%) patients survived to discharge among whom 25 (23.4%) patients survived with a favorable neurological outcome. The in-hospital mortality was 66.7% (36/54 patients) for in-hospital cardiac arrest vs. 73.6% (39/53 patients) for out-of-hospital cardiac arrest. Mild therapeutic hypothermia was used in 42 (39.3%) patients, among whom 11 patients had good neurological recovery. Percutaneous coronary intervention was performed on 56 (52.3%) patients. Complications included 26 (24.2%) cases of hemorrhage and 6 (5.6%) cases of limb ischemia. V-A ECMO was urgently initiated in 3 patients with aortic dissection, which is a contraindication of V-A ECMO. The stepwise regression analysis showed that a low lactate level, normal pupil light reflex, absence of hemorrhage, and use of mild therapeutic hypothermia are predictive of neurologically intact survival, although out-of-hospital cardiac arrest is not a risk factor for poor prognosis.
Conclusion: By performing resuscitation with V-A ECMO support, 1 out of 4 patients who were otherwise in a near-fatal condition were rescued. V-A ECMO was effectively used not only for in-hospital cardiac arrest, but also for out-of-hospital cardiac arrest. The prognosis of cardiac arrest patients who receive V-A ECMO support can be estimated using simple routine examinations.

P2973 | BEDSIDE
A systematic diagnostic and therapeutic approach for the treatment of patients after cardio-pulmonary resuscitation: a prospective evaluation of 212 patients during 5 years

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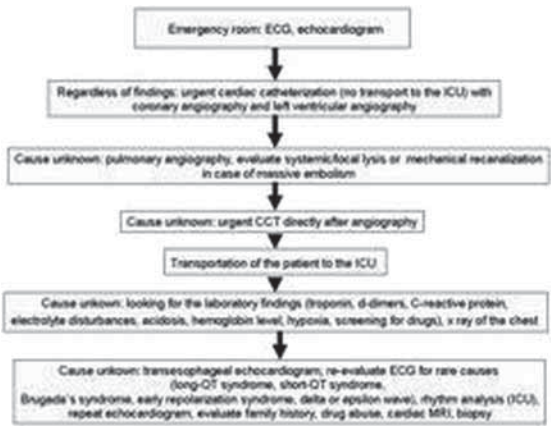
Purpose: There is a need for a systematic treatment protocol for patients after resuscitation.
Methods: A systematic diagnostic approach including ECG, echocardiogram, urgent cardiac catheterization ("STEMI-like" workflow), pulmonary angiography, CT scans, pre-defined laboratory findings, IABP, hypothermia and cMRI prospectively during the last 5 years was in our cardiology department evaluated (see figure). The primary endpoint was the Cerebral Perfomance Category Scale (CPCS).
Results: From January 2008 to December 2012, 212 patients were included. Mean age was 66.7 years, 71.2% were male, the mean EF was 42.9%, mean time from first medical contact to start of catheterization was 76.6 min.
A significant coronary artery stenosis was found in n=130 (61.3%), a PCI in 101 pts (47.6%). An ACS was diagnosed in 100 patients (47.2%), 91 patients (42.9%) had a cardiomyopathy.
Rare diagnoses were pulmonary embolism (n=8, 3.8%), a congenital defect (n=4, 1.9%), LQTS (n=4, 1.9%), an early repolarization syndrome (n=2, 0.9%) and aortic dissection (n=1, 0.5%).
A mechanical recanalization of a thrombus of the pulmonary artery was done in one pt.
An extracardiac cause for cardiac arrest was observed in 12 patients (5.7%), mostly stroke.
Results endpoints: The survival rate was n=76 (35.9%), a CPCS of 1/2 was seen in 67 patients (31.8%).
In pts after succesful PCI, a significant difference in mortality was found (65.4% vs. 95.7, p<0.05). The difference in mortality with IABP vs. no IABP was not



Diagnostic and therapeutic algorithm

significant (p=0.6). Hypothermia reduced mortality significantly (52.7% vs 68.2%, p<0.05).
Conclusion: A systematic diagnostic and therapeutic algorithm using a "STEMI-like" workflow which includes urgent catheterization is feasible, safe and can improve prognosis.

P2974 | BEDSIDE
Long-term neurological outcome of extracorporeal cardiopulmonary resuscitation for out of hospital cardiac arrests

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Purpose: To investigate one-year neurological outcome of patients who have undergone extracorporeal cardiopulmonary resuscitation (ECPR) and make comparison to neurological outcome at the time of hospital discharge.
Methods: Patients were included in this single center retrospective study between 2003 and 2012, when they met following criteria: 1. Out of hospital cardiac arrest without return of spontaneous circulation on arrival to the hospital, 2. Undergone emergent ECPR using veno-arterial extracorporeal membrane oxygenation (VA ECMO) as an adjunct to conventional CPR. Initial rhythm could be any rhythm and implementation of ECPR was on physician's discretion. Trauma cases were excluded. Patients were grouped in 3 neurological outcomes based on cerebral performance category (CPC), neurologically intact (CPC1, 2), severely disabled (CPC3, 4), and dead (CPC5). Neurological outcomes were assessed at the time of discharge and one year from cardiac arrest. Also, in order to investigate tolerable time duration for ECPR, proportions of favorable (CPC1, 2) to unfavorable (CPC3, 4, 5) outcome were compared in five-minute interval from collapse to start VA ECMO.
Results: 70 patients were eligible for this study. 4 patients were lost during follow up. Out of 70 patients, 19 (27%) were neurologically intact, 15 (21%) were severely disabled, and 36 (51%) were dead on hospital discharge. Out of 66 patients at one year follow up, 18 (27%) were neurologically intact, 10 (15%) were severely disabled, and 38 (58%) were dead. When the cut off was set at 45 minutes, patients who were on ECMO prior to 45 minutes from collapse had 62% favorable outcome and 38% unfavorable outcome on hospital discharge. On the contrast, patients who were on ECMO after 45 minutes from collapse had 11% favorable outcome and 89% unfavorable outcome on hospital discharge.
Conclusions: Long-term neurological outcome of ECPR is acceptable compared to neurological outcome at the time of hospital discharge, yielding same rate of 27% favorable outcome.

P2975 | BEDSIDE
Does prolonged cooling or lower temperature provide improved outcomes for cardiac arrest?

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Purpose: The optimal durations of cooling and target temperatures in therapeutic hypothermia for cardiac arrest patients are still unclear. We assessed the hypothesis that lower target temperature and/or longer cooling and rewarming durations provide improved outcomes for cardiac arrest patients.
Methods: This observational study was conducted in tertiary care hospitals. Adult comatose survivors of cardiac arrest without obvious extra-cardiac cause treated with hypothermia were enrolled in this study. We assessed the association between durations of cooling, target temperatures, and favourable outcomes. Favourable outcomes were defined as 90-day post-cardiac arrest cerebral performance category of 1 or 2. P<0.05 was defined as statistically significant.
Results: The study patients (N=218) had a median age of 61 years, 77% were male, and 57% had initial shockable rhythm. In the study patients, 138 patients (63%) were treated with target temperature of 34℃ or more, duration of cooling were median 24.5 h (interquartile range 18.9 – 47.0 h) and duration of rewarming were 19.8 h (5.9 – 42.0 h). There were no significant differences of the 90-day favourable neurological findings between the patients whose target temperature were 34℃ or more and that of less than 34℃ (35% vs. 41%, P=0.34). Because of hemodynamic instability, therapeutic hypothermia protocols were terminated before cooling period in 51 patients. The patients who were survived up to completion of rewarming (N=167), 59 patients (37%) were treated with hypothermia of duration of cooling more than 36 h, and 58 patients (35%) were treated with hypothermia of duration of rewarming more than 36 h. there were no significant differences in 90-day favourable findings between the patients whose duration of cooling <36 h and that of >36 h (45% vs 54%, P=0.27) and whose duration of rewarming <36 h and that of >36 h (47% vs 52%, P=0.54). The rate of pneumonia were significantly lower in patients whose duration of cooling <36 h (27% vs. 49%, P=0.004) and whose duration of rewarming <36 h (26% vs. 52%, P<0.001).
Conclusions: Prolonged cooling and rewarming >36 h may not improve outcomes in post cardiac arrest therapeutic hypothermia, but may increase pneumonia. The target temperature <34℃ may not improve outcomes.

P2976 | BEDSIDE
Serial measurement of neuron-specific-enolase and S-100 improves prognostication in cardiac arrest patients treated with hypothermia

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Purpose: The neurological outcome of patients after cardiopulmonary resuscitation is poor. Currently available prognostic parameters, including single measurements of Neuron-Specific-Enolase (NSE) and S-100 are unreliable, especially when patients are treated by controlled hypothermia.
Methods: We prospectively enrolled 50 patients resuscitated from out-of-hospital cardiac arrest. Hypothermia (33°) was initiated on admission and maintained for 24h. Serum values of NSE and S-100 were measured 0h and 6h after admission and daily for six days. The Cerebral Categories Scale (CPC), determined on the day of discharge was used as the outcome measure (CPC 4-5: poor outcome; CPC 1-3: good outcome).
Results: A favourable neurologic outcome was achieved in 18 patients (36%), while 32 patients (64%) had a poor outcome. Age was significantly higher in patients with poor outcome (66±1 vs. 63±2 years; p=0.04), gender distribution was not different. Mean NSE levels at 24h were 72.7 ng/mL (poor outcome) vs. 41.8 ng/mL (good outcome). The maximum NSE value in patients with good outcome was reached at 24h and it was well above the threshold typically assumed to indicate poor prognosis (33 ng/mL). Maximum NSE in poor outcome was reached at 72h, best discrimination between both groups was present at 48h (see table). Maximum values for S-100 in patients with poor outcome were observed on admission, and remained higher compared to the group with good outcome throughout all time points. Maximum S-100 in good outcome was at 0h, best discrimination between both groups was also present at admission.
Conclusions: Analysis of NSE values following successful resuscitation has limited predictive value in patients treated with hypothermia and should not be limited to a single time point. S-100 values show best discriminatory power to identify poor vs. good outcome at the time of admission.

NEW INSIGHTS IN PERIPHERAL INTERVENTION

P2977 | BEDSIDE
Meta-analysis of non-randomized comparative studies of use of BMS vs. DES for extracranial vertebral artery disease

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Purpose: Although the use of drug-eluting stents (DES) is well established for the reduction of restenosis compared to bare-metal stents (BMS) in the coronary system, its role within the extracranial vertebral artery disease is less well defined.
Materials and methods: We performed a search strategy using the terms "extracranial", "vertebral", "stenosis", "stenting", "bare-metal stents" and "drug-eluting stents" through Medline. In order to reduce interperformer variability, only those studies were included where both BMS and DES were used in the same setting and restenosis was evaluable during follow-up. Follow-up was considered evaluable when at least the clinical course or one reliable imaging method, e.g. duplex sonography, computed tomography angiography (CTA), magnetic resonance angiography (MRA) or catheter-based angiography, respectively, or a combination of these were available for both BMS and DES.
Results: A total of 9 studies were identified that met the inclusion criteria. Reported technical success rate was high (range: 99.2-100%) and comparable between BMS (100%; 276/276) and DES (166/167; 99.4%). The use of DES was associated with significant lower overall restenosis rates (8.2%; 14/170; mean follow-up 16-43 months) compared to BMS (23.7%; 68/287; mean follow-up 19-46 months; p<0.0001). Moreover, DES showed significant lower symptomatic restenosis rates as compared to BMS (4.7%; 8/169 for DES vs. 11.6%; 32/275 for BMS, respectively; p=0.005).
Conclusion: This meta-analysis demonstrates that the use of DES for EVA stenting significantly reduces both the rate of restenosis and recurrence of symptoms

Abstract P2976 – Table 1. NSE and S-100 kinetics

		0h	6h	24h	48h	72h	96h	120h
NSE poor outcome	mean±sd	36.5±16.0	41.7±9.6	72.7±95.6	116.8±94.2	187.7±228.7	137.6±162.6	128.7±134.4
good outcome	mean±sd	31.1±8.7	32.0±5.2	41.8±17.6	32.0±16.2	27.0±12.6	22.4±11.5	15.5±5.9
	p-value	0.38	0.03	0.24	<0.01	0.02	0.03	0.02
S-100 poor outcome	mean±sd	3.2±2.6	2.7±7.3	1.6±2.9	1.0±1.6	0.9±2.1	0.4±0.6	0.9±2.5
good outcome	mean±sd	1.2±1.4	0.3±0.1	0.2±0.1	0.1±0.1	0.1±0.1	0.1±0.1	0.1±0.01
	p-value	0.02	0.36	0.05	0.03	0.16	0.03	0.36

as compared to BMS. In future, randomized trials are needed to support these findings.

P2978 | BEDSIDE
Carotid artery stenting through transradial approach in high risk patients

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Purpose: The aim of this prospective study was to compare the difference in outcome of transradial (TRA) carotid artery stenting (CAS) in patients at high risk for endarterectomy.
Methods: In a prospective, single-center study designed to evaluate the feasibility and safety of TRA CAS, the periprocedural outcome of 541 consecutive patients, mean age 65, male 400 (74%), were analyzed. There were 246 patients (45,5%) at high-risk for endarterectomy according to SAPPHIRE criteria. Symptomatic patients were statistically more frequent in the group of high-risk patients 192 (78%) vs no high-risk group 173 (59%). Most of the procedures were performed using distal protection 399 (74%) with only 12 (3%) that underwent CAS with MoMa proximal protection device.
Results: In terms of intervention related characteristics as the type and size of the guiding catheter or guiding sheath, (5Fr-8Fr) there was no statistically significant difference between both groups. Cannulation of target common carotid artery with anchoring technique 457 (84%) was more frequent in both groups instead of telescopic technique 84 (16%). Crossover rate from TRA to brachial or femoral approach was only 2%.

Procedural data and complications

Procedural data	Total 541 (100%)	High-risk 246 (45,5%)	No high-risk 295 (54,5%)	P
Radial access	419 (77%)	169 (75%)	250 (78%)	ns
Ulnar access	99 (18%)	48 (20%)	51 (18%)	ns
Femoral access	10 (2%)	5 (2%)	5 (2%)	ns
Brachial access	13 (3%)	7 (3%)	6 (2%)	ns
Interventional time (min)	15–120	15–120	15–120	ns
Complications				
Death	1 (0,2%)	1 (0,4%)	0 (0%)	ns
Major stroke	2 (0,4%)	1 (0,4%)	1 (0,3%)	ns
Minor stroke	3 (0,6%)	1 (0,4%)	2 (0,7%)	ns
Intraprocedural TIA	7 (1,3%)	3 (1,2%)	4 (1,3%)	ns
Severe hypotension	1 (0,2%)	0 (0%)	1 (0,3%)	ns
Major vascular complications	1 (0,2%)	1 (0,4%)	0 (0%)	ns

Conclusion: Transradial carotid artery stenting is feasible and safe procedure in high-risk patients with a low complication rate when performed by an experienced operator.

P2979 | SPOTLIGHT
Simultaneous bilateral carotid artery stenting versus unilateral carotid artery stenting: early and long-term results

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Objective: Currently, the majority of clinical data on carotid revascularization reflected unilateral procedures, the optimal procedural strategy for bilateral carotid stenosis remains controversial. The purpose of this study was to evaluate the clinical outcomes of simultaneous bilateral carotid artery stenting (SBCAS) compared with unilateral carotid artery stenting (UCAS).
Methods: We retrospectively reviewed the prospective database of 637 consecutive patients who were underwent carotid artery stenting (CAS) in our institution from Jan. 2005 to Dec. 2012. 120 patients (18.8%) of them underwent SBCAS, and the others (n=517) received UCAS. The primary end point was the composite of stroke, myocardial infarction, or death during the periprocedural period or any stroke on the intervened side within 8-year follow up.
Results: In a median follow-up of 41 months, there was no significant difference in the estimated 8-year rates of the primary end point between the SBCAS group and the UCAS group (7.5% vs. 5.0%; P=0.282). The 8-year rate of primary end points among symptomatic patients was 8.0% in the SBCAS group and 5.4% in the UCAS group (P=0.367), and the rates among asymptomatic patients was 6.3% and 4.5% respectively (P=0.615). During the periprocedural period, rates of the primary end point did not differ significantly between the SBCAS group and the UCAS group among all patients ((5.8% vs. 4.4%, P=0.479), symptomatic patients (6.8% vs. 5.0%, P=0.594) and among asymptomatic patients (3.1% vs. 3.5%, P=1.000). After this period, the incidences of any stroke on the intervened side were similarly low (1.7% and 0.6%, respectively; P=0.85). Multivariable Logistic regression revealed that SBCAS (P=0.501) and symptomatic carotid stenosis (P=0.287) did not have a significant association with the primary end points during the perioperative period.
Conclusions: The patients underwent SBCAS had no more adverse events than those underwent UCAS within 8-year follow up, whether or not symptomatic of carotid atherosclerosis. Our findings suggest that this one-stage strategy may become a valuable alternative in the treatment of patients with bilateral carotid stenosis.

P2980 | BEDSIDE
Long-term clinical outcomes after vertebral artery angioplasty in the prospective randomized STOVAST (STenting for Ostial Vertebral Artery STenosis) Trial population

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Background: Vertebrobasilar (VB) strokes account for 25% to 35% of all ischemic cerebrovascular events. Symptomatic (prior VB stroke/TIA, drop attacks, severe vertigo/dizziness, vision disturbances) vertebral artery stenosis (VAS) is a significant risk factor for stroke. In patients with ongoing symptoms despite optimal medical therapy, vertebral artery stenting is attractive treatment modality.
Material and methods: From 2008 to 2011, 100 consecutive patients (age 66.1±8 years, 65 men) with symptomatic ostial VAS were included in the STOVAST Trial. The outcomes of ostial vertebral artery stenting with a randomized allocation to drug-eluting stents (DES) vs. bare-metal stents (BMS) were prospectively evaluated. Each patient was examined by an independent neurologist prior to, after angioplasty and at 12 months. Procedural success was achieved in 99 patients, 49 DES and 50 BMS were implanted. Results from the trial showed no evidence for in-stent restenosis reduction with DES vs BMS use (20.9% vs 23.8%, p=0.75).
Results: (table): Only one periprocedural complication was noted - episode of transient global amnesia. At one-month 92% patients remained asymptomatic. As 6 patients died, 93 patients were available for long-term clinical follow-up. At one-year five cardiac- and one cancer-death occurred. One VB stroke and one episode of VB TIA were observed. Both ischemic events were associated with a significant progression of contralateral VAS, that were, therefore, treated with angioplasty of the vessel contralateral to the index one. 65% patients remained asymptomatic. Vertebrobasilar ischemia symptoms recurrence was found significantly more often in the group with angiographically-confirmed restenosis (68,7% vs 30.3%, p=0,003).

Symptoms	Before VAS (n=100)	1 month after VAS (n=99)	1 year after VAS (n=93)
Vertebrobasilar stroke	11 (11%)	0 (0%)	1 (1,1%)
Vertebrobasilar TIA	13 (13%)	0 (0%)	1 (1,1%)
Severe vertigo/dizziness	93 (93%)	7 (7,1%)	33 (35,5%)
Drop attacks	8 (8%)	0 (0%)	2 (2,2%)
Vision disturbances (cortical blindness, diplopia)	9 (9%)	0 (0%)	2 (2,2%)

Conclusions: Vertebral artery stenting is safe and effective in symptom relief. Most of the patients remains symptom-free in long-term follow-up. Vertebrobasilar ischemia symptoms recurrence is the predictor of restenosis.

P2981 | BEDSIDE
Percutaneous interventions for brachiocephalic trunk occlusive disease

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Occlusive disease of brachiocephalic trunk (BCT) is a rare condition, accounting for 7.3% of subjects with subclavian steal syndrome. Percutaneous angioplasty (PTA) became method of choice in the treatment of subclavian artery (SA) and BCT stenosis, likewise in carotid artery occlusive disease. Cerebral neuroprotection system (NS) is mandatory during internal carotid artery (ICA) stenting, but guidelines do not address the problem of NS use in BCT PTA. The study aimed to evaluate the immediate and long term results of PTA for BCT stenosis, with focus on the safety and its efficacy.
Methods: The study comprised 23 (13M) patients in the mean age of 59.7±9y. (38-74y.) referred for PTA due to a symptomatic BCT stenosis (mean diameter stenosis: 75.8±16%), related to atherosclerosis in 20 and Takayasu arteritis in 3 cases. A concomitant ipsilateral ICA occlusion was noted in 3 (13%) and contralateral SA disease in 9 (39%) subjects. Previous ischemic stroke (IS) related to BCT stenosis was found in 8 (35%) patients. NS was used in selected cases with high plaque burden, thrombus or soft plaque. The incidences of periprocedural and long-term cardiovascular (CV) events: CV death (CVD), myocardial infarction (MI), IS, and recurrent stenosis (RS) (>50% diameter stenosis) were recorded.
Results: In 22 (96%) subjects, planned stenting was performed, while in 1 patient only a balloon PTA was performed due to unsuccessful stent delivery. NS was used in 6 (26%) cases, including right common carotid artery (RCCA) protection in 4 subjects, double NS to RCCA and right vertebral artery (RVA) in 2 patients. IS occurred in 2 (8.7%) subjects. One major embolic IS was observed in the territory of anterior and posterior cerebral circulation together with acute right upper limb ischemia in patient without NS. A minor embolic IS in the posterior cerebral circulation area was observed in 1 (4.3%) case, in which NS was used only for protection of RCCA. During mean follow-up period of 56±36 months (2-123 months), RS was noted in 5 (24%) of 21 subjects with at least 6 month follow-up. RS and non-RS group differed only with respect to lower stent diameter (7.4±1.1

vs. 8.4±0.7mm, p=0.046) and hs-CRP (13.9±20 vs. 4.2±5.2 mg/L, p=0.08). We observed 2 (8.7%) ISs: one due to restenosis and one due to RCCA stenosis progression. No CVD or MI were noted.
Conclusions: Despite a selective use of NS, periprocedural IS rate was unexpectedly high. Thus, we believe that NS should be used routinely for both RCCA and RVA territories protection. Despite the large diameter of BCT, RS rate is higher, as compared to SA PTA.

P2982 | BEDSIDE
Repeat intervention for repeat restenosis after femoropoplitial stenting

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Purpose: Repeat intervention for repeat in-stent restenosis (ISR) after femoropoplitial (FP) stenting has not been well described. The aim of this study is to investigate efficacy of repeat intervention for repeat ISR and predictor of repeat ISR after FP stenting in a real world.
Methods: All patients undergoing a first intervention procedure with stenting from January 2004 to April 2013 were identified. Lesions and limbs required first target lesion revascularization (TLR) after FP stenting were 153 lesions and limbs. The incidence of second, third ISR and TLR were investigated. Cox multivariate regression analysis was used to determine predictors for third ISR.
Results: Male was 63.1% and mean age was 72.5±8.2 years old. (Mean follow up period 41±17 months) Of 153 ISR lesions, 79 lesions (51.6%) required second ISR and 69 lesions (45.0%) required second TLR. Of 69 lesions required second TLR, 43 lesions (62.3%) required third ISR and 33 lesions (47.8%) required third TLR. After controlling for confounding risk factors, risk-adjusted Cox proportional hazards regression showed that total occlusion ISR and over 75 years old were predictors of third ISR (hazard ratio[HR], 1.96; 95% confidential interval [CI] 1.02-3.76; adjusted P=0.04, HR2.06; 95%CI 1.08-4.08; adjusted P=0.03).

Univariate and multivariate predictors of third ISR

Variables	Univariate analysis			Multivariate analysys		
	HR	95%CI	p value	HR	95%CI	p value
BMI over 30	3.29	0.79–9.14	0.09	4.21	0.65–15.74	0.11
Age over 75	2.38	1.30–4.48	<0.01	2.08	1.09–4.11	0.03
Use of insulin	0.42	0.14–0.98	0.04	0.55	0.18–1.33	0.19
Lesion length	1.00	1.00–1.01	0.03	1.00	0.99–1.01	0.31
Total stent length	1.00	0.99–1.01	0.09	0.99	0.99–1.01	0.67
Number of stents	1.27	0.98–1.62	0.07	0.56	0.69–2.00	0.51
Total occulusion ISR	1.70	0.92–3.10	0.09	1.91	1.01–3.62	0.04

Conclusion: Repeat intervention decreased ISR and TLR in stages. Total occlusion ISR and the elderly were predictors of repeat ISR after FP stenting.

P2983 | BEDSIDE
Efficacy of stent placement versus balloon angioplasty in small and short femoropopliteal lesion

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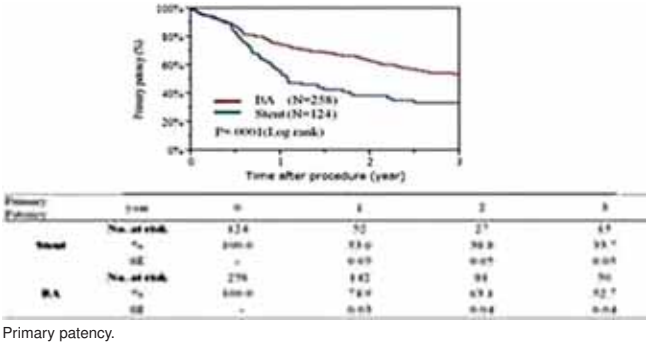
Purpose: The aim of this study was to investigate the efficacy of stent placement versus balloon angioplasty (BA) for femoropopliteal (FP) lesions of 4.0mm or less in diameter.
Methods: Through a multicenter retrospective analysis, we enrolled 2742 consecutive patients (3471limbs) with FP disease and analyzed 345 patients (382 limbs) with femoropopliteal lesions of 4.0 mm or less in diameter and 150mm or less in length in current study; 124 limbs (32.5%) were implanted the self-expanding nitinol stent, 258 limbs (67.4%) were balloon angioplasty alone.
Results: The mean follow-up term was 2.3±1.7 years. The mean reference vessel diameter was 3.8±0.4 mm. The mean lesion length was 64.6±43.7 mm. Based on treated limb-based analysis, primary patency of balloon angioplasty alone group and stent group was, respectively, 74.9% and 53.6% at 1 year, and 52.7% and 33.7% at 3 years, and it was significantly higher in the BA group than in the stent group (P=0.0001).Assisted-primary patency and MALE were also significantly higher in the BA group than in the stent group (P<0.0001 and P=0.001, respectively), while secondary patency was similar between the two groups. Independent predictors of primary patency were use of thienopyridine, a procedure with BA alone, and a lesion length greater than 75.0 mm.
Conclusions: In small and short FP lesions, implantation of the self-expanding nitinol stent does not improves primary, assisted-primary and secondary patency and decrease MALE compared with balloon angioplasty alone.



Primary patency.

BODYWEIGHT – FROM RISK FACTOR TO MORTALITY PREDICTOR

P2984 | BEDSIDE
Birth weight and high sensitivity C-reactive protein in young and healthy adults

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Purpose: Low birth weight is a strong predictor of the occurrence of ischemic heart disease and other cardiovascular events. However, the underlying mechanisms are poorly understood. We hypothesized that inflammation, an independent risk factor for cardiovascular disease, might be implicated in this relationship.
Methods: Healthy individuals of the Principality of Liechtenstein aged 25 to 41 years were enrolled in a population based study. Individuals with diabetes, prevalent cardiovascular disease or a body mass index >35kg/m^2 were excluded. We performed a cross-sectional analysis among 1844 individuals with available information on high sensitivity C-reactive protein (hs-CRP) and birth weight. Birth weight data were obtained by self-report. Multivariable linear regression models adjusting for potential confounders were used to assess the relationship between birth weight and hs-CRP.
Results: Median age of our population was 36 years. Median birth weight levels (interquartile range) across quartiles of birth weight were 2900 (2700; 3030), 3350 (3250; 3470), 3652 (3580; 3750) and 4047 (3921; 4300) grams for men and 2720 (2500; 2850), 3150 (3050; 3200), 3400 (3330; 3500) and 3810 (3680; 4000) grams for women. The main results are shown in the Table. In the fully adjusted models, the β-regression coefficients (95% CI) for log-transformed hs-CRP per 100g increment in birth weight were -0.02 (-0.02; -0.01), p=0.001, and -0.01 (-0.02; -0.00), p=0.007 after additional adjustment for body composition. Adjustment for body composition partly attenuated these findings (Table).
Conclusion: Our data demonstrate that birth weight is inversely associated with hs-CRP levels in adult life, suggesting that inflammation may be a potential mechanism relating intrauterine growth restriction to the occurrence of cardiovascular events. Differences in body composition may be involved in these relationships.

P2985 | BEDSIDE
Anthropometric indices in relation to the prediction of 10-year incidence (2001-2011) of cardiovascular disease in apparently healthy individuals: a classification analysis of the Attica study

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Objective: To evaluate the role of anthropometric indices in 10-year incidence of cardiovascular disease (CVD).
Methods: During 2001-2, 1514 men and 1528 women (>18 years) without any clinical evidence of cardiovascular disease (CVD) at the basline examination, living in Athens greater area, Greece, were enrolled in the ATTICA study. In 2011-12, the 10-year follow-up was performed. Weight, height, waist and hip circumferences, as well as body mass index (BMI) and waist-to-height (WHtR) and waist-to-hip (WHR) ratio were tested in relation to the development of a fatal or non-fatal cardiovascular disease event as defined according to WHO-ICD-10 criteria.

Abstract P2984 – Table 1. Multivariable linear regression analyses

	Continuous[†] (n=1844)	Quartile 1 (n=466)	Quartile 2 (n=516)	Quartile 3 (n=419)	Quartile 4 (n=443)	P for trend[‡]
High-sensitivity C-reactive protein (hs-CRP, Log); β (95% CI)						
Sex, age adjusted	−0.01 (−0.02; −0.00)*	Ref.	0.05 (−0.07; 0.17)	−0.10 (−0.23; 0.03)	−0.16 (−0.33; 0.00)	0.008
Fully adjusted[$]	−0.02 (−0.02; −0.01)**	Ref.	0.06 (−0.06; 0.17)	−0.11 (−0.23; 0.01)	−0.16 (−0.32; −0.01)	0.002
Fully adjusted[+]	−0.01 (−0.02; −0.00)**	Ref.	0.08 (−0.04; 0.19)	−0.08 (−0.20; 0.04)	−0.12 (−0.28; 0.03)	0.03

[$]All coefficients are adjusted for sex, age, body mass index, systolic blood pressure, low density lipoprotein cholesterol, high density lipoprotein cholesterol, estimated glomerular filtration rate (CKD-EPI-formula), HbA1c, physical activity, education level, smoking, alcohol consumption, fruit/vegetable consumption. (n=1799). [+]Additionally adjusted for body composition (n=1773). *P-value < 0.05; **P-value < 0.01; [†]Log-transformed variable, per 100g increment in birth weight; [‡]p for trend across quartiles of birth weight.

Results: The 10-year incidence was 14.3% in men and 9% in women ($p<0.001$). Based on hierarchical classification analysis, using Fisher linear discriminant function, all anthropometric indices were highly associated with the 10-year prediction of CVD events; the most dominant predictor was WHtR (Wilks' Lambda = 0.957, $p<0.001$), followed by WHR (Wilks' Lambda = 0.963, $p<0.001$), waist circumference (Wilks' Lambda = 0.966, $p<0.001$), BMI (Wilks' Lambda = 0.963, $p<0.001$) and hip circumference (Wilks' Lambda = 0.994, p=0.001). Moreover, 80.9% of men and 48.1% of women had WHtE <0.5, a threshold that has been proposed by WHO as an indicator of acceptable values. Gender-age specific analysis confirmed that the aforementioned ranking was irrespective of participants' sex or age.
Conclusions: The present analysis stated a hypothesis that this ratio should be implemented in clinical practice or research for better identifying the potential CVD candidate, instead of the commonly used BMI. This ratio incorporates muscle distribution in relation to body fat and may better reflect fat allocation to the body; a factor that promotes atherosclerosis.

P2986 | BEDSIDE
Abdominal obesity and low skeletal muscle mass jointly predicted total mortality and cardiovascular mortality in elderly population

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Background: We aimed to investigate the jointed impacts of abdominal obesity and low skeletal muscle mass for cardiovascular and total mortality in elderly population.
Materials and methods: A total of 1485 elderly from the National and Health Survey in Taiwanese Elderly (1999-2000) was enrolled, and the survival status was followed using the data from the National Death Registry. The skeletal muscle mass index (SMMI) was calculated by dividing skeletal muscle mass by high in meters squared. The first quartile of SMMI was defined low skeletal muscle mass. Abdominal obesity was defined by simultaneous with high triglycerides (TG) (≥150 mg/dL) and high waist circumference (WC) (≥90 cm for men and ≥80 cm for women). The Cox proportional hazard model was used to evaluate the jointed impacts of abdominal obesity and low skeletal muscle mass index for cardiovascular disease and total mortality.
Results: During the follow-up (median time: 9.2 years), one-third elderly died (n=493) by any cause and 34% of them was cardiovascular mortality (including diabetes; ICD-9-CM: between 390 and 459 for CVD; 250 for diabetes). The total mortality and cardiovascular mortality was 4.2 and 1.4 per 100 person-years. Total mortality in men and women were 4.01 and 2.72, respectively, for normal-TGWC and normal SMMI, 5.73 and 2.82, respectively, for high-TGWC and normal SMMI, 7.07 and 5.91, respectively, for normal TGWC and low SMMI, and 13.92 and 5.77, respectively for high-TGWC and low SMMI. Low SMMI (Hazard ratio and 95% confidence intervals: 1.45; 1.13-1.87) and high-TGWC (1.61; 1.13-2.29) were independently associated with total mortality in elderly men, but only low SMMI (1.63; 1.20-2.22) was significant in elderly women. Furthermore, combined low SMMI and high-TGWC had more than 6.8-fold and 3.2-fold risk for cardiovascular mortality, respectively in men and women, compared to the controls (normal SMMI and normal -TGWC).
Conclusions: Elderly persons with both abdominal obesity and low skeletal muscle mass were higher mortality risk. Resistance training to maintain muscle mass may prolong life among the elderly persons.

P2987 | BENCH
Association between naps, snore, sleep duration and obesity in the population of INTER-HEART China Study

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Purpose: The relationship between sleep and obesity has been discussed a lot and it is still unclear and controversial. Most studies only assessed the association of sleep duration with obesity or just adjusted few covariates. In this paper, we aim to explore the association of naps, snore and sleep duration with obesity after more confounding variables including demographics, disease, diet and physical activity were controlled.
Methods: We used data from the INTER-HEART China study. A total of 2909 cases (AMI patients) and 2947 controls (None AMI patients) were recruited from 17 cities. Sleep information, social demographics, diet, physical activity, disease history were collected by standardized questionnaires. Physical examinations were conducted by trained personnel in a standardized manner. Body mass index (BMI) and waist circumferences (WC) were used to define general or abdominal obesity. Multiple linear regression and logistic regression were employed to assess the associated between sleep and obesity after controlling for important covariates (Model1) or all available covariates (Model2).
Results: Among the 5856 subjects, 2968 (50.1%) naps, 1271 (21.76%) never snore, 4353 (75.2%) sleep 6~8 hours, 693 (11.5%) were general obesity and 3483 (60.0%) were abdominal obesity. Results from multiple linear regression showed that snore frequency was associated with BMI ($P<0.0001$); naps duration (P=0.0213) and snore severity ($P<0.0001$) were associated with WC. Logistic regression showed that snore frequency (OR and 95%CI: 1.272 (1.113-1.454) in model1; 1.323 (1.154-1.516) in model 2) and short sleep duration (OR and 95%CI: 1.642 (1.101-2.450) in model1, 1.737 (1.149-2.625) in model2) were found to be significantly associated with general obesity. Snore severity (OR and 95%CI: 1.244 (1.094-1.415) in model 1; 1.243 (1.092-1.415) in model 2) and long sleep duration (OR and 95%CI: 1.311 (1.056-1.628) in model1, 1.294 (1.040-1.611) in model2) were found to be significantly associated with abdominal obesity.
Conclusions: Snore frequency was significantly associated with BMI, naps duration and snore severity was associated with WC. Snore frequency and short sleep duration were associated with general obesity; snore severity and long sleep duration were associated with abdominal obesity. Future well designed longitudinal studies are needed to confirm our findings.

P2988 | BEDSIDE
Body mass index and changes in weight are associated with risk of atrial fibrillation and cardiovascular mortality: a longitudinal cohort study of 7,169 patients with newly diagnosed type 2 diabetes

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Purpose: Obesity is associated with an increased risk of type 2 diabetes (T2D) and cardiovascular (CV) disease. Our aim was to explore the impact of body mass index (BMI) at baseline, and weight change, on the risk of atrial fibrillation (AF) and CV mortality in patients with T2D.
Methods: A total of 7,169 primary care patients with newly diagnosed T2D and without previous history of CV disease were grouped separately according to baseline BMI and their change in BMI within 18 months after diagnosis. The relative weight change was grouped as follows (1 BMI unit ~ 3.6 kg): "weight gain" (>1 BMI unit), "stable weight" (±1 BMI unit) and "weight loss" (<1 BMI unit). Follow-up time was 9 years, and risks of AF and CV mortality were estimated using adjusted Cox regression models.
Results: Mean age was 60 years at time of diabetes diagnosis and patients were on average slightly obese (mean BMI 30.2 kg/m^2). During follow-up, overweight and obese patients had significantly higher risk of AF, compared with those with normal BMI. For CV mortality there was an apparent "obesity paradox" situation with similar risk independent of BMI category. From time of T2D diagnosis, few patients (15%) increased weight while the majority lost or maintained weight. Risks of both AF and CV mortality were significantly higher in patients increasing weight compared to weight stable patients.

Table 1

		Atrial fibrillation, n=287		CV mortality, n=203	
		HR	95% CI	HR	95% CI
Weight categories*					
Normal weight, n=750	BMI <25 kg/m^2	Reference	Reference	Reference	Reference
Overweight, n=2579	BMI 25–30 kg/m^2	1.85	1.10 to 3.09	0.72	0.47 to 1.12
Obese, n=3840	BMI >30 kg/m^2	2.85	1.73 to 4.71	0.96	0.63 to 1.46
Weight change**					
Weight gain, n=1023	>1 BMI unit	1.53	1.10 to 2.12	1.84	1.28 to 2.66
Weight stable, n=3736	±1 BMI unit	Reference	Reference	Reference	Reference
Weight loss, n=2410	>1 BMI unit	1.06	0.81 to 1.38	1.03	0.75 to 1.43

*Adjusted for age, gender and systolic blood pressure. **Additional adjustments for baseline BMI.

Conclusions: Obesity/overweight or weight gain in patients with newly diagnosed T2D may be more hazardous than previously recognized, and efforts should be made to control weight in diabetes patients.

P2989 | BEDSIDE
Impact of fat free mass on cardiac prognosis in patients with heart failure

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Background: Heart failure (HF) is thought to be as a catabolic state, since cardiac cachexia emerges with advancing HF stage. Fat free mass (FFM) consists of skeletal muscle, organs, bone, and connective tissue and is widely used as an indicator of resting energy expenditure. However, little is known about the impact of FFM on cardiac prognosis in patients with HF. The purpose of this study was to clarify whether decreased FFM can predict unfavorable prognosis in patients with HF.
Methods: We evaluated FFM and measured serum brain natriuretic peptide (BNP) levels in 294 consecutive patients admitted to our hospital for treatment of worsening HF at admission. FFM is calculated by the following estimated formula. FFM (kg) = 7.38 + 0.02908×urinary creatinine (mg/day). We used percentage of FFM (FFM%) normalized by their body weight. Subjects were divided into three

groups according to their FFM% tertile. The patients were prospectively followed for a mean duration of 13.3 months (interquartile range 3.0-20.3).
Results: Twelve patients who underwent cardiac surgery during the follow-up period were excluded from analysis, and 15 patients were lost to follow-up. The remaining 267 patients were included in final analysis. There were 160 males (60%), and the mean age was 71±12 years old. The median serum BNP level was 390 pg/ml (interquartile range: 142-965) and mean left ventricular ejection fraction was 50±18%. There were 83 cardiac events (31%) including 19 cardiac deaths and 64 readmissions during the follow-up period. Patients with cardiac events were older and in a more severe New York Heart Association functional class than in those without. Moreover, they also showed lower serum albumin, total cholesterol, triglyceride, hemoglobin, and FFM% compared with those without. Serum BNP levels were decreased according to their FFM% tertile (Kruskal-Wallis, $P<0.001$). Furthermore, multivariate Cox hazard analysis revealed that decreased FFM% was associated with cardiac events (adjusted hazard ratio 1.52, 95% confidence interval 1.09-2.12). Kaplan-Meier analysis revealed that significantly higher cardiac event rate was observed in the lowest tertile (T1) (log-rank test, $P<0.001$).
Conclusions: Decreased FFM% was independent predictor of unfavorable prognosis in patients with HF.

PATHOPHYSIOLOGY OF HYPERTENSION

P2990 | BEDSIDE
Excessive salt intake induces future development of hypertension in general population of our country

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Purpose: Both hypertension and high levels of dietary salt are associated with cardiovascular diseases including coronary artery disease and stroke. In salt-sensitive hypertension, excessive salt intake causes an increase in blood pressure and salt restriction has a depressor effect. The present study was designed to investigate whether excessive salt intake predicts future development of hypertension in the general population of our country.
Methods: Normotensive 6,232 subjects who visited our hospital for a physical check-up were enrolled in this study (male=61.9%, 53.4±11.4 year-old). Individual salt intake was estimated by calculating 24-hour urinary salt excretion using a method reported. After baseline examination, they were followed up for the median of 1,089 days with the endpoint being the development of hypertension. Hypertension was defined as systolic blood pressure ≥140mmHg, diastolic blood pressure ≥90mmHg, or the use of antihypertensive medications.
Results: During the follow-up, hypertension developed in 1,190 subjects (69.8 per 1000 person-year), with the incidence being more frequent in male than in female subjects (82.4 vs. 49.2 per 1000 person-year). The incident of hypertension was increased across the gender-specific quartiles of baseline salt intake (47.9, 72.6, 75.9, and 83.5 per 1,000 person-years in the first to fourth quartiles, respectively). After adjustment for age, gender, body mass index, systolic blood pressure, heart rate, serum creatinine, uric acid, impaired glucose tolerance, dyslipidaemia, haemoglobin, current smoking habit, and family history of hypertension, the hazard ratio of incident hypertension (first quartile as reference) in the second, third and fourth quartiles was 1.30 (95% confidence interval 1.09-1.55), 1.20 (1.01-1.44) and 1.15 (0.96-1.37), respectively. Multivariable Cox hazard analysis, where salt intake was taken as a continuous variable, indicated that salt intake at baseline (hazard ratio 1.06, 95% confidence interval 1.02-1.09) and a yearly increase in salt intake (1.18, 1.12-1.24) were significant predictors for future incident of hypertension after adjustment for possible risk factors.
Conclusions: Not only excessive salt intake at baseline, but also chronic increase in salt intake, is closely related with incident hypertension, suggesting that effort to reduce dietary salt consumption is necessary to prevent the development of hypertension in normotensive general population.

P2991 | SPOTLIGHT
New markers for risk evaluation of pre-diabetic hypertensive patients without coronary artery disease

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Introduction: Hypertension is one of the most important causes of premature death worldwide. Pre-diabetic state, mainly impaired glucose tolerance (IGT), is a risk factor for coronary artery disease (CAD) and sudden death. Aortic function plays a significant prognostic role for cardiovascular (CV) events. The resistive index (RI) reflects local wall extensibility and the related vascular resistance.
Objectives: The purpose of this study was to find new accessible markers for the initial CV risk evaluation of newly diagnosed pre-diabetic hypertensive patients without known previous CAD. We analyzed the relationship between aortic distensibility (AD), carotid RI, BP, abnormal ECG stress test and cardiac events in those pts.
Methods: We enrolled 258 consecutive newly diagnosed hypertensive pre-diabetic (IGT) pts without CAD. All pts were evaluated by ambulatory blood pressure monitoring, carotid RI (Doppler ultrasound), AD, ECG stress test for non-cardiac or atypical chest symptom, rest ECG and/or cardiac echo abnormalities, presence of major CV risk factors. Echocardiographic indices of AD were calculated using the equation: 3.14 x (AoS – AoD) x AoD/(2 x (SBP – DBP)), where AoS and AoD are the systolic and diastolic diameters of aortic root, and SBP and DBP are the systolic and diastolic blood pressure levels. We analyzed the association between AD, RI, BP, abnormal exercise ECG, several clinical parameters and cardiac events during a mean follow-up period of 4.2±0.6 ys.
Results: The mean age of the population was 46.8±15.7 years. 24-hour SBP was 152±34 mmHg and 24-hour DBP was 93±12 mmHg. Abnormal stress ECG showing inducible ischemia was noticed in 21% pts. Univariate analysis has shown the following parameters significant associated with abnormal exercise testing: age ($p<0.01$), family history of premature CV events ($p<0.02$), SBP ($p<0.02$), dyslipidaemia ($p<0.02$), AD ($p<0.03$), carotid RI ($p<0.04$), and plasma glucose ($p<0.04$). Multi-adjusted analysis revealed that LDL cholesterol ($p<0.01$), SBP ($p<0.02$), higher values of RI ($p<0.02$) and lower values of AD ($p<0.03$) were significant independent predictors of abnormal ECG exercise test. Multivariate Cox proportional analysis revealed that abnormal stress ECG (HR=2.3, 95%CI: 1.3–6.2, p=0.034) and post-load glucose (2-hPG) (HR=2.8, 95%CI: 0.9–6.8, p=0.041) were good predictors of the cardiac events.
Conclusions: Two simple and effective markers – aortic distensibility and resistive index can be extremely useful in every day clinical practice in the initial risk evaluation of newly diagnosed pre-diabetic hypertensive patients without known previous CAD.

P2992 | BEDSIDE
Body fat distribution and elevated blood pressure in 22051 youths: The pep family heart study

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Objective: Because adiposity is considered as a driving force for cardiovascular disease (CVD) the purpose of this study was to assess the association between elevated blood pressure (BP) and fat patterning in a large sample of urban children and adolescents.
Subjects and methods: We estimated body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), percentage body fat (%BF) and the sum of subscapular and triceps skinfold thickness (SFT) in 14213 children and 7838 adolescents aged 3-18 years using Slaughter-equations, SPSS 18, $p<0.05$ for significance.
Results: The prevalence of elevated BP was similar in all age groups. However, the prevalences of elevated BMI, %BF and WC continuously increased whereas WHtR decreased significantly by age in both genders. From normal-weight via overweight (BMI 85th-<95th percentile) to obese (BMI >95th percentile) the prevalence of prehypertension increased from 13.2% via 18.3% to 21.9% in males and from 12.9% via 18.7% to 24.9% in females. The prevalences of manifest hypertension increased similarly from normal weight via overweight to obesity from 5.7% via 10.4% to 18.6% in males and from 5% via 9.1% to 24.4% in females. Compared to normal-weight, the risk of being prehypertensive was significantly increased in overweight males and females (OR 1.6 and OR 1.8, respectively) and obesity (OR 2.4 and OR 3.3, respectively). We found the strongest associations between hypertension and adverse fat patterning (females, males) for BMI >95th (OR 5.9, 4.3), SFT sum >35 cm (OR 5.8, 4.6), %BF >95th (OR 5.6, 3.4) WHtR >0.5 (OR 3.9, 3.8), WC >90th (OR 3.5, 3.1), BMI 85th-95th (OR 2.7, 2.1) and %BF 85th-95th (OR 2.0, 1.8).
Conclusion: The strong association of hypertension with body fat distribution suggests that improvement of adverse fat patterning is a promising tool for preventing and treating elevated blood pressure.

P2993 | BEDSIDE
Left ventricular mass versus pulse wave velocity as predictors of coronary artery disease in essential hypertension: data from a Greek 6-year-follow-up study

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Purpose: 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. 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$110 g/m^2 in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.
Results: The incidence of CAD over the follow-up period was 2.8%. Hypertensives who developed CAD (n=29) compared to those without CAD at follow-up (n=1004) had at baseline higher LVMI (124.5$\pm$27.9 vs 103$\pm$26.2 g/m^2, p$<$0.0001), prevalence of LVH (48% vs 25%, p=0.022) and prevalence of high PWV levels (69% vs 48%, p$<$0.05). No difference was observed between hypertensives with CAD and those without CAD with respect to baseline office BP, renal function and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that baseline PWV levels predicted CAD (hazard ratio=1.218, p=0.025). However, in multivariate Cox regression model baseline glomerular filtration rate (hazard ratio=1.020, p=0.026) and LVMI (hazard ratio=1.021, p$<$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 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.

P2994 | BEDSIDE
Ambulatory hypotensive effect of physical training: a reappraisal through a meta-analysis of selected moderators

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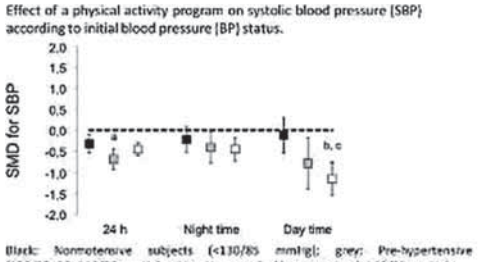
Background: The effectiveness of chronic exercise to decrease both systolic and diastolic blood pressure (SBP and DBP) is well established. However, this hypotensive effect may be altered by a number of variables including the participants' characteristics, the physical activity program characteristics and other co-interventions including diet or medication. Therefore, the purpose of this study was to assess the effect of these moderators on ambulatory blood pressure (BP) through a meta-analysis of the existing literature.
Methods and results: Three databases were searched using relevant terms and strategies (from 1945 to 2013-Oct-19). Twenty-eight studies from 676 identified records met following inclusion criteria: randomized controlled trials with quality score using PEDro scale or van Tulder scale $\geq$5, presence of relevant details about training intervention and subjects' characteristics, and pre and post-training measurements of ambulatory blood pressure (ABPM). The overall effect was a weighted mean difference reached for day-time systolic/diastolic ABPM -3.82/-3.29 mmHg (95% CI -5.15 to -2.49 and -4.59 to -1.99 respectively; P$<$0.01). Moderators associated with ABPM improvement were the following: an initial casual BP $\geq$140/90 mmHg (hypertensive or uncontrolled BP subjects), diet co-intervention, training program duration $>$12 weeks, and cumulative number of exercises $>$40 sessions. These improvements were significant or higher for day-time SBP than other BP variables. We found no differences for gender, age, or presence of antihypertensive drugs.



Conclusions: Antihypertensive effects of aerobic training assessed by ABPM appear modest but significant, and our meta-analysis highlights favorable moderators as initial high BP, diet, and training cumulative duration.

P2995 | BEDSIDE
MiR-1 and miR-133 are downregulated in patients with essential hypertension and left ventricular hypertrophy

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Purpose: MicroRNAs (miRs) are essential regulators of gene expression implicated in cardiovascular function and disease and they are emerging as potential biomarkers and therapeutic targets in cardiovascular disease. MiR-1 and miR-133 have been shown in animal models to play a role in heart hypertrophy mainly having anti-hypertrophic function. Their downregulation in rodent models has been reported to be involved in the pathogenesis of myocardial hypertrophy, while overexpression attenuates hypertrophy. Thus they maybe involved in the pathogenesis of left ventricular hypertrophy in hypertensive patients. We evaluated miR-1 and miR-133 levels in peripheral blood mononuclear cells of patients with essential hypertension in relation to left ventricular mass index.
Methods: 68 untreated hypertensive patients and 28 healthy volunteers were included for comparison. All patients 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-1 levels were found to be higher (26.66$\pm$4.08 versus 11.79$\pm$2.13, p=0.025), while miR-133 levels were found to be lower (5.97$\pm$0.61 versus 12.53$\pm$2.19, p$<$0.001) in hypertensive patients compared to healthy controls. In hypertensive patients, miR-1 (r=-0.329, p=0.006) and miR-133 (r=-0.356, p=0.003) levels showed strong negative correlations with left ventricular mass index.
Conclusions: MiR-1 and miR-133 levels in PBMCs of hypertensive patients differ from healthy controls and show strong negative correlations with left ventricular mass index in hypertensive patients. Our data define that miR-1 and miR-133 are probably involved in the pathogenesis of left ventricular hypertrophy in hypertensive patients maybe having anti-hypertrophic function, thus they might be promising therapeutic targets in hypertension.

P2996 | BEDSIDE
The prevalence of primary aldosteronism in patients with uncontrolled hypertension: challenges of interpretation of aldosterone-renin ratio

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Purpose: Primary aldosteronism (PA) is considered to be far more frequent reason for elevated blood pressure (BP) or resistance to antihypertensive therapy that it had been believed several decades ago, but still the precise rate is unknown and data from different centers are contradictory. Aldosterone-renin ratio (ARR) is a preferred screening test for PA and showed to be suitable even in patients on most anti-hypertensive agents. On the other hand subgroups of patients with high risk of this disease are associated with aldosterone excess, sometimes resulting in false-positive ARR, and actually the confirmation of the PA in patients with positive ARR test rarely exceeds 30%. The aim of the present study was to assess the prevalence of PA in patients with uncontrolled hypertension (HTN) and the utility of ARR and its components for detection of PA in routine practice of specialized hypertension excellence center.
Design and method: We examined 314 patients with HTN [161 males (51.3%) and 153 females (48.7%)] referred to our medical research centre (HTN Excellence Center of ESH). Ambulatory blood pressure monitoring, renal ultrasound with Doppler were performed as well as blood testing for creatinine level with calculation of GFR by MDRD formula, potassium, glucose, cortisol, metanephrines, plasma aldosterone, renin concentration with calculation of ARR. In case of elevated ARR the patients proceeded to confirmatory saline infusion test.
Results: ARR was high in 141 (52.2%) patients with HTN (n=314), which may be explained by a high proportion of severe and resistant HTN, obesity, obstructive sleep apnea (63.1%). In a group of patients with high ARR (n=141) concurrently increased aldosterone level was observed in 90 (63.8%) patients and in most cases renin was lower (68.1%) or within normal values. In 51 (36.2%) patients ARR was increased due to the low renin concentration without aldosterone excess, most of them were older, with mild hypertension and on beta-blockers. The diagnosis of PA was confirmed in 27 patients (8.6% of all hypertensive patients, 19.2% of patients with elevated ARR), all of them were characterized by long-term moderate-to-severe hypertension or resistance to antihypertensive treatment.
Conclusions: The prevalence of PA constitutes 8.6% in patients with uncontrolled hypertension and 19.2% in patients with elevated ARR. False-positive ARR results could be explained by low renin levels without aldosterone excess or secondary aldosteronism, indicating importance of evaluation of ARR in combination with aldosterone and renin concentrations.

BIOLOGY AND FUNCTION OF STEM CELLS

P2997 | SPOTLIGHT
Cell-in-cell proliferation of resident cardiac stem cells inside mature cardiomyocytes in the primary culture of rat myocardial cells

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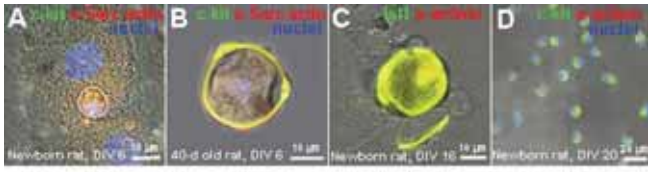
"Cell-in-cell structures" (CICSs) usually defined as specific inclusions within the cells containing living cells of the same or distinct type have been described in hematopoietic, immune, tumor and other cells. In this report, we first demonstrated the formation of CICSs in the mammalian cardiac myocytes. Vacuoles containing multiple cardiac stem cells (CSCs) belonging to c-kit+ -, Sca+ - and Isl1+ subtypes were identified within mature cardiac myocytes in the primary culture of myocardial cells of newborn, 20- and 40-day-old rats. CSC-containing vacuoles were localized near the host cell nucleus or between two nuclei (Fig. 1A). The rate of CICSs occurrence was found to be ~1–2 per 100.000 myocardial cells. CSCs confined to CICS expressed Ki67 antigen, what is suggestive of their proliferation and growth within the vacuoles inside CICSs (Fig. 1B, C). Over the time of culturing, the outer membrane of CSC vacuoles has been shown to become more thick and rigid, forming a hard capsule to isolate CSCs from host cell cytoplasm. Two to five small openings (micropyles) have been identified in the outer membrane of advanced CICSs, potentially serving the purpose of gas and metabolite exchange between the CSCs and a host cell (Fig. 1B). Expression of cardiac-specific proteins (α-sarcomeric actin and sarcomeric α-actinin) suggests that the host cells are mature cardiac myocytes (Fig. 1A-C). It was also found that CICSs development is finalized by the rupture of the capsule, followed by the release of cardiac marker-positive CSCs-derived transitory cells (Fig. 1D).



Cardiac "cell-in-cell structures" (CICSs) containing cardiac stem cells as identified in vitro (A) and ex vivo (B). The opening of the CICS (C) followed by the release of c-kit+ CSC-derived transitory cells (D).

Figure 1. Cell-in-cell CSC development.

On the basis of these data, we hypothesized that self-renewal of mammalian myocardium may, at least in part, occur by means of proliferation and partial differentiation of CICSs-embedded CSCs inside the mature cardiomyocytes.

P2998 | BENCH
Characterization and differentiation potential of porcine induced pluripotent stem cells

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Purpose: Up to now, the promising regenerative potential of induced pluripotent stem (iPS) cells is mostly investigated in small animal models. Therefore, we aimed to generate porcine iPS cells as a first step towards a large animal model.
Methods: Induced pluripotent stem cells were generated by lentiviral transduction of huOCT4, huSOX2, huKLF4 and huc-MYC in adipose tissue-derived fibroblasts. Quantitative RT-PCR was used to validate the expression of pluripotency markers like pGDF3 and pNANOG as well as mRNA levels of endogenous and exogenous reprogramming factors. Additionally, pluripotency was demonstrated in living cells by application of gene-specific nanoflares. Undirected differentiation of piPS cells was performed in analogy to human protocols. Gene expression of all three germ layers as well as cardiac transcription factors and cardiac TropT was analyzed by quantitative RT-PCR.
Results: First colonies appeared 16 days after transduction and could be successfully established after 3 weeks. Further culturing of generated porcine iPS was possible for more than 60 passages. Beside the expression of all four exogenous and endogenous reprogramming factors, the established piPS cell lines stained positive using specific GDF3 and NANOG nanoflare probes. Upon differentiation the expression of marker genes for ectoderm (KRT14), endoderm (AFP) and mesoderm (HAND1) were strongly increased confirming the capacity of the iPS cells to differentiate into all three germ layers. The expression of NKX2.5 and TBX5 peaked during undirected in vitro differentiation at day 6. Surprisingly an early peak of the mesodermal marker MESP1 could not be detected over time. Corresponding to an increased expression of the cardiac transcription factors TBX5 and NKX2.5 an induction of cardiac TropT could be documented after three weeks.
Conclusion: Our results show that piPS cell lines could retain a long-term stable phenotype and harbor the potential to differentiate into all three germ layers. The expression kinetics of the cardiac transcription factors NKX2.5 and TBX5 nicely correlate with the situation in human and murine in vitro models.

P2999 | BENCH
Transplantation of adipose tissue mesenchymal cells conjugated with PLGA microspheres promotes revascularization and tissue repair in a murine model of acute myocardial infarction

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Objective: Adipose tissue-derived mesenchymal stromal cells (AT-MSCs) may contribute repairing ischemic cardiovascular tissue. We examined whether poly (lactide-co-glycolide) (PLGA) microspheres functionalized with vascular endothelial growth factor (VEGF) enhance survival, growth, and differentiation of AT-MSCs, and the therapeutic efficacy of transplanted AT-MSCs conjugated with VEGF-microspheres or injection of conditioned medium from AT-MSCs in a murine model of acute myocardial infarction (AMI).
Methods: Twelve month-old male C57BL/6 mice underwent coronary artery ligation, followed by randomization into 7 groups (n=5/group): Sham operation, AMI control (saline 20 μl), intramyocardial injection with AT-MSCs only (2.5x105 cells/20 μl), or concentrated medium from AT-MSCs (CM, 20 μl), or AT-MSCs (2.5x105 cells/20 μl) conjugated with empty microspheres or VEGF-microspheres.
Results: VEGF-microspheres did not impact proliferation or osteogenic and adipogenic differentiation of AT-MSCs. Conversely, H2O2-induced apoptosis was inhibited in AT-MSCs conjugated with VEGF-microspheres, and this effect was dependent on the VEGF/Akt axis. AT-MSCs conjugated with VEGF-microspheres were more pro-angiogenic than AT-MSCs alone. AT-MSCs conjugated with VEGF-microspheres and CM decreased the area of fibrosis and increased myogenic marker expression, arteriogenesis, number of cardiac-resident c-Kit positive cells and fractional shortening when transplanted into the infarcted hearts of C57 mice (Fig. 1; N=5, **vs no ligation; °°<0,01 °<0,05 vs ligation-PBS treated).

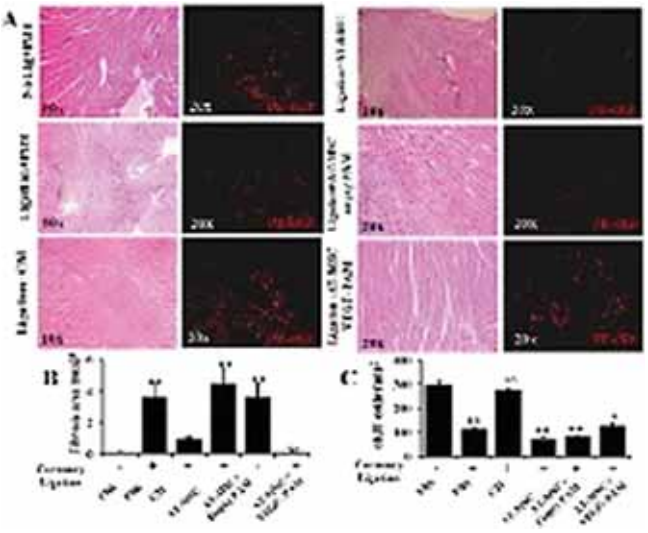

Figure 1. Fibrosis area and cKit-pos cells

Conclusions: The delivery of the AT-MSCs conjugated with VEGF-microspheres or injection of CM may have therapeutic applications for enhancing arteriogenesis and survival of AT-MSCs and for improving left ventricular function after AMI.

P3000 | BENCH
Intravenous transplantation of c-kit-positive resident cardiac stem cells ameliorates left ventricular remodeling in pressure overload

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Aims: Recent investigations demonstrate participation of c-kit (CD117)pos resident cardiac stem cells (RCSC) in myocardial repair. Hence, we investigated the influence of intravenous transplantation of c-kitpos RCSC on cardiac remodeling induced by pressure overload.
Methods and results: c-kitpos linneg GFPposRCSC were isolated by magnetic activated cell sorting from enzymatically dispersed whole hearts of 10-week-old male C57Bl/6-Tg (ACTb-EGFP)1Osb/J mice expressing green fluorescent protein (GFP) ubiquitary. RCSC were cultured and expanded in cell culture. Immunostaining revealed that 80% of cells expressed Oct3/4 in the nucleus. RCSC cultivated for 5 weeks in differentiation medium expressed mark-

ers of endothelial cells (podocalyxin 16.7±5%), smooth muscle cells (α-smooth muscle actin 28.2±5.2%) and cardiomyocytes (cardiac troponin 9.7±2%). 10-week-old male C57/Bl6N wildtype (WT) mice were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation (SHAM). For transplantation, 5x105 RCSC or stem cell buffer were infused in the tail vein 24 h post TAC and divided into four groups: SHAM+RCSC, TAC+RCSC, SHAM+buffer, TAC+buffer (n=6-13 per group) and analysed after 35 days. TAC significantly increased the number of the c-kitpos linneg GFPposRCSC in the left ventricle (LV) (TAC+RCSC 571±16.5/mm^2 vs. SHAM+RCSC 237±27/mm^2, $p<0.05$). GFPpos cardiomyocytes were identified in 4 TAC+RCSC mice. GFPposcells were also found in the bone marrow, spleen, lungs, kidneys and liver of RCSC-transplanted mice. In the liver of 5 RCSC-transplanted animals GFPpos hepatocytes were detected. Transplantation of RCSC in TAC mice prevented hypertrophy and fibrosis: cardiomyocyte cross-sectional area (TAC+RCSC 301±20, TAC+buffer 380±22, SHAM+RCSC 255±16.8, SHAM+buffer 261±23μm^2, $p<0.05$), LV fibrosis assessed by picrosirius red staining (TAC+RCSC 5±0.7, TAC+buffer 9.2±1.3, SHAM+RCSC 1.5±0.3, SHAM+buffer 2.7±0.5%, $p<0.01$), collagen Iα2 mRNA (TAC+RCSC 83.6±10, TAC+buffer 139±31, SHAM+RCSC 92±19, SHAM+buffer 100±22%, $p<0.05$) were reduced. Density of endothelial (CD31pos) cells (TAC+RCSC 5730±302, TAC+buffer 4718±156, SHAM+RCSC 5158±311, SHAM+buffer 4069±365 per mm^2, $p<0.05$) and brain natriuretic peptide (BNP) mRNA (TAC+RCSC 1071.8±347.7, TAC+buffer 439±144, SHAM+RCSC 274±105.8, SHAM+buffer 100±14.8%, $p<0.05$) were increased in the LV of animals transplanted with RCSC.

Conclusions: Intravenous transplantation of c-kitposlinneg resident cardiac stem cells ameliorates left ventricular remodeling in pressure overload by decreasing cardiomyocyte hypertrophy, fibrosis and increasing endothelial cell density and BNP expression.

P3001 | BENCH
Inhibition of microRNA-195 ameliorates aged stem cell function for cardiac repair through telomere re-lengthening

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Background: Decline in stem cell function aggravates aging process. Recently, we found age-induced microRNA (miR)-195 targets telomerase reverse transcriptase (TERT) in bone marrow-derived mesenchymal stem cells (BMSCs), and inhibition of miR-195 induced telomere re-lengthening in aged BMSCs. However, the effect of miR-195 on stem cell function and in cardiac repair is unknown.

Methods and results: We transfected aged BMSCs isolated from 24month-old mice with lentiviral anti-miR-195 to knockdown. Inhibition of miR-195 significantly reactivated Tert and Sirt1 along with telomere re-lengthening in aged BMSCs. Furthermore we injected BMSCs transfected with miR-195 inhibitor into the infarcted heart using mouse left anterior descending artery ligation model. 4 weeks after transplantation, LVEF, LVEDV, TEI index were significantly improved in transplantation of anti-miR-195 transfected group as compared to scramble control group, as assessed by echocardiography. Histological analysis of anti-miR-195 transfected group indicated less fibrosis and smaller infarction size along with higher angiomyogenesis as compared to control group. Moreover, significant telomere lengthening (Q-FISH analysis) and higher expression of anti-aging factors were observed in the heart lacking miR-195 (RT-PCR and Western blot).

Conclusions: Inhibition of age-induced miR-195 significantly restored telomerase expression in aged BMSCs, and transplantation of BMSCs lacking miR-195 improved cardiac function. The ability to use autologous, rejuvenated aged BMSCs by miR-195 inhibition is a novel therapeutic strategy for cardiac disease.

P3002 | BENCH
Purified exosomes from human cardiac progenitor cells improve cardiac function after myocardial infarction in vivo

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Background: Cardiac progenitor cell (CPC) transplantation improves cardiac function after myocardial infarction. Exosomes (Exo) are secreted nano-sized membrane vesicles that act as intercellular carriers of proteins and RNAs. Here, we investigated the role of Exo in the paracrine secretion by human CPCs (Exo-CPC), as compared to those from normal human fibroblasts (Exo-NHDF).

Methods: CPC were derived from atrial explants of patients who underwent heart valve surgery. Exo were precipitated with ExoQuickTM. Cytoprotective and proangiogenic assays were performed with mouse cardiomyocytes (CM) and human endothelial cells (HUVEC), respectively. The in vivo effects of Exo- CPC and Exo-NHDF were tested in a rat model of acute myocardial infarction.

Results: In vitro, Exo- CPC significantly reduced starvation-induced CM apoptosis by 59% ($p<0.05$), whereas Exo-NHDF did not. They also stimulated tube formation by HUVEC in Matrigel (total tube length 7912.38±1076 a.u.) compared with Exo-NHDF (total tube length 5095.25±747 a.u.; $p<0.05$). When injected into infarcted rat hearts, Exo-CPC, but not Exo-NHDF, significantly reduced infarct scar (0.58±0.08 a.u. vs. Exo-NHDF, 0.76±0.01 a.u.; $p<0.05$) while increasing new vessel formation (84±13 vs. 34±5 vessels/mm^2; $p<0.01$). Left ventricular ejection fraction decreased from baseline to 7 days in hearts injected with PBS (-21.3±4.5%) or Exo-NHDF (-12±6.3%) but was maintained in those injected with Exo-CPC (+0.8±6.8%; $p<0.05$ vs. PBS).

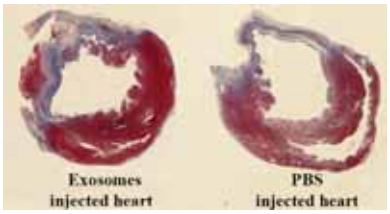

Figure 1. Exo.

Conclusions: Exo accounts for proangiogenic and antiapoptotic activities of human CPCs. Exo-CPC injected into infarcted hearts improves cardiac function early after MI. As a cell-free product, Exo-CPC has a potential for circumventing many of the limitations of cell therapy for cardiac repair.

P3003 | BENCH
Protein disulfide isomerase is a fundamental regulating factor of cardiac stem cell survival during hypoxia

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The human heart is a self-renewing organ characterized by the presence of c-kit-positive cardiac stem cell (hCSC) stored in niches and widespread within the 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 protein misfolding during stress, as occurs during ischemia.

The objective of this work was to determine whether PDI is present and functional in CSC and it is involved in the preservation of the stem cell pool during hypoxia. Surgical specimens were collected from the atrial and ventricular myocardium of 21 patients and hCSCs and myocytes were isolated. This cohort of patients included 10 women and 11 men affected by ischemic cardiomyopathy; 11 patients also had diabetes. Age was comparable in women and men. The yield of CSCs harvested from each sample did not vary with age or diabetes.

The PDI was very low expressed in the myocytes, sampled from the ventricles and atria of the patients investigated. Interestingly, by qRT-PCR, a 2000-fold difference was found in PDI expression comparing CSC and myocytes. Subsequently, the effects of hypoxia (1% O2) were studied in hCSCs in vitro and analyzed at 12, 24, 48 and 96 hours. With respect to differentiated cells, CSC showed consistently higher expression of PDI both at RNA and protein levels. Moreover, hypoxia led to upregulation of HIF1α transcripts in a time dependent manner. This results were coupled with an increase of the transcripts for the stemness associated genes Oct4, Nanog and IGF-1R in hCSC. Moreover, a high correlation was found between the expression of PDI in the CSC and the left ventricular remodeling evaluated 5 months after revascularization. A significant direct correlation between improvement of ejection fraction at FU and hCSC length of telomeres ($p<0.01$; R2 0.33) telomerase activity ($p<0.05$; R2 0.38) and PDI expression was observed ($p<0.05$; R2 0.41).

In conclusion, our data indicate PDI is a key regulator of CSC response to hypoxia and favors the conservation of their undifferentiated phenotype and most importantly their potential activation after injury.

ILLUMINATING THE VALVE WITH CARDIOVASCULAR MAGNETIC RESONANCE

P3004 | BEDSIDE
Biventricular heart remodeling after percutaneous and surgical pulmonary valve implantation: a CMR study

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Purpose: Percutaneous pulmonary valve implantation (PPVI) is an alternative to surgical pulmonary valve replacement (SPVR) in selected patients with congenital right ventricular outflow tract (RVOT) obstruction. Objective of this study is to evaluate the medium-term impact of PVVI and SPVR on biventricular function as assessed by cardiac magnetic resonance (CMR).

Methods: From 2008 to 2013, 33 patients (20±8 yy) underwent PPVI, while 16 patients (30±11 yy) underwent SPVR. A cono-truncal disease was present in 29/49 patients, previous Ross operation in 9/49. CMR was performed before and after an average of 10 months (range 3-15). Ventricular measurements were made on short-axis SSFP cine images.

Results: Results are summarized in table 1. The right ventricular end-diastolic

volume index (RVEDVI) decreased significantly for both procedures. Right ventricular ejection fraction (RVEF) increased significantly in the SPVR group compared to the PPVI patients. The left ventricular end-diastolic volume index (LVEDVI) increased more significantly after the procedure in the PPVI group; while changes were less evident and delayed in the SPVR patients. Left ventricular stroke volume index (LVSVI) increased in both groups after the procedure. There was an inverse correlation between the RV and LVEDVI: as the RVEDVI decreased in the follow-up, the LVEDVI increased.

Pre and post pulmonary valve replacement

	PVVI pre	PPVI post	P value	SPVR pre	SPVR post	P value
RVEDVI (ml/m^2)	81±37	68±16	0.03	142±34	88±21	≤0.01
RVESVI (ml/m^2)	43±35	32±13	≤0.01	75±29	41±15	≤0.01
RVSVI (ml/m^2)	36±11	35±9	NS	71±40	47±13	≤0.01
RVEF (%)	49±14	53±1 2	NS	46±11	53±9	0.03
LVEDVI (ml/m^2)	66±16	74±17	≤0.01	61±7	66±12	≤0.05
LVESVI (ml/m^2)	28±10	32±12	≤0.01	24±7	25±7	NS
LVSVI (ml/m^2)	38±12	41±11	0.04	35±10	40±8	≤0.05
LVEF (%)	57±10	56±11	NS	60±9	62±6	NS

Conclusions: Improvement of RVOT function is associated with reduction of RV volume and positive effects on ventricular–ventricular interaction supported by the increased LVSVI after the procedure. In the follow-up LV function improvement is delayed in the SPVR group. Medium-term follow-up shows permanent beneficial effect of pulmonary valve replacement in both groups.

P3005 | BEDSIDE
Which cardiac magnetic resonance derived parameter predicts better the need for invasive treatment in aortic coarctation?

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Severity of aortic coarctation (AC) is actually evaluated using clinical and imaging parameters in a comprehensive manner. We aim to analyze which cardiac magnetic resonance (CMR) derived parameters predicts better the need for surgical or percutaneous treatment of aortic coarctation.
Methods: Consecutive patients (p) with AC referred for CMR were selected. Patients with significant degree of aortic hypoplasia or loss of follow up were excluded. Clinical data were obtained reviewing medical records with a range of follow up of 6-70 months. CMR protocol includes: 1.Angiographic evaluation with multiplanar reconstructions to estimate the minimum diameter indexed by body surface area (MDi) and relative stenosis (RE) referred to the diameter of distal descending aorta; 2. Physiological evaluation with phase-contrast sequences quantifying maximum velocity post-coarctation (MV), derived gradient and flow pattern in descending aorta expressed as flow increase rate (FIR = distal descending aorta flow – proximal descending aorta flow)/proximal descending aorta flow %.)
Results: Eighty patients (p), mean age (25+ 15 years), 9 excluded, 42 (59%) male, 36 (50%) native coarctation, 20 p required treatment during follow-up and in 13 of them it was surgical. MDi, RE and FIR were significantly associated with the need of surgical or percutaneus treatment. Area under receiver operator characteristics curves (AUC), statistical significance, cut-off points and confidence limits are shown in the table.

Diagnostic performance of CMR variables

Variable	AUC	Significance	Confidence	Cut-0ff	Sens	Spe
MDi	0,71	0,01	0.53–0.89	7 mm^2/m^2	71%	70%
FIR	0,89	0,001	0.78–0.9	15%	84%	95%
RE	0,83	0,001	0,52–0.9	48%	81%	75%

MDi, minimum diameter indexed by body surface area; FIR, flow increase rate; RE, relative stenosis.

Conclusions: 1. Flow pattern in descending aorta expressed as flow increase rate is the CMR parameter that predicts better the need for invasive treatment of aortic coarctation 2. FIR ≥15% predicts the need for invasive treatment with Sens 84% Esp 95%.

P3006 | BEDSIDE
Diagnostic performance and severity criteria of cardiac magnetic resonance methods to evaluate mitral regurgitation related to comprehensive echocardiographic assessment

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Cardiac magnetic resonance (CMR) derived quantitative and semi-quantitative methods to asses severity of mitral regurgitation (MR) had been validated in several reports but their diagnostic performance and severity criteria are not fully established.
Objectives: To study diagnostic performance and to develop severity criteria of usual CMR methods related to comprehensive echocardiographic assessment.
Methods: Consecutive patients (p) with MR referred for a CMR and echocardiographic study were prospectively included. Patients with other causes of volume overload were excluded. Echocardiographic severity was determined using a comprehensive protocol recommended by ASE. Left and right ventricular stroke volume (LVSV, RVSV) were obtained by CMR short axis cine sequences. Regurgitant volume index (RVi) determined by ventricular stroke volume difference and regurgitant fraction (RF) were also analyzed. Regurgitant orifice area was measured by planimetry in a phase encoded sequence obtained at the level of the mitral valve leaflets and indexed to body surface area (ROi).
Results: Sixty seven p were included, 51 males (76%). Of them, 35 (52%) had mitral valve prolapse, 11 (16%) coronary artery disease, 9 (16%) dilated cardiomyopathy, 4 (6%) hypertrophic cardiomyopathy and 8p (11%) other aetiologies. Fifty three patients had severe MR. Area under receiver operator characteristic curves (AUC), best cut-off points of sensitivity, specificity, confidence interval and statistical significance are shown in the table.

	AUC	Significance	Confidence	Cut-off	Sensitivity	Specificity
RV	0.82	0.009	0.61–0.96	46ml	73%	86%
RVi	0.85	0.003	0.73–0.97	22ml/m^2	81%	86%
RF	0.78	0.01	0.61–0.95	34%	81%	72%
RO	0.85	0.004	0.72–0.97	0.65cm^2	64%	100%
ROi	0.88	0.002	0.76–0,99	0.25cm^2/m^2	78%	86%

RV: Regurgitant volume; RVi: Regurgitant volume index; RF: Regurgitant fraction; RO: Regurgitant orifice área; ROi: Regurgitant orifice area indexed to body surface area.

Conclusions: 1. CMR methods had good diagnostic performance related to echocardiography. 2. ROi is the method with best diagnostic performance and a ROi greater than 0,25cm^2/m^2 predicts severe MR with sensitivity of 78% and specificity of 86%.

P3007 | BEDSIDE
Determination of turbulent kinetic energy via phase-contrast-MRI for the assessment of aortic stenosis severity

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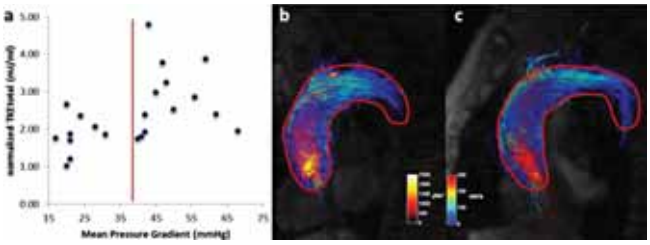
Introduction: In patients with aortic stenosis, cardiac load is increased due to energy losses in post-stenotic turbulent flow patterns. Clinical measures to determine the significance of aortic stenosis are either invasive or often found to misclassify disease severity. Phase-contrast MRI (PC-MRI) offers the possibility to quantify turbulent kinetic energy (TKE) which is a measure of the energy dissipated in turbulent flow. This energy is hypothesized to provide a more exact indicator of the additional work load of the heart. As part of an ongoing study, this work investigates the total TKE in the aorta in patients with different stages of aortic stenosis.
Methods: Time-resolved 3D PC flow measurements with multiple first gradient moments were employed to quantify velocities and turbulence intensities. For analysis, the TKE over all voxels in the aortic arch were integrated (TKE_total) and normalized by the stroke volume. 22 patients (69.8±13.3 years) were evaluated in this study. According to echocardiographically assessed mean pressure gradient, 12 patients had severe (>40 mmHg) and 10 patients had mild to moderate aortic stenosis (≤40 mmHg). Data is given as mean ± SD.
Results: In the group with severe aortic stenosis (2.87±0.91) mJ/ml and in the group with mild to moderate aortic stenosis (1.81±0.48) mJ/ml the mean total TKE differs highly significantly (P<0.003, Fig. 1a). However, there are patients with identical pressure gradients and highly different energy losses (Fig. 1b & c) and vice versa.



Figire 1. (a) TKE vs MPG; (b, c) TKE + flow patterns.

Conclusion: TKE differs highly significantly between patients with severe and patients with mild to moderate aortic stenosis. The potential for improved classification of patients with discrepant energy losses and pressure gradients has to be evaluated in larger clinical trials.

P3008 | BEDSIDE
Early onset of retrograde flow in the pulmonary artery measured by cardiac mri as follow up marker in pulmonary hypertension

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Background: Phase contrast gradient echo (PC-GRE) flow measurements have become integral part in the work up of patients with pulmonary hypertension (PH) by cardiac MRI. With increasing hypertension and vascular remodeling laminar flow in the PA becomes turbulent. A vortex develops, which also contains negativ flow. Exact quantification of flow is therefore hampered. However the onset of negativ flow can be used as a marker of PH itself. To study the onset of negativ flow as a follow up marker of PH we studied 26 patients with chronic thrombembolic pulmonary hypertension (CTEPH) before and after pulmonary endarterectomy (PEA).
Methods: 26 patients with CTEPH were studied on a 1.5 T Scanner before and after PEA by PC-GRE measurements in standard fashion. The onset of negative flow was computed as relative to the cycle duration, relative onset time (ROT). Results were correlated with invasive measurements of PA mean pressure.
Results: Of the 26 patients examined, 18 showed negative flow before PEA, while only 12 of the patients showed negativ flow after PEA (p=0.01). In those patients which exhibited negative flow before and after PEA, the onset was significantly delayed after PEA (ROT before PEA 9% vs. 15% after PEA, p=0.01). ROT was intermediately correlated with PA mean pressure r=0.39 but because of the limited sample only as a trend p=0.1.

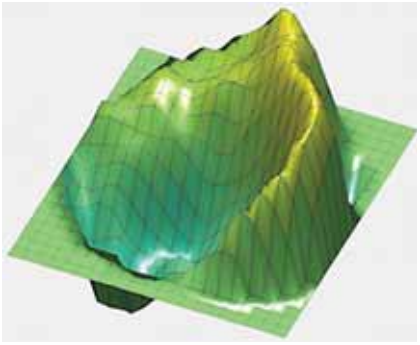

Figure 1. 3D representation of flow (+/–)

Conclusion: The onset of negative flow is well suited as a follow up marker for pulmonary hypertension, which could be shown in a cohort of CTEPH patients before and after PEA.

P3009 | BEDSIDE
Quantification by CMR of peri-prosthetic aortic regurgitation after TAVI

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Aims: Peri-prosthetic aortic regurgitation (Peri-AR) after TAVI has been associated with increased mortality. Quantification of Peri-AR is difficult after TAVI and needs the combination of hemodynamic, angiographic and echocardiographic parameters. The aim of this study is to assess the value of cardiovascular magnetic resonance (CMR) with the technique of phase contrast velocity mapping for the quantification of Peri-AR.
Methods: 30 patients underwent TAVI (COREVALVE (CV), n=10; or EDWARDS SAPIEN XT (EDXT), n=20) in our center between November 2012 and august 2013. AR severity was assessed using both transthoracic echocardiography (TTE), following the VARC criteria, and CMR. Both CMR and TTE were performed 5 days after TAVI. Invasively measured Aortic Regurgitation index (AR index) was obtained during TAVI in 26 patients.
Results: 30 patients were included, 20 with ED XT and 10 with CV. Peri-AR were graded by TTE as mild in 22, moderate in 3 and severe in 5 patients. The mean regurgitant volume and the mean regurgitant fraction by CMR were 5.5 ml and 9.2% for mild Peri-AR, 16.7 ml and 20.3% for moderate and 34.6 ml and 46.8% for severe Peri-AR, respectively, with significant differences between the three groups ($p<0.005$). A regurgitant fraction $<14\%$, discriminates mild from moderate/severe peri-AR with a 100% sensivity and 82% specificity (AUC 0.95). The reproducibility of CMR was excellent, with a coefficient of correlation at 0.99 for the intra and inter-operators variability. The mean AR index was 29.4 for mild Peri-AR and 13.8 for moderate/severe Peri-AR. Three patients were classified as mild Peri-AR by TTE but moderate/severe Peri-AR by AR index. For these 3 patients, FR by CMR was $>14\%$, suggesting a possible underestimation of Peri-AR severity by TTE in some cases.
Conclusion: CMR is a reliable method for assessing the severity of peri-AR using FR determination. In some cases CMR can correct an underestimation by TTE. A future prospective study should assess the FR as a predictor of morbidity and mortality in the follow up after TAVI.

P3010 | BEDSIDE
Associations between native myocardial T1 and diastolic function evaluated by PC-CMR in patients with severe aortic valve stenosis

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Purpose: To assess the relationship between the presence of myocardial interstitial fibrosis as reflected by the increase in native T1 values and alterations in left ventricular (LV) diastolic function evaluated by phase contrast cardiac magnetic resonance (PC-CMR), in subjects with severe aortic valve stenosis (AVS).
Methods: We studied 20 subjects (71 ± 10 years) with severe AVS including 19 with a preserved ejection fraction. All patients underwent transthoracic echocardiogram (TTE) and cardiac magnetic resonance (CMR) exams. CMR included conventional LV systolic function and delayed enhancement evaluations as well as a native T1 mapping acquisition using the modified Look-Locker inversion recovery sequence and velocity encoding data of the transmitral inflow for the evaluation of LV diastolic function. These latter CMR data were analyzed using custom software resulting in segmental T1 values and diastolic parameters such as transmitral peak velocities (E, A), peak flow rates (Ef, Af), filling volume (FV), and myocardial peak velocities.
Results: For all patients, TTE revealed the presence of severe AVS according to ESC criteria (aortic valve area indexed to BSA= 0.43 ± 0.09 cm^2/m^2 and mean gradient 54 ± 14mmHg). When compared to CMR data of 34 elderly controls (60 ± 8 years) despite the preserved ejection fraction (patients=$66\pm10\%$; controls=$66\pm4\%$), diastolic parameters indicated an impaired LV relaxation in patients with severe AVS. Importantly, while dense fibrosis volume quantified from delayed enhancement images was not related to diastolic function parameters, a significant relation was found between native myocardial T1 values and parameters of LV filling such as: the ratio between the peak filling rate and the peak atrial rate EfMR/AfMR ($r=0.51$; $p<0.05$); the ratio between the peak atrial rate and the filling volume Af/FVMR ($r=0.67$; $p<0.05$); and the peak atrial rate Af ($r=0.63$; $p<0.05$).
Conclusions: Interstitial myocardial fibrosis assessed non-invasively by native T1 is related to the severity of diastolic dysfunction in subjects with severe AVS.

IMPROVING OUTCOMES IN STEMI

3034 | BEDSIDE
A national PCI network and a pharmacoinvasive strategy, keys of success of the Romanian STEMI program

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Background: 1. A national network for interventional therapy (PCI) in patients (pts) with ST-elevation myocardial infarction (STEMI) was opened in Romania in August 2010. 2. In real life it is difficult to perform primary angioplasty (PPCI) within the first 2 hours after the first medical contact (FMC) as guidelines recommend. In these circumstances the pre-transfer therapy (thrombolysis, antiplatelets, anticoagulants) are recommended.
Objective: To evaluate the in-hospital mortality in STEMI pts treated in Romania between January 1st 2009–December 31st, 2013, respectively before the implementation of the national STEMI network and for the first 4 years after opening the Romanian national program for interventional therapy in STEMI pts.
Methods: Romania has a 19 million inhabitants. According to the our RO-STEMI registry (opened in 1997) 15000 STEMI pts are admitted every year in the Romanian hospitals. In 2010 the national STEMI network was based on 10 PCI centers organized in a 24/7 system. The number of PCI centers increased to 14 in 2013. Based on a regional dispatch system the STEMI pts were either directly transported to the PPCI centers (if within the first 2 hours after the first medical contact) or after local thrombolysis (if time of transport was longer). The protocol recommended aspirin, bolus of unfractionated heparin and loading dose of clopidogrel in all pts. before transfer to the PCI centers. Data of STEMI pts were recorded in the central database of the Romanian registry on STEMI (RO-STEMI).
Results: Between 2009 – 2013 the RO-STEMI registry recorded data from 33222 STEMI pts. Pts treated by PCI progressively increased from 19.5% (2009) to 60.9% (2013). The culprit coronary artery was found as opened in 40% of pts before the angioplasty and stenting. Pts treated by thrombolysis decreased from

21.7% (2009) to 5.6% (2013) and pts. not undergoing reperfusion therapy decreased from 58.8% (2009) to 33.22% (2013). The in-hospital mortality decreased from 13,5% (2009) to 12,2%, 9,93%, 8,19% and 8,20% in 2010, 2011, 2012 and 2013, respectively.
Conclusion: Implementation of a pharmacoinvasive strategy consisting in a limited number of PCI centers but a large scale pre-transfer administration of antiplatelets, anticoagulants with/without thrombolysis was followed in 3 years by a 40% decrease of the global in-hospital mortality with persistence of this result.

3035 | BEDSIDE
More rapid platelet inhibition with prehospital administration of 60 mg prasugrel compared to 600 mg clopidogrel in patients with STEMI and primary PCI. The double-blind, randomized ETAMI trial

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Objective: This study compared the onset of antiplatelet action of early treatment with clopiogrel and prasugrel in patients with ST elevation myocardial infarction (STEMI) scheduled for primary percutaneous coronary intervention (PCI).
Background: Little is known about the timing of onset of antiplatetet action after a pre-PCI loading dose of clopidogrel or prasugrel in patients with STEMI.
Methods: This double-blind prospective study randomized 62 patients with STEMI scheduled for primary PCI in the ambulance or the emergency department to 60 mg prasugrel (n=31) or 60 mg clopidogrel (n=31). The primary endpoint was the platetet reactivity index (PRI) measured with the VASP assay 2 hours after intake of the study medication. Secondary endpoints were PRI after 4 hours, TIMI patency of the infarct related artery before and after PCI and clinical events until day 30.
Results: The PRI after 2 hours (50.4+ 32.7 versus 66.3 + 22.2; p=0.035) and after 4 hours (39.1 + 27.5 54.5 + 49.3; p=0.038) were significantly lower with prasugrel compared to clopidogrel. In addition the rate of patients with a PRI <50% was higher with prasugrel compared to clopidogrel after 2 hours (46.7% versus 28.6%) and after 4 hours (63.0% versus 38.9%). There were no significant differences in TIMI 2/3 patency before PCI (45.2% versus 35.5%, p=0.43) and TIMI 3 patency after PCI (88.5% versus 89.3%, p=0.92).
Conclusions: The pre-PCI administration of prasugrel in patients with STEMI undergoing primary PCI was associated with a significant faster inhibition of ADP-receptor inhibition compared to clopidogrel.

3036 | BEDSIDE
Is upstream heparin useful in patients with STEMI undergoing primary intervention?

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Purpose: Antiplatelet and antithrombotic agents in patients with STEMI are often started in ambulance. However, data supporting upstream administration of heparin are very limited. We sought to evaluate the outcomes of STEMI patients receiving upstream heparin in comparison to patients who were given heparin during the procedure.
Methods: Data of all STEMI patients presenting to our Hospital from January 2006 to December 2013 were analysed. After excluding patients treated with upstream IIb/IIIa GP inhibitors, we evaluated 836 patients, who were divided in 2 groups according to the timing of heparin administration.
Results: Baseline characteristics were similar in the 2 groups. Patients receiving upstream heparin showed a lower use of procedural abciximab, a nonsignificant trend towards both a higher rate of open vessel before PCI and TIMI III flow after PCI, and a lower 30-day mortality (see table).

	Upstream heparin	Procedural heparin
No. of patients	425	411
Age	67±13.3	68±13.2
Females	30%	31%
Diabetes	22%	26%
Systolic BP	138±32	137±33
Killip class II–IV	10%	7%
Anterior STEMI	34%	34%
MV disease	43%	42%
Use of abciximab	50%	59%*
Symtom onset-to-balloon time	198 [133–301]	208 [134–365]
1st med contact-to-balloon time	83 [69–104]	78 [60–101]
TIMI flow II–III before PCI	35%	29%
TIMI flow III after PCI	85%	78%
Peak CKMB (ng/ml)	192±182	170±169
Pre-discharge LVEF	50±11	50±13
30-day mortality	4.5%	10.2%*

*P=0.001.

Conclusions: Upstream heparin in STEMI patients treated with primary PCI might be associated with better reperfusion and even with lower mortality. Further data are needed to confirm those observations.

3037 | BEDSIDE
Influence of early administration of heparin on initial patency of the infarct related artery in patients with ST-elevation myocardial infarction treated with primary angioplasty

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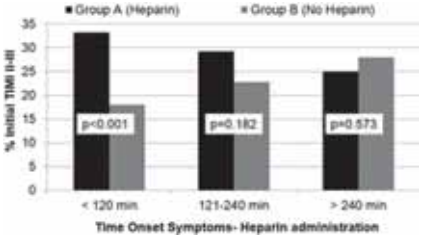
Background: Initial Thrombolysis in Myocardial Infarction (TIMI) flow is related to mortality in ST-Elevation Myocardial Infarction (STEMI) patients treated with primary angioplasty (PPCI). Although adjunctive treatment with unfractioned heparin improves coronary patency, the benefit of early administration remains unclear.
Objectives: To investigate the effect of early administration of heparin compared with administration in the cathlab in patients transferred from another hospital on the initial patency of the infarct related artery (IRA) in patients treated with PPCI.
Methods: Retrospective analysis of 1326 consecutive patients treated with PPCI (February 2007-December 2013) transferred to our centre, allocated in two groups (group A: heparin administration before transfer, 758 patients (57%); B: administration of heparin in the cathlab, 568 patients (43%). The effect of time between symptoms onset and heparin administration (TS-HA) on artery patency was assessed.
Results: Initial TIMI II-III flow grade in the IRA was 29.6% in group A vs 20.6% in group B (p=0.002). TS-HA was related to initial TIMI II-III [33.2% vs 18% (p<0.001) when administered <120 minutes; 29.2% vs 22.8% (p=0.03) between 120-240 minutes; 25% vs 28% >240 minutes (p=0.87)]. There were no differences in major bleeding. Multivariate analysis showed administration of heparin before transfer as an independent predictor factor for initial TIMI II-III flow grade (RR 1.64 IC (95%) [1.25-2.15], p<0.0001).



Early heparin administration-TIMI II-III.

Conclusion: In patients with STEMI transferred for PPCI, early administration of heparin resulted in a higher initial patency of the IRA.

3038 | BEDSIDE
Post PCI anticoagulation after primary PCI: widely used but only increases bleeding. Insights from a pooled analysis of the HORIZONS-AMI and EUROMAX trials

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Background: After successful primary PCI, many sites routinely continue anticoagulation despite an unclear risk to benefit ratio. The outcomes of this approach have not been studied.
Methods: EUROMAX and HORIZONS-AMI were two international randomized trials comparing bivalirudin to heparin with or without glycoprotein IIb/IIIa inhibitors in patients with STEMI treated with primary PCI. We collected the use of post procedural anticoagulation (defined as unfractionated or low-molecular-weight heparins or fondaparinux given after the catheterization laboratory) and analyzed outcomes.
Results: Overall 5792 patients were available for analysis of whom 2387 (41.2%) received post procedure anticoagulation. The composite outcome of death, reinfarction or major bleeding (not related to bypass surgery) occurred in 10.7% of patients who received anticoagulation post PCI vs 8.2% of those who did not (RR: 1.31; 95%CI: 1.11-1.54). This was largely driven by an increase in protocol-defined non-CABG related major bleeding (RR: 1.56; 95%CI: 1.28-1.92), which was also observed when using other definitions for bleeding (TIMI major bleeding: RR 1.83; 95%CI: 1.3-2.59). Logistic regression analysis showed that post-PCI anticoagulation was an independent correlate of 30-day non-CABG protocol defined major bleeding (OR: 1.357; 95%CI: 1.062-1.734) or TIMI major bleeding (OR: 1.647; 95%CI: 1.122-2.416) but not of the composite outcome. There were no significant differences in death, cardiac death, reinfarction or stent thrombosis between the 2 groups.
Conclusion: In these two recent randomized international trials of primary PCI, a sizeable fraction of patients (more than 40%) received prolonged anticoagulation after primary PCI. This practice is associated with increased bleeding risk

but no clear clinical benefit, and should be abandoned unless a clear indication exists.

3039 | BEDSIDE
Intracoronary bivalirudin bolus during primary angioplasty improves postprocedural angiographic flow and myocardial reperfusion indexes

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Aim: We prospectively investigated the feasibility and safety of intracoronary bivalirudin bolus administration during primary percutaneous coronary interventions (PCI), comparing it with the standard intravenous route.
Background: Bivalirudin efficacy in the very first hours after primary PCI has been questioned, due to increased acute stent thrombosis rates. Intracoronary administration of the bivalirudin bolus might furnish an extremely high local drug concentration without changing the global dose administered to the patient, with a potential favorable effect over the pro-thrombotic milieu of the infarct related artery.
Methods: In 245 consecutive patients treated with primary PCI we administered intracoronary bivalirudin bolus followed by standard intravenous infusion. Postprocedural coronary blood flow indexes and clinical reperfusion markers of these patients were compared with a propensity score-matched cohort of primary PCI patients treated with standard intravenous bivalirudin bolus plus infusion.
Results: Our study suggests safety similar bleeding episodes were observed in the two groups. However we observed better TIMI frame count values (14.7 vs 17.9, P=0.001), higher rates of $\geq$70% ST resolution (72.7 vs 60.0%, p=0.004) and lower postprocedural peak CK-MB levels (188.3$\pm$148.7 vs 242.1$\pm$208.1 Ui/dL, P=0.025) in the intracoronary bolus group. Acute stent thrombosis was observed only in 3 cases, all in the intravenous bolus group (P=NS). The results were substantially confirmed when analysis was restricted to patients with evidence of an occluded infarct related artery before PCI.
Conclusion: In the population studied intracoronary bivalirudin bolus during primary PCI is safe and might improve results obtained through the standard intravenous route over postprocedural coronary flow and clinical myocardial reperfusion.

3040 | BEDSIDE
The impact of thrombus aspiration on luminal expansion: the intra-vascular ultrasound study of thrombectomy in ST elevation myocardial infarction patients

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Purpose: Primary PCI is the optimal treatment for STEMI patients and thrombus aspiration is widely used as adjuvant therapy, aiming to protect the microcirculation, reduce infarct size and distal embolization. Routine thrombus aspiration is debated and mortality benefit was not demonstrated in a recent cohort study. Our aim was to assess the effects of thrombus aspiration in STEMI patients undergoing primary PCI and to gain insight into the mechanism of luminal expansion. Intravascular ultrasound (IVUS) was done prior to and after thrombus aspiration and the aspirate analysed by histopathology
Methods: 40 STEMI patients undergoing primary PCI were recruited and informed consent obtained. Blood was sampled at the beginning of the procedure and after 12 hours. IVUS was done prior to and after thrombus aspiration and stenting. Vessel lumen and external elastic membrane were measured at 0.5 mm intervals throughout the lesion and proximal and distal reference segments. Histopathology assessment was carried out on the aspirated thrombus material.
Results: Majority (81%) were male and mean age 59 years with troponin T at 12 hours 4114$\pm$3297 ng/L. Most procedures were carried out via radial access (94%) using drug eluting stents (97%, mean diameter 3.8$\pm$0.4 mm). 36 out of 40 patients had IVUS suitable for analysis. All patients had reduced or no flow in the target vessel at the beginning with 30 out of 36 patients having TIMI 0 flow at baseline. All patients had TIMI 3 flow post intervention.
The luminal volume at the lesion increased by a third after aspiration (93$\pm$64 to 128$\pm$111 mm^3, P=0.0009), attributed to a reduction in the plaque-thrombus volume from 212$\pm$122 to 174$\pm$96 mm^3, P=0.0017) There was no change in the vessel volume defined by the external elastic membrane (307$\pm$175 to 302$\pm$193 mm^3, P=NS), demonstrating that lumen enlargement is not caused by vasodilatation. The aspirated material consisted largely of blood components, but was on average relatively small, 40.07$\pm$29.9 mg. There was no association between changes in lumen areas and the mass of the aspirated thrombus (P=NS).
Conclusions: Passage of a thrombectomy catheter in STEMI patients increases luminal volume at the culprit lesion by a third by IVUS assessment. The lack of changes in the external elastic membrane volume indicates that vasodilatation is not mechanically involved in this process. Only a small amount of the thrombus is removed from the vessel as a clot and a larger amount appears to travel downstream in the vessel. This is likely to explain the lack of demonstrable mortality benefit with thrombus aspiration.

3041 | BEDSIDE
Ruptured versus eroded plaques at the culprit site of ST-elevation myocardial infarction: incidence, morphological characteristics and response to primary percutaneous coronary intervention

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Purpose: To define in-vivo morphology features, thrombus characteristics and response to primary stenting of ruptured compared with non ruptured/eroded plaque at culprit site of ST-elevation myocardial infarction (STEMI).
Methods: In the OCTAVIA trial (NCT01377207) 140 patients with STEMI$<$6 hours from symptom onset underwent optical coherence tomography (OCT) of the infarct-related artery before primary angioplasty, after everolimus-eluting stent (EES) implantation and at 9-month follow-up. Serum biomarkers, histopathology and immunohistochemistry of thrombus aspirates were assessed at baseline. All analyses were performed by dedicated core laboratories.
Results: A fully identifiable culprit plaque morphology was adjudicated in 97 patients: plaque rupture in 63 (64.9%), eroded plaque in 32 (33.0%) and spontaneous dissection in 2 (2.1%). Patients with plaque erosion (ER) had similar clinical characteristics but lower peak level of CK-MB (66.6 UI/L) compared with ruptured plaques (RP, 149.8 UI/L, p=0.025). Serum inflammatory and platelets biomarkers were comparable between groups (p=NS for all). ER compared with PR had lower lipid content (22.6% vs. 37.3% lipid areas p$<$0.001) and less plaque material retrieved with manual thrombus aspiration (7.1% vs. 54.8% p=0.002). Histology and immunohistochemistry of thrombus aspirates did not show differences between groups, with the only exception of a higher content of the eosinophil marker interleukin-5 (IL-5) in the ER group (IL-5 cells/5HPF 1 vs. 0, p=0.01). The presence of any additional thin-cap fibroatheroma along the infarct-related artery was significantly less in ER (47% vs. 94% PR, p$<$0.001). ER had less remaining thrombus after manual thrombus aspiration (both white 0.41 μm^3 vs. 1.52 μm^3, p=0.001 and red thrombus 0 μm^3 vs. 0.29 μm^3, p=0.001). At 9-month after EES implantation there were no differences between ER and PR for rate of strut coverage (92.5% vs. 91.2%, respectively, p=0.15) and percentage of stent volume obstruction (12.6 vs. 10.2%, p=0.27). No significant differences in outcomes were observed at 1 yr.
Conclusions: Patients with plaque erosion vs. plaque rupture at culprit site of STEMI did not show major differences in clinical characteristics and serum biomarkers of inflammation and platelet activation. Eroded compared with ruptured plaques showed less remaining thrombus, less lipid component, and fewer thin-cap fibroatheromas along the culprit vessel. No differences in healing response to current generation drug-eluting stent was observed at 9 months between eroded and ruptured plaques.

3042 | BEDSIDE
Collateral blood flow influences the effect of remote ischemic conditioning in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

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Purpose: Remote ischemic conditioning (RIC) increases myocardial salvage in patients with ST-elevation myocardial infarction (STEMI). We investigated the influence of collateral blood flow (CBF) on the effect of RIC in STEMI patients undergoing primary percutaneous coronary intervention (PPCI).
Methods: In a prospective, single-blinded randomised controlled trial (n=140), we studied the subgroup of patients with STEMI and occluded culprit vessel (TIMI flow grade 0-1) on arrival, randomised to treatment with either RIC+PPCI or PPCI alone. RIC was performed as 4 cycles of 5 min upper arm ischemia followed by 5 min of reperfusion. Myocardial salvage index (MSI) was assessed by single photon emission computerized tomography (SPECT). Pre-procedural CBF was assessed from the pre-PPCI coronary angiography, and patients were grouped as either having CBF (Rentrop score 1-3) or no CBF (Rentrop score 0).

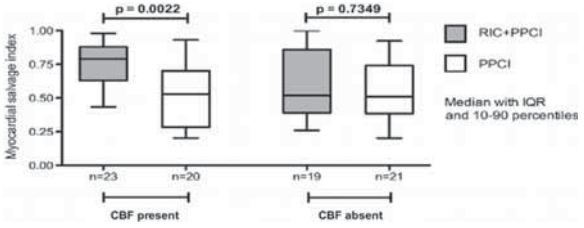

Figure 1

Results: A total of 83 patients were included in the study. 43 patients had CFB visible on coronary angiography. Of these, 23 patients were treated with RIC+PPCI, 20 with PPCI alone. AAR was similar in patients treated with RIC+PPCI or PPCI alone (p=0.7155). The presence of CBF did not affect AAR, either in patients treated with RIC+PPCI or PPCI alone (p=0.5776 and p=0.3472). In patients with CBF, RIC+PPCI significantly increased MSI compared to PPCI alone (P=0.0022), whereas in patients without CBF, RIC+PPCI did not affect MSI compared to PPCI alone (p=0.7349) (Fig. 1).
Conclusion: CBF on coronary angiography seems necessary for the cardioprotective effect of RIC in STEMI patients undergoing PPCI. This finding suggests that CBF facilitates delivery of a humoral cardioprotective factor to the myocardium threatened by reperfusion injury and may differentiate RIC from local ischemic conditioning.

3043 | BEDSIDE
Impact of right bundle branch block on long-term mortality in patients with symptoms suggestive of acute myocardial infarction

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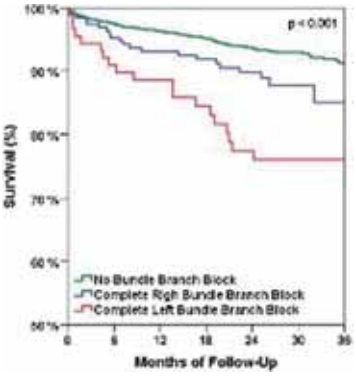
Background: Left bundle branch block (LBBB) is a well known predictor of impaired outcome in patients with symptoms suggestive of acute myocardial infarction (AMI). The prognostic impact of right bundle branch block (RBBB) in these patients is less well defined.
Methods: In a prospective multicenter study, we enrolled 2930 consecutive patients with symptoms suggestive of AMI. Patients were stratified according to presence of a complete RBBB, LBBB or absence of BBB. Final diagnoses were adjudicated by two independent cardiologists. The primary endpoint was all-cause mortality during 3 years of follow-up.
Results: RBBB was present in 7% and LBBB in 3% of patients. Patients with RBBB and LBBB were older compared to patients without BBB (median 71 vs. 78 vs. 60 years, $p<0.001$). Overall, AMI was the final diagnosis in 19% of patients. Rates of AMI were 19% in patients with RBBB and 39% in patients with LBBB. A total of 199 patients died during 3 years of follow-up. Kaplan-Meier analysis revealed that mortality in patients with RBBB was high compared to patients without BBB (15% vs. 9%), but lower compared to patients with LBBB (24%). The association was similar in patients with and without AMI (mortality rates 23%, 19% and 32% in patients with AMI and 13%, 7% and 19% in patients without AMI, $p<0.001$ for all comparisons). After adjusting for age, this association was no longer significant, neither for RBBB nor for LBBB, neither in the overall cohort nor in the subgroups of patients with and without AMI.



Conclusions: The presence of an RBBB is a predictors of a worse outcome in patients with symptoms suggestive of AMI, but to a lesser extent than LBBB. Patients with BBB were generally older and the association with a worse outcome was no longer significant after adjustment for age.

ATRIAL FIBRILLATION ABLATION: LOOKING FOR THE HOLY GRAIL

3052 | BEDSIDE
Clinical and ECG characteristics of super-responder for catheter ablation in patients with longstanding persistent atrial fibrillation

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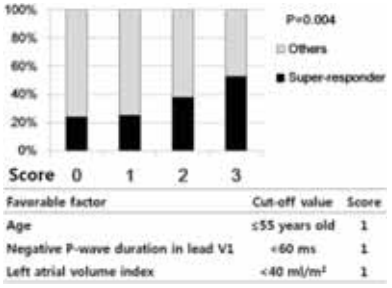
Purpose: The radiofrequency catheter ablation (RFCA) for longstanding persistent atrial fibrilation (L-PeAF) is technically challenging and has a high recurrence. Therefore, determination of clinical factors for super-responder before procedure might be valuable to reduce un-necessary procedure.
Methods: We included consecutive 361 patients with L-PeAF (77.8% male, age 58.0±10.5 years) who underwent RFCA. Super-responder was defined as no AF symptom nor ECG documented recurrence during follow-up. We evaluated pre-procedural clinical, ECG, and echocardiographic factors associated with super-responders.
Results: 1. During 782±451 days follow-up interval, 116 (32.1%) patients were categorized as super-responders, 201 (55.7%) as partial responder (remain in sinus rhythm with AAD), and 44 (12.2%) as failure. 2. Super-responders were younger (56.0±11.4 vs. 59.0±9.9 years old, p=0.010), and had shorter negative P-wave duration in lead V1 (58.5±26.4 vs. 65.5±25.1 ms, p=0.019) and smaller left atrial volume index (LAVI; 39.6±11.1 vs. 43.2±11.7 ml/m^2, p=0.008). 3. LAVI (OR=0.974, p=0.020), negative P wave duration in V1 (OR=0.989, p=0.020), and age (OR=0.973, p=0.011) were independently associated with super-responders in logistic regression analyses. Their cut-off values were determined by ROC curve analyses (40mL/m^2, 60ms, and 55 years old, respectively). 4. The number of favorable factors had significantly positive correlation with the frequency of super-responders (figure, p=0.004).



Favorable factor	Cut-off value	Score
Age	≤55 years old	1
Negative P-wave duration in lead V1	<60 ms	1
Left atrial volume index	<40 ml/m²	1

Conclusion: The super-responders were associated with lower LAVI, shorter duration of negative P-wave duration in V1, and younger age in patients with L-PeAF. Further prospective clinical study is warranted to validate whether pre-selection of potential super-responders may improve clinical outcome.

3053 | BEDSIDE
The impact of left atrial electroanatomical substrate on atrial fibrillation recurrence after radiofrequency pulmonary veins isolation: a prospective observational study

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Background: There is a lack of data regarding how the left atrial (LA) electroanatomical remodeling can predict the clinical outcome after index and redo pulmonary vein (PV) isolation in patients with atrial fibrillation (AF). Our aim was to assess the extent of LA electroanatomical substrate (EAS) in patients with AF and its impact on recurrence rate following PV isolation.
Methods: We prospectively analyzed electroanatomical high density bipolar maps (HDBM) in 111 subjects with paroxysmal (14 pts) and persistent (97pts) AF. Bipolar signals ≤0.75mV, associated with local conduction velocity delay (table 1) were tagged on LA maps and considered as EAS. Relative EAS area outside PV ostia were consistently measured. AF recurrences were documented using Holter monitoring every 3 months and symptom-based observations.
Results: A mean number of points for LA HDBM was 420±184. A mean relative EAS area was 13.8±10.3% and 32.6±18.5% in patients with paroxysmal and persistent AF, respectively (P=0,003). During a mean follow-up of 21±8 months, AF recurrence was diagnosed in 43 (39%) of patients. Following a redo ablation in 31 (28%) of patients, subsequent AF recurrence developed in 21 pts (19%). Multivariate analysis (table 2 and 3) showed that only relative EAS areas was independently associated with AF recurrence (HR 1.05, CI 95% 1.02-1.09, P=0.002); and relative EAS areas, AF history longevity and LA enlargement were independently associated with recurrences after redo ablations (HR 1.09, CI 95% 1.05-1.14, P=0.00018;HR 1.11, CI 95% 0.99-1.24, P=0.05;HR 1.28 CI 95% 1.07-1.52, P=0.005, relatively). Each 10% increase in the extent of relative EAS area was associated with a 1.6-fold elevation of AF recurrence rate after the index ablation; and with a 2.4-fold elevation of AF recurrence rate after a redo ablation.

Table1. Local conduction velocity

Voltage zones	Local conduction velocity (LCV), m/s	P-value
VZ1 (0,06–0,75 mV)	1,07±0,44	0,00001*
VZ2 (0,76–1,5 mV)	2,33±0,61	0,0008**
VZ3 (>1,5 mV)	2,37±0,52	0,67***

*p for the comparison between LCV1 and LCV3; **p for the comparison between LCV1 and LCV3; ***p for the comparison between LCV 2 and LCV3.

Conclusion: The presence of EAS areas (≤0.75mV) outside PV ostia in patients undergoing PV isolation is a significant and independent predictor of AF recurrence.

3054 | BEDSIDE

Unusefulness of image integration in radiofrequency catheter ablation of paroxysmal atrial fibrillation with multielectrode mapping systems

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Purpose: Pulmonary veins isolation (PVI) is the cornerstone of catheter ablation (CA) of paroxysmal atrial fibrillation (PAF). In the last years 3D mapping (3DM) systems developed image integration (IMI) tools to improve left atrium (LA) navigation and CA outcome. We investigated the role of IMI in the era of multielectrode (ME) 3DM.
Methods: We enrolled 210 consecutive patients (Pts) (155 M, 74%; mean age 59±11 yrs) suffering PAF, undergoing first PVI with RF CA between Jan 2010 and Mar 2013. In 114 (54.3%) cases 3DM was performed with CARTO 3; in 96 (45.7%) with NavX 3.0 system; in all cases LA points were collected with a ME catheter (Lasso/AFocus). In 142 (67.6%) cases IMI with CT or MRI scan was performed (Group A); in 68 (32.4%) CA was guided by 3DM alone (Group B). We recorded skin-to-skin time (SKT), fluoroscopy time (FST) and Dose Area Product (DAP). Acute (complete PVI) and long-term outcome data (any AF recurrence in follow-up after a blanking period of 3 months) were analyzed for both groups.
Results: The two groups did not differ in clinical and anatomical characteristics (including mean age, LVEF and LA area, gender, incidence of PV variants, level of anesthesia). Skin-to-skin time was similar with median 150 min (120-180) in Group A and 160 min (120-180) in Group B (p=0.66). Imaging significantly increased FST and DAP with respectively in Group A and B: 38 (27-50) vs 29 (22-42) min and 132 (77-212) vs 74 (44-139) Gy/cm^2 ($p<0.01$). Sub-analysis showed that these differences in FST and DAP were significant only in first 80 cases (2010) and not when analyzing the subsequent period, suggesting a process learning curve-related. No differences in acute and long-term clinical outcome were reported analyzing survival free from AF recurrences for Group A or B (Log-rank p=0.45), at a median F-U of 12 (3-32) months.
Conclusions: In our study ME 3DM without IMI achieved similar procedural results (SKT, FST and DAP) with no differences in clinical success rate. This may favor the only use of 3DM for the first CA procedure of PAF, achieving the same clinical long-term success rate and reducing both cost and X-ray pre-procedural exposure.

3055 | BEDSIDE

Robotic or conventional atrial fibrillation ablation? Comparison during long term follow up

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Background: Different robotic devices are available for atrial fibrillation (AF) ablation although the long-term efficacy is not well established. The aim of this prospective study is to evaluate the efficacy of pulmonary vein isolation using magnetic navigation comparing to a non-robotic conventional ablation.
Methods: We studied 809 consecutive patients who underwent 905 AF ablation procedures by the same medical team in two different centers (one using only magnetic navigation and the other manual approach). 3D mapping systems (CARTO for magnetic navigation and CARTO or NAV-X for manual approach) and circular Lasso catheter were used in all patients. Recurrence was defined by the presence of symptoms or AF documented by ECG or 24h Holter recording lasting longer than 30sec.
Results: The mean age of the patients was 57±11 years, 72% were male, 36% hypertensive, and 70.5% had paroxysmal AF. The mean left atrium volume was 104±38ml. Ablation was performed with magnetic navigation in 491pts (54%). There were no differences between robotic vs. conventional treatment regarding sex, type of AF at presentation or prevalence of hypertension, but patients in the magnetic navigation group were significantly older (58.4±11 vs. 56.8±11 years, p=0.033) and had smaller left atriums (91±34 vs. 119±35 ml, $p<0.001$). Magnetic navigation procedure lasted longer (189.3±41.3 vs. 153.5±58.4min, $p<0.001$) but needing lower fluoroscopy time (15±12 vs. 28±17 min; $p<0.001$). During a mean follow up of 2.2±1.7 years after each patient's last procedure, there were 284 AF recurrences (35.1%). After adjusting for age, sex, hypertension, type of AF and left atrium volume, the mode of ablation was not an independent predictor of freedom from AF. The only independent predictors of recurrence were larger indexed left atrium volume (HR 1.015 for each ml/m^2, 95%CI 1.01-1.02, $p<0.001$), female gender (HR 1.58, 95%CI 1.21-2.06, p=0.001), and non-paroxysmal AF (HR 1.29, 95%CI 1.01-1.66, p=0.044).
Conclusions: In our registry of patients submitted to pulmonary vein isolation, magnetic navigation used lower fluoroscopy times and the outcome was not inferior during long-term follow up when compared to manual approach.

3056 | BEDSIDE

Does the isolation of left atrial posterior wall improve clinical outcomes after radiofrequency catheter ablation for persistent atrial fibrillation? a prospective randomized clinical trial

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Introduction: Although posterior wall (PW) of left atrium (LA) has been known to be arrhythmogenic focus, little is known about the effect of PW isolation in patients who underwent catheter ablation (CA) for persistent AF (PeAF).
Methods: We randomly assigned 114 consecutive patients with PeAF to PW isolation (n=56) or control (n=58) group. In all patients, linear ablation was performed following circumferential antral pulmonary vein isolation (PVI). Linear lesions included roof, anterior perimitral, and cavotricuspid isthmus lines with conduction block. In PW isolation group, additional posterior inferior linear lesion was conducted. Creatine kinase-MB (CK-MB) and troponin-T levels were measured 1 day following CA. LA emptying fraction (LAEF) was assessed by 2D-echocardiography before and 12 months after CA.
Results: A total of 114 subjects were followed until the end of the study period (12 months following CA). There were no significant differences between 2 groups in baseline demographics, CHADS2 score, left atrial volume (LAV), and LAEF. Although ablation time was slightly longer in PW isolation group than control, the levels of CK-MB and troponin-T, and procedure time were not different between 2 groups. AF termination during CA was more frequently observed in PW isolation group than control (P=0.018). Twelve months after a single procedure, recurrence occurred in 10 (17.9%) patients in PW isolation group and 21 (36.2%) in control group (P=0.036). Change in LAEF was not different between 2 groups. On multivariate logistic analysis, LAV and ablation strategy were independently associated with arrhythmia recurrence.
Conclusions: Additional PW isolation to PVI + linear lines was an efficient ablation strategy without deterioration of LA pump function in patients who underwent CA for PeAF.

3057 | BEDSIDE

Identification of rotors and ablation after pulmonary vein isolation following restoration of sinus rhythm prior to catheter ablation in patients with persistent atrial fibrillation

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Purpose: Mapping of the electrical propagation to identify the underlying mechanisms that perpetuate atrial fibrillation (AF) is difficult. The purpose of this study was to demonstrate that the restoration and maintenance of sinus rhythm (SR) pre-ablation would facilitate the identification of rotors or focal sources (AF sources) and the termination of AF.
Methods: We prospectively enrolled 56 patients undergoing an initial ablation for persistent AF. SR was restored for at least 2 weeks prior to ablation. If SR could not be maintained, pulmonary vein isolation (PVI) and linear ablation were performed. Radiofrequency ablation was performed during induced AF. If AF was sustained or induced after the PVI, activation maps to identify AF sources (Rotor map) were created by a 64-pole basket catheter and 20-pole circular mapping catheter with the use of the Velocity system. A rotor was defined as follow: reproducible reentrant atrial activity which was repeatedly present for more than 40% of the 3.8 second observation time. A macro-rotor was defined as an activation circuit, which extended around the Line of the PVI or the mitral annulus. A micro-rotor was defined as an activation circuit other than a macro-rotor. Focal sources of AF were identified as sites with a centrifugal activation pattern, which was repeatedly present for more than 40% of the 3.8 second observation time. The accuracy of the Rotor map was confirmed by the termination of AF. The endpoint of the procedure was the non-inducibility of AF lasting for more than 5 minutes. Recurrent AF was evaluated through the use of an auto-triggered external loop recorder (ELR) for 7 days (3 and 6 months after the procedure).
Results: SR was maintained in 32 patients (57%). Only PVI was performed in 13 patients (23%). Fourteen AF sources were identified in 13 patients. The sources were left atrial in 13 patients, and right atrial in 1, and 12 were rotors. Non-inducibility was confirmed in 24 patients (43%). After the first procedure, the clinical success rate at 6 months without any antiarrhythmic drugs was 73% (15/56), and the clinical success rate at 6 months with or without antiarrhythmic drugs was 80% (11/56).
Conclusions: Ablation at the sites guided by Rotor maps could terminate AF after the PVI in patients with restoration and maintenance of SR prior to catheter ablation. This method was a feasible persistent AF strategy.

3058 | BEDSIDE

Procedural vagal reactions predict AF recurrence following cryoablation

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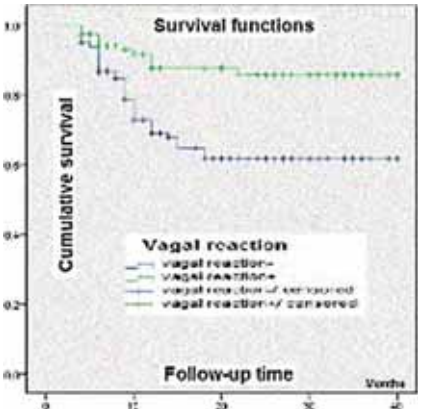
Purpose: Ablation of ganglionated plexi has been reported to improve outcome

of patients undergoing AF ablation. The mid and long-term success rates have been demonstrated in previous studies. In this study, we aim to demonstrate the relationship between occurrence of vagal reactions, probably due to increased modification of ganglionated plexi during cryoablation, and AF recurrence in patients after cryoablation.
Methods: 265 patients with AF and preserved left ventricular systolic function (56.20±11.62 years, 48% male, 80.3% paroxysmal) who were symptomatic despite treatment with ≥1 antiarrhythmic drug underwent cryoballoon-based ablation. Occurrence of vagal reactions were recorded during the procedure.
Results: Vagal reactions were observed in 104 patients (39.3%). At a mean follow-up of 27.3±8.6 months, 63 patients (23.7%) had developed AF recurrence. Procedural vagal reactions were common in patients without AF recurrence (45.77% vs. 18.75%, p=0.000). On multivariate regression analysis, procedural vagal reactions (HR: 0.282, 95%CI: 0.140-0.569, p=0.000), LA diameter (HR: 4.114, 95%CI: 2.398-7.059, p=0.000), alcohol consumption (HR: 3.362, 95%CI: 1.355-8.344, p<0.05), duration of AF (HR: 1.056, 95%CI: 1.020-1.094, p<0.05), and early recurrence (HR: 8.602, 95%CI: 4.548-16.271, p=0.000) were found to be independent predictors of AF recurrence after cryoablation. Kaplan-Meier analysis of freedom from AF recurrence regarding procedural vagal reactions is shown in figure.



Kaplan-Meier analysis for AF freedom.

Conclusion: Higher incidence of vagal reactions, probably due to increased modification of ganglionated plexi during cryoablation, was associated with lower AF recurrence rate following catheter-based cryoablation.

3059 | BEDSIDE
Comparison of two different doses of single bolus steroid injection to prevent atrial fibrillation recurrence after radiofrequency catheter ablation

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Purpose: Steroids may be able to prevent the early recurrence of atrial fibrillation (AF) after radiofrequency catheter ablation (RFCA). However, the optimal doses and route of steroid delivery have not been determined. This study evaluated the effect of two different doses of a single bolus injection of steroids on AF recurrence after RFCA.
Methods: Of 448 consecutive AF patients who underwent RFCA, a single steroid bolus was injected in 291 patients. A low-dose steroid group (n=113) received100 mg hydrocortisone and a moderate-dose steroid group (n=174) received 125 mg methylprednisolone. We used propensity-score matching to select patients as follows: control (n=95), low-dose (n=95) and moderate-dose steroid groups (n=97).
Results: Pericarditis developed in 1 (1.1%) control patient, 2 (2.1%) low-dose patients and 0 moderate-dose patients. Maximum body temperature and C-reactive protein (CRP) were significantly decreased in the moderate-dose steroid group compared to the other groups (p<0.01). The number of patients with immediate AF recurrence (≤3 days) was 13 (14%) in the control, 7 (8%) in the low-dose and 11 (11%) in the medium-dose groups (p=0.37). Compared with the control group, low-dose or moderate-dose steroid treatment did not effectively decrease post-RFCA AF recurrence that was early-(3–30 days) (11 [12%] vs. 15 [16%] vs. 11 [11%]; p=0.59) or mid-term (1–12 months) (22 [23%] vs. 13 [14%] vs. 21[22]; p=0.49).
Conclusions: A single injection of moderate-dose steroid significantly decreased inflammation. However, single bolus injections of low-dose or moderate-dose steroids were not effective in preventing immediate, early or midterm AF recurrence after RFCA. Our study suggests that a single dose of corticosteroid may not be effective to prevent AF after RFCA.

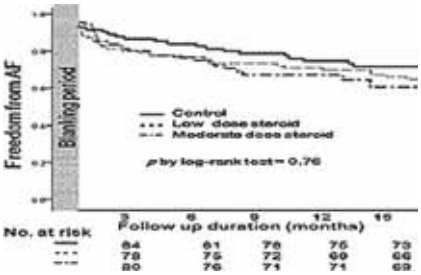

Figure 1. Survival curves for AF recurrence.

3060 | BEDSIDE
Silent cerebral thromboembolism in catheter ablation for atrial fibrillation under the use of novel oral anticoagulants versus therapeutic warfarin

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Purpose: Cerebral thromboembolism (CE) is one of the serious complications in left atrial catheter ablation for atrial fibrillation (AF). Prior our study has reported that the incidence of silent CE in AF ablation was not rare and continuous warfarin during AF ablation decreased thromboembolic events. Recently, the use of novel oral anticoagulants (NOACs) as periprocedural anticoagulant for AF ablation is increasing. We aimed to evaluate the incidence of thromboembolic event and bleeding complication related to the procedure, and compare the safety of AF ablation under the use of NOACs versus therapeutic warfarin.
Methods: 106 consecutive patients who underwent AF ablation were taking anticoagulant with warfarin or NOACs (dabigatran or rivaroxaban) more than one month prior to the procedure. In 65 patients warfarin was continued with international normalized ratio (INR) maintained between 2.0 and 3.0 during ablation (group W). In 41 patients NOAC was held on the morning of the procedure and resumed just after vascular hemostasis (group N). Throughout AF ablation procedure, heparin was administered to maintain activated clotting time (ACT) between 300 and 400 seconds. ACT was checked every 15 minutes. Head magnetic resonance imaging (MRI) was performed in all patients within 24 hours after the procedure regardless of symptomatic or asymptomatic.
Results: In 5 (7.7%) patients of group W and in 7 (17.0%) patients of group N, diffusion weighted imaging of head MRI showed embolic lesions without neurological symptom (P=0.21). The major bleeding complication occurred in one patient in each group, including cardiac tamponade (group N) and hematoma needed transfusion (group W) respectively (P=0.74). Although the amount of heparin during the procedure in group W was significantly less than in group N (8942±2039 U vs. 17098±4827 U; P<0.0001), mean ACT during the procedure in group W was maintained higher level than in group N (358.3±28.6 sec. vs. 327.3±17.9 sec.; P<0.0001).
Conclusions: The incidence of silent CE under continuous therapeutic warfarin during AF ablation was lower than NOACs, although the risk of bleeding complications was equivalent to each other. In AF ablation, warfarin continuation may be preferred rather than NOACs as a periprocedural anticoagulant in regard to risk reduction of thromboembolic complications.

3061 | BEDSIDE
Impact of systolic and diastolic dysfunction on the outcome of catheter ablation in patients with atrial fibrillation

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Introduction: Patients with left ventricular (LV) systolic dysfunction have worse results of atrial fibrillation (AF) ablation than those with a preserved systolic function. On the other hand, LV diastolic dysfunction is the independent predictor of AF recurrence after AF ablation. The impact of both LV systolic dysfunction and diastolic dysfunction on the outcome of catheter ablation in patients with AF remains unclear. We clarified the outcomes of circumferential pulmonary vein isolation in patients with LV systolic dysfunction and diastolic dysfunction.
Methods: We included 240 consecutive patients who underwent circumferential pulmonary vein isolation (CPVI) for drug-refractory symptomatic AF between March 20008 and March 2012. All patients underwent successful circumferential pulmonary vein isolation. Additional ablation for non-PV foci triggering AF and induced atrial tachyarrhythmias (ATAs) or atrial flutter was performed as necessary. Systolic dysfunction and diastolic dysfunction were defined as an LV ejection fraction of <50% and mitral inflow early filling velocity to early diastolic medial mitral annular velocity ratio (E/e') of >10, respectively. All patients were followed up for more than 1 year. We evaluated any ATA recurrences without any antiarrhythmic drugs after a single or final ablation procedure.
Results: Forty-one patients (17%) had LV systolic dysfunction, 84 (35%) had LV diastolic dysfunction, and 16 (7%) had both. After the final procedure, 31 of 41 (76%) patients with systolic dysfunction maintained sinus rhythm and 161 of 199 (81%) those without. The outcome in the patients with and without systolic dysfunction was similar (the log-rank test P=0.15). In the patients with and without diastolic dysfunction, 133 (85%) and 60 (70%) maintained sinus rhythm, respectively. The rate of pulmonary vein reconnections and type of ATA recurrence

was similar. The presence of diastolic dysfunction increased the ATA recurrence ($p<0.01$). However, among the patients with a normal systolic function, diastolic dysfunction alone did not affect the ATA recurrence. The patients who had both systolic dysfunction and diastolic dysfunction had a significantly higher ATA recurrence rate (p=0.02).
Conclusion: Patients with both systolic and diastolic dysfunction had a worse outcome of AF ablation. Diastolic dysfunction alone did not predict an ATA recurrence in patients with normal systolic function.

MULTIMODALITY IMAGING IN CORONARY ARTERY DISEASE

3062 | BEDSIDE
Transmural myocardial perfusion gradients in relation to coronary artery stenoses severity assessed by cardiac multidetector computed tomography

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Purpose: We aimed to assess the relationship between epicardial coronary artery stenosis severity and the corresponding regional transmural perfusion at rest and during adenosine stress, using multidetector computed tomography (MDCT).
Methods: We evaluated the relationship between the severity of coronary artery diameter stenosis assessed by MDCT angiography and semi-quantitative myocardial MDCT perfusion in 200 symptomatic patients. The perfusion index (PI= mean myocardial attenuation density / mean left ventricular lumen attenuation density) at rest and during adenosine stress, the myocardial perfusion reserve (MPR = stress PI/rest PI), and the transmural perfusion ratio (TPR= subendocardium/subepicardium) were calculated.
Results: A coronary artery stenosis ≥50% was present in 49 patients (25%). Rest PI and rest TPR values were similar in patients with and without a coronary artery stenosis ≥50%, whereas stress PI, stress TPR and MPR were significantly reduced in patients with a stenosis ≥50% ($p<0.001$, $p<0.0001$ and p=0.02, respectively). Subendocardial PI was significantly higher than subepicardial PI at rest and during stress for patients without a significant stenosis, whereas this difference was blurred during stress in patients with ≥50% stenosis. In a broad spectrum of stenosis severity groups, TPR at rest remained unchanged until the group of patients with total occlusions, whereas TPR during stress decreased progressively when a threshold of 50% was superseded.

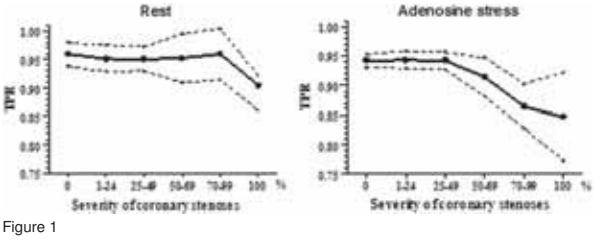

Figure 1

Conclusion: The transmural myocardial perfusion ratio by MDCT is a potential strong functional index of coronary artery stenosis severity.

3063 | BEDSIDE
A CT-based score to predict the success of interventional revascularization of chronic total coronary occlusions

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Purpose: Interventional revascularization (PCI) of chronic total occlusions (CTO) is technically challenging. Success rates vary substantially and failure is difficult to predict. Coronary computed (CT) angiography has demonstrated its utility as a strategic tool for procedure planning and prediction of procedure success. The purpose of our study was the development of a new score which summarizes relevant factors concerning CTO success.
Methods: In a two center study, 135 patients with 137 CTOs underwent contrast-enhanced coronary CT angiography before PCI. In consensus, two experienced observers analysed the occlusion length (in mm) as well as the degree of calcification at entry and exit of the CTO, the maximal degree of calcification of the vessel cross-section, the percentage calcified length of the CTO and the presence of visible contrast pools in the course of the occluded segment (visual scale 0 to 4). Furthermore, vessel tortuosity, minimal visible vessel diameter, the minimal visible non-calcified vessel diameter (visual scale 0 to 4) and positive remodelling were analysed. All parameters were compared between patients in whom revascularization was successful and those in whom revascularization failed.
Results: The maximal degree of calcification of the vessel cross-section (score 1.5±1.3 vs. 2.2±1.5 for success vs. failure, p=0.005) and the percentage length of calcification (score 1.2±1.2 vs. 1.7±1.4 for success vs. failure, p 0.02) were statistically different between both groups. A score which combined all analysed parameters was significantly lower for success than for failure (8.4±5.2 vs. 10.8±6.3 p=0.02), with an area under the ROC curve of 0.61. When using a score of 11 as cut-off value for revascularization success, sensitivity, specificity, positive and negative predictive value were 72.8%, 46.4%, 66.3% and 54.1%, respectively. Multiple regression analysis revealed that the maximal percentage vessel cross section calcification was the only independent predictor for revascularization success or failure (p=0.004).
Conclusions: Coronary CT angiography can help predict revascularization success of CTO patients. The degree of maximal percentage vessel cross section calcification seems to be the major predictor of success vs. failure.

3064 | BEDSIDE
Does preoperative myocardial perfusion imaging (MPI) impact perioperative patient management and mortality?

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Purpose: The positive predictive value of preoperative stress testing is uncertain. We sought to explore the clinical impact of a positive MPI on the perioperative management and outcomes of patients referred for risk stratification prior to non-cardiac surgery.
Methods: Retrospective data from our institutional stress, nuclear, left heart catheterization (LHC) and percutaneous coronary intervention (PCI) databases were reviewed. All patients undergoing MPI from 10/2004 to 06/2012 for preoperative risk assessment were included. Patients with an abnormal MPI were divided into ischemic and non-ischemic (scar, TID or RV dilation) groups. The catheterization databases were then queried to assess whether ischemic patients underwent LHC and/or PCI within 60 days of the MPI. Mortality data was compiled using the United States Social Security Death Index.
Results: 5657 patients underwent preoperative MPI; of which 1809 (31.9%) had an abnormal result. Overall, 992 out of the 1809 patients (54.8%) had ischemia on their MPI. Amongst patients with ischemia 46.2% underwent LHC, compared to 2.3% ($p<0.0001$) of patients with normal test and 7.1% ($p<0.0001$) of patients with an abnormal MPI. Mortality at 1 year was lower for ischemic patients who underwent LHC (8.9% vs. 13.6%; $p<0.027$) compared to those that did not, regardless of PCI (Table).

Mortality and MPI Results

	Number of patients	Number of deaths within 1 year	Mortality (%)
Normal stress test	3848	302	7.8%
Abnormal stress test	1809	227	12.5%
Abnormal stress test without ischemia	817	113	13.8%
Abnormal stress test with ischemia	992	114	11.5%
Ischemia without LHC	534	73	13.6%
Ischemia with LHC	458	41	8.9%
Ischemia with LHC + PCI	103	10	9.7%
Ischemia with LHC but without PCI	355	31	8.7%

MPI, myocardial perfusion imaging; LHC, left heart catheterization; PCI = percutaneous intervention.

Conclusions: MPI testing and results influenced rates of LHC in patients undergoing preoperative testing. Preemptive revascularization does not appear to alter mortality outcomes. MPI results identify a moderate (normal MPI) and high risk groups (abnormal MPI). A normal MPI does not confer low mortality at one year.

3065 | BEDSIDE
Comparison of two-dimensional and three-dimensional speckle tracking echocardiography for the assessment of myocardial viability

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Background: Late-enhancement magnetic resonance imaging (LE MRI) is considered to be the reference method for the assessment of myocardial viability. 2D (two-dimensional) and 3D (three-dimensional) speckle tracking echocardiography (STE) are recently developed quantification techniques that can be used for the objective evaluation of the regional myocardial function.
Purpose: To evaluate the diagnostic value of 2D and 3D STE for the assessment of myocardial viability using LE MRI as a reference method.
Methods: 53 patients (41 male, mean age 60±10 years) with first acute myocardial infarction (AMI) treated successfully with primary percutaneous coronary intervention were included in the study. 7-10 days after AMI, all patients underwent transthoracic 2D and 3D resting echocardiography with subsequent measurement of systolic longitudinal strain (SLS) using 2D and 3D STE. Additionally,

patients underwent LE MRI with semiquantitative assessment of the thickness of late enhancement (LE) region in left ventricular segments. Segments vere considered viable if LE region occupied ≤50% or ≤75% of myocardial thickness.
Results: In the analysis of 727 segments of sufficient image quality from 2D STE and 723 segments from 3D STE, SLS measurements with both techniques had similar diagnostic value for the detection of viability defined as LE extent of ≤75% myocardial thickness by MRI (AUC 0.72 and 0.67, respectively; p=0,23). Diagnostic accuracy of the criterion SLS ≤ -14,99% was 83,3% for 2D and SLS ≤ -11% was 81,5% for 3D.
When segments with LE ≤50% of myocardial thickness were considered viable, diagnostic accuracy of the criterion SLS ≤ -15,25% was 90,1% for 2D and SLS ≤ -11% was 89,3% for 3D. In addition, 2D STE had significantly higher diagnostic value for the detection of viability than 3D SLS STE (AUC 0.75 and 0.64, respectively; p<0,001).
Conclusions: 2D and 3D strain echocardiography with SLS measurements seem to be promising tools for myocardial viability assessment based on resting echocardiography. There is a noticeable trend towards greater diagnostic value of 2D technique compared to 3D.

3066 | BEDSIDE
Global longitudinal strain predicts outcome in patients undergoing stand alone coronary artery bypass grafting

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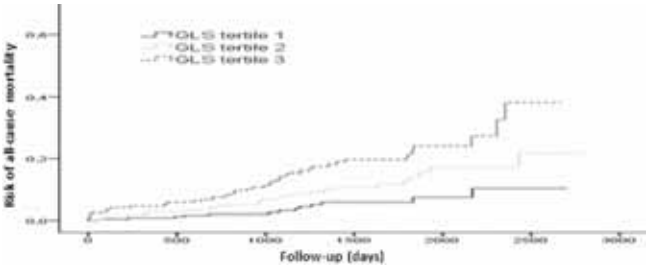
Background: Left ventricular systolic function is a key determinant of outcome after coronary artery bypass grafting (CABG) and routinely estimated by left ventricular ejection fraction (LVEF) or wall motion score index (WMI). Global longitudinal strain (GLS) is a new method of estimating systolic function, which appears superior to both LVEF and WMI. The present study tested the hypothesis, that GLS would predict outcome after CABG superiorly.
Methods: We included all patients (n=723) treated with stand-alone CABG from 2006 through May 2011 at a single tertiary cardiac centre. Before surgery, all patients underwent echocardiography, including measurement of GLS. Patients were followed for a median of 4 years (3-5years). Endpoints were all-cause mortality (n=86), cardiovascular mortality (n=50) and the composite endpoint MACE (cardiovascular mortality or hospitalization due to myocardial infarction, ischemic stroke or heart failure) (n=136).
Results: GLS predicted all three endpoints independent of all other echocardiographic parameters including both LVEF and WMI (all, p<0.001). Importantly, neither LVEF nor WMI remained significant when GLS was included (both p>0.50). Even when further adjusted for standard risk-factors, blood-tests and coronary angiographic results, GLS remained an independent predictor of all three outcomes (all, p<0.001), HR per 1 tertile increase for all-cause mortality, 2.15 (1.58-2.93). Importantly GLS also improved NRI for all endpoints, when added to currently used risk-scores, including euroscore II, reclassifying about 30% of the patients.



GLS predicts all-cause mortality

Conclusions: GLS performs superior to LVEF and WMI and predicts both all-cause mortality, cardiovascular mortality and MACE independently. Importantly GLS also improves NRI from current risk scores, including euroscore II.

3067 | BEDSIDE
Regional longitudinal myocardial deformation provides incremental prognostic information in patients with ST-segment elevation myocardial infarction

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Purpose: Global longitudinal systolic strain (GLS) has recently been demonstrated to be a superior prognosticator to conventional echocardiographic measures in patients after myocardial infarction. The purpose of this study was therefore to evaluate the prognostic value of regional longitudinal myocardial deformation (RLMD) in comparison to GLS, conventional echocardiography and clinical information.
Method: In total 391 patients were admitted with ST-Segment elevation myocardial infarction (STEMI), treated with primary percutaneous coronary intervention and subsequently examined by echocardiography. All patients were examined by tissue Doppler imaging (TDI) and two-dimensional strain echocardiography (2DSE).
Results: During a median-follow-up of 64 (IQR 30-73) months the primary endpoint (death, heart failure or a new MI) was reached by 145 (38.9%) patients. In univariable and multivariable (adjusted by age, gender, peak TnI, diabetes, complex lesion and culprit lesion) Cox proportional hazards regression models, a decrease in longitudinal performance in almost all regions determined by all RLMD parameters were significantly associated with an increased risk of an adverse outcome. However, after adjustment for significant clinical confounders and conventional echocardiographic parameters (LVEF, diastolic dysfunction and LVMI), a pattern appeared. Decreasing longitudinal performance in the anterior septal and inferior myocardial regions seemed to be superior prognostic markers, since RLMD parameters (longitudinal deformation (LD), strain and Strain Rate s (SRs)) obtained from these myocardial walls (not GLS) remained as independent predictors of the combined outcome (Inferior LD: HR 1.12 (1.03-1.22), p=0.011; inferior strain: HR 1.04 (1.00-1.07), p=0.043; anterior septal SRs: HR 2.07 (1.05-4.09), p=0.036). Furthermore, inferior myocardial LD provided incremental prognostic information to clinical and conventional echocardiographic information (Harrell's c-statistics: 0.63 vs. 0.67, p=0.032). In addition, impaired RLMD outside the culprit lesion perfusion region was significantly associated with an adverse outcome (p<0.05 for all deformation parameters).
Conclusion: RLMD measures, regardless if determined by TDI or 2DSE, are superior prognosticators to GLS. In addition, impaired longitudinal deformation in the inferior myocardial segment provides prognostic information over and above clinical and conventional echocardiographic risk factors. Furthermore, impaired longitudinal deformation outside the culprit lesion perfusion region seems to be a paramount marker of adverse outcome.

3068 | BEDSIDE
Cost evaluation and comparison of three decision strategies to revascularize: results of the suspected CAD protocol of the european CMR registry

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Background: Cardiac magnetic resonance (CMR) is accepted as a method to assess suspected coronary artery disease (CAD). Nonetheless, invasive coronary angiography (CXA) combined or not with fractional flow reserve (FFR) remains the main diagnostic test to evaluate CAD. Little data exist on the economic impact of the use of these procedures in a population with a low to intermediate pre-test probability.
Objective: To compare the costs of 3 decision strategies to revascularize a patient with suspected CAD: 1) strategy guided by CMR 2) hypothetical strategy guided by CXA-FFR, 3) hypothetical strategy guided by CXA alone.
Method: Costs were calculated from a health care payer perspective for a cohort of 2'604 patients who underwent an ischemia work-up using CMR within the European CMR registry (57 centers in 15 countries). For these 2'604 patients the costs included those for the CMR examination as well as those for primary treatments (percutaneous coronary interventions; PCI and coronary artery bypass grafting; CABG) and for treatment of major adverse cardiac events (MACE: non-fatal myocardial infarction, stroke, aborted sudden cardiac death, and death) during a 1-year follow-up. Costs associated with death and medications were not included in the modeling. After CMR, 22% of patients had ischemia and 21% of those were revascularized (15% PCI, 5% CABG, 1% PCI+CABG), while 2.8% of the CMR-negative patients were revascularized. MACE occurred in 2.5% and 2.1% of the CMR-positive and CMR-negative patients, respectively. The costs for the hypothetical CXA-FFR strategy included costs for CXA as the primary test followed by costs for FFR for patients with stenosis >50%. Assuming 22% of FFR positive patients (= proportion of ischemia-positive CMR in the registry) the proportion of patients with stenoses was estimated as 76% calculated from the literature. Costs were also calculated for a CXA-only strategy, where revascularization is based on stenosis degree only. Costs for all diagnostic tests were calculated as out-patient procedures.
Results: The average costs per patient for CMR, CXA-FFR, and CXA-only were € 870/1'730/4'573 in Germany, £ 1'058/2'041/4'274 for the United Kingdom, and CHF 3'230/6'611/18'317 for Switzerland. Thus, for Germany, UK, and Switzerland, the utilization of CMR achieves theoretical cost reductions of 48%, 50%, and 51% vs CXA-FFR, respectively, and of 75%, 81%, and 82%, vs CXA-only, respectively.
Conclusions: In a real-world population with a low to intermediate pretest like-

lihood for CAD, CMR offers a cost-saving approach when treatment costs and costs for complications are considered.

3069 | BEDSIDE
Myocardial perfusion evaluated by stress cardiac magnetic resonance as a predictor of major adverse cardiac events in patient with acute myocardial infarction

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Background: It has been well known that microvascular obstruction (MVO) and infarct size evaluated by late gadrinium enhancement (LGE) were associated with left ventricular (LV) remodeling and adverse cardiac outcomes after acute myocardial infarction (AMI). Whereas, the role of stress cardiac magnetic resonance (CMR) in predicting the prognosis of patients with AMI remains to be uncertain.
Objective: The aim of this study is to investigate the prognostic value of adenosine stress CMR in patients with AMI.
Methods: 154 consecutive patients with AMI (66±12yrs, 34 females) treated with primary percutaneous coronary intervention (PCI) were enrolled between March 2009 and August 2012. The cohort was followed for major adverse cardiac events (MACE). CMR was performed 5.9±2.3days after PCI and 114 patients with residual coronary artery stenosis (>50%) were assessed by adenosine stress perfusion imaging. Each segmental perfusion was scored on the basis of the transmural extent of any perfusion defect (0= no defect, 1= 1 to 50%, 2= 51 to 100%). Summed stress score (SSS) and rest score (SRS) were calculated by summing up the transmural score of all segments and their difference yielded the summed difference score (SDS). The wall motion score (WMS), and the segment number of LGE and MVO were also evaluated.
Results: During median follow up of 963±418 days, 13 MACE including 3 cardiac deaths, 4 nonfatal myocardial infarctions and 6 readmissions for heart failure were documented. The SSS (10.0±6.9 vs. 5.0±4.8, p=0.004), SRS (4.5±2.9 vs. 3.3±4.2, p=0.036), SDS (6.0±7.4 vs. 1.9±2.7, p=0.048), summed WMS (28.1±6.2 vs. 24.6±5.3, p=0.026) and the segment number of LGE (6.4±2.6 vs. 4.8±2.5 segments, p=0.018) were higher in patients with MACE than those in patients without MACE. There was no significant relation between MACE and LV volume, ejection fraction, medications and the extent of MVO. In multivariate analysis, SDS was the best independent predictor of MACE (hazard ratio: 1.263 [95% confidence interval: 1.050 to 1.520], p=0.013) among age, hemoglobin concentration on admission, history of previous PCI and CMR parameters.
Conclusion: The presence of residual myocardial ischemia evaluated by adenosine stress CMR was superior to other CMR findings with respect to the prediction of MACE in patients with AMI.

3070 | BEDSIDE
T1 and T2 mapping have a higher diagnostic accuracy for the ischaemic area at risk in NSTEMI patients compared with dark blood imaging

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Background: Myocardial injury mapping with T1 and T2 relaxometry MRI have shown great promise for the identification of acute myocardial infarction. Most of this work has been performed in patients with ST-elevation myocardial infarction (STEMI) with fewer data available in NSTEMI. We prospectively studied the diagnostic accuracy of two novel (T1, T2 mapping) and one established (short tau inversion recovery [STIR]) MRI techniques for imaging the ischaemic area-at-risk (AAR) in patients with recent NSTEMI.
Methods: NSTEMI patients underwent contrast-enhanced cardiac MRI at 3.0 Tesla (Siemens MAGNETOM Verio) before or after coronary angiography. The presence/extent of infarction was assessed with late gadolinium enhancement imaging 15 min after contrast administration (Gadovist, 0.1 mmol/kg). The infarct-related territory was identified independently using a combination of angiographic, ECG and clinical findings. AAR was assessed with T1 (MOLLI; Siemens Healthcare), T2 (bSSFP; Siemens Healthcare) and T2 STIR methods by 2 observers, blind to clinical data. Comparisons were made between MRI and clinical findings.
Results: 73 NSTEMI patients (mean age was 57±10yrs, 78% male) underwent 3T MRI. The mean infarct size was 5.5±7.2% of left ventricular (LV) volume. The AAR T1 and T2 times (ms) were 1323±68 msec and T2 57±5 msec, respectively. The extent of AAR (% of LV volume) estimated with T1 (15.8±10.6%) and T2 maps (16.0±11.8%,) was similar (p=0.838), and moderately well correlated (r=0.82, P<0.001). The 95% limits of agreement for mean area-at-risk estimated with T1 versus T2 maps were -13% and 13%.
Mean AAR estimated with T2 STIR (7.8±11.6%) was significantly lower than that estimated with T1 (P<0.001) or T2 maps (P<0.001). There were moderate correlations between AAR estimated with T1 maps versus T2 STIR (r=0.54, P<0.001), and AAR estimated with T2 maps versus T2 STIR (r=0.46, P<0.001). The 95% limits of agreement for mean myocardial AAR estimated with T1 vs. T2 STIR maps were -28% and 12% and for T2 vs. T2 STIR maps -32% and 16%.
The infarct-related artery was correctly identified in 52 patients (71%) when using T1 maps, 56 (77%) for T2 maps, and 32 (44%) for T2 STIR maps. There was no difference in diagnostic accuracy with T1 and T2 maps (P=0.125). A difference in diagnostic accuracy was observed between T1 maps and T2 STIR (P<0.001), and T2 maps and T2 STIR (P<0.001) for detecting infarct-related artery.
Conclusion: In NSTEMI patients, MRI with T1 and T2 mapping have much higher diagnostic accuracy than T2 STIR which is more prone to problematic artifact and misdiagnosis.

3071 | BEDSIDE
Analysis of the inflammatory response after acute myocardial infarction by PET/MRI

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Purpose: The inflammatory response after acute myocardial infarction determines the quality of infarct healing and might be a target of future therapies. Preclinical models suggest that cardiac inflammation can be quantified by FDG-PET. Translation of this strategy into a clinical setting using simultaneous 18F-FDG-PET imaging and cardiac MRI may enable visualization of inflammatory processes in relation to functional and tissue specific parameters.
Aim of this study was to evaluate this imaging strategy in patients with acute myocardial infarction.
Methods: 29 patients with a first ST-elevation myocardial infarction were imaged 5.0±1.3 days after PCI by simultaneous FDG-PET/MRI. Myocardial FDG uptake was suppressed by low-carbohydrate diet on the day before the scan, overnight fasting, and administration of unfractionated heparin before image acquisition. FDG uptake was quantified in the infarct area, remote myocardium, spleen, bone marrow (BM), and aortic wall and expressed as %injected dose/100 ml. Furthermore, using cardiac MRI, the scar size was assessed by the late gadolinium enhancement (LGE) technique and the ejection fraction (EF) was determined.
Results: The FDG uptake was significantly higher in the infarct area vs. remote myocardium (0.4±0.1 vs. 0.1±0.06; p<0.0001). There was a significant correlation between FDG uptake in the infarct area and the aortic wall (R=0.50,p<0.01) as well as the spleen (R=0.44,p<0.02), while no correlation was observed with FDG uptake in the BM. Furthermore, there was no correlation between FDG uptake in the infarct area and infarct size or ejection fraction. Also, there was no correlation with peak serum creatine kinase or peripheral blood monocyte count.
Conclusions: The inflammatory response after myocardial infarction can be imaged and quantified by FDG-PET/MRI in patients. Weak correlation of cardiac FDG signal with measures of cardiac function or inflammation in the peripheral blood suggest, that this novel imaging strategy might add useful information about the quality of cardiac healing after myocardial infarction.

GROWING RELEVANCE OF FIBROSIS: DIVE DEEP INTO MECHANISMS

3085 | BENCH
The Raf kinase inhibitor protein protects from pressure overload-induced heart failure

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Background: The Raf kinase inhibitor protein (RKIP) was found to inhibit mitogen activated protein kinase Raf1 as well as G protein coupled receptor kinase 2. Phosphorylation of RKIP at serine 153 coordinates the inhibitory function of RKIP towards Raf1 or GRK2, respectively. Interestingly, both, Raf1 and GRK2, are central kinases in the heart: Raf1 protects from myocyte death, and GRK2 is involved in the desensitization of G protein coupled receptors, e.g. β-adrenergic receptors.
Objective: The aim of this study was to investigate the physiological role of RKIP in the heart and its effects on β-adrenergic signaling and cardiac contractility.
Methods and results: We generated mice with cardiac overexpression of wild-type RKIP (TgRKIP) and found that RKIP significantly reduces cardiac GRK activity. In line with these results, downstream targets of β-adrenergic receptors such as phospholamban and troponin I, important players in the contraction-relaxation cycle, showed increased phosphorylation signals in heart lysates of TgRKIP mice compared to wild-type mice. Cardiac function and morphology of TgRKIP mice were characterized by echocardiography and left ventricular catheterization with and without dobutamine stress. These studies revealed significantly increased fractional shortening (P<0.01) as well as increased speeds of left ventricular contraction (P<0.01) and relaxation (P<0.01) in 8-week-old TgRKIP mice compared to control mice. To assess the effects of RKIP in heart failure, we analysed cardiac function and structure of TgRKIP as well as of RKIP–/– mice in response to chronic pressure overload (TAC). Wild-type, TgRKIP and RKIP–/– mice developed similar extents of left ventricular hypertrophy upon TAC. In contrast to wild-type mice, RKIP overexpression preserved cardiac contractility and even prevented increased expression of the heart failure markers BNP and ANP as well as fibrosis and apoptosis in response to TAC. RKIP knockout mice (RKIP–/–), how-

ever, developed severe heart failure in response to TAC: cardiac contractility was markedly decreased, left ventricles were dilated, interstitial fibrosis, apoptosis as well as heart failure markers were significantly increased.
Summary: In conclusion, RKIP enhances β-adrenergic signaling and induces cardiac contractility, but also protects from pressure overload induced heart failure. A detailed understanding of the rescue mechanism of RKIP may help to find new therapeutic strategies to improve cardiac contractility in heart failure.

3086 | BENCH
Beta3 adrenergic receptors protect from cardiac fibrosis through inhibition of paracrine signalling from cardiac myocytes to fibroblasts: proteomic analysis of the myocyte secretome

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Background: Cardiac fibrosis is an integral part of myocardial remodelling in response to stress. Mice with cardiac myocyte-specific overexpression of beta3-adrenergic receptor (β3-AR) are protected not only from the development of hypertrophy but also cardiac fibrosis. As overexpression was restricted to cardiac myocytes (CM), we postulated that the protection involved a paracrine cross-talk to cardiac fibroblasts (CF).
Methods: We developed a model of superfusion of CF in serum-free conditions with media conditioned by cultured CM with adenoviral expression of the human β3AR and treated or not with phenylephrine (PE). Cardiac extracts were analysed in wild type (WT) and heterozygote transgenic mice with cardiac myocyte-specific overexpression of human β3AR (hβ3TG) submitted to transaortic constriction (TAC) for 9 weeks.
Results: Incubation of CF with medium conditioned by control CM treated with PE stimulated their proliferation, migration, myofibroblats differentiation (α-SMA expression) and pro-collagen I expression compared with medium from CM not treated with PE. This was associated with activation of the ERK pathway in CF. All these effects were abolished by heat inactivation of the media, suggesting implication of paracrinally secreted peptides. The effects of medium conditioned by untreated β3AR overexpressing CM were similar to those untreated controls. However, incubation of CF with medium of β3AR overexpressing CM treated with PE did not activate their differentiation into myofibroblats (0.35±0.1 (β3AR) vs 0.89±0.2 (GFP), $p<0.05$) or pro-collagen I expression (1.10±0.2 (β3AR) vs 1.75±0.4 (GFP), $p<0.05$). Activation of the ERK pathway was also absent. To unravel the idendity of paracrine factors, the secretome of CM was submitted to shotgun proteomic analysis by LC tandem MS. Top candidates significantly downregulated in β3AR-PE conditioned medium compared with GFP-PE included CTGF, galectin-3 binding protein, plasminogen activator inhibitor 1, collagen I and III, fibronectin, thrombospondin-1. Accordingly, β3AR was associated with decreased mRNA expression of CTGF in CM in vitro. These results were confirmed in vivo after TAC stress in mice at mRNA and proteins levels (cTGF protein expression: 1.03±0.1 (WT) vs 0.51±01 (β3AR), $p<0.01$).
Conclusion: We conclude that β3AR decreases the expression of pro-fibrotic paracrine factors such as CTGF, resulting in protection from myocardial fibrosis in response to neurohormonal stimulation.

3087 | BENCH
Identification of bio-active pectins to prevent galectin-3 mediated fibrosis in a murine heart failure model

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Purpose: Galectin-3 is a mediator of fibrosis and is believed to play an important role in heart failure development. Galectin-3 has a carbohydrate recognition domain (CRD) and carbohydrate binding to the CRD modulates galectin-3 activity. Pectins are heterogeneous polysaccharides present in plants, fruits and vegetables. Pectic fragments bind to the CRD and may reduce its activity. Our aim was to identify pectins with strong inhibitory activity, which may one day play a role in prevention or treatment of heart failure.
Methods: Multiple (>40) pectins of various food crops were screened and compared to two known galectin-3 inhibitors - modified citrus pectin (MCP) and lactose. We studied galectin-3 induced monocyte chemotaxis and, second, we tested the pectins in an enzyme-linked lectin assay, studying the binding affinity of pectins for galectin-3. We selected the pectin with strongest inhibitory effects, and then tested its efficacy in vivo in a murine model of angiotensin II (AngII) infusion (2.5 mg/kg/day, 14 days). End points were cardiac function and fibrosis, determined by echocardiography, invasive hemodynamic monitoring and analysis of the cardiac tissue.
Results: The in vitro tests revealed 7 pectins to have superior inhibitory capacity over MCP, and we further tested the most potent pectin, which was an enzymatically modified plant pectin (EMPP). EMPP was shown to be superior in inhibiting galectin-3 induced monocyte chemoattraction (61% vs. 31% for MCP, $P<0.01$). Furthermore, EMPP inhibited galectin-3 affinity for lectin by 77% ($P<0.001$); MCP inhibited this by 43%. In vivo, in hypertensive mice, AngII increased fibrosis 4.9-fold compared to control, which was attenuated to a 3.5-fold increase by MCP and a 2.3-fold increase by EMPP ($P<0.05$ vs. AngII alone). Functionally, AngII-treated mice had lower fractional shortening (33%) compared to control (41%); MCP improved this to 35% (non-significant), while EMPP improved this to 40% ($P<0.05$). Gene expression profiles showed that the protective effects of EMPP were not associated with a reduction in blood pressure, or markers of cardiac stretch (ANP), but we observed a striking reduction in inflammatory status.
Conclusion: We demonstrate the feasibility of novel in vitro assays as a tool to identify biologically active pectins with superior galectin-3 inhibitory capacity. We propose that this approach may be useful in identifying functional foods or therapeutics for prevention or treatment of galectin-3 mediated conditions. The newly identified EMPP, might be an interesting candidate to prevent cardiac fibrosis.

3088 | BENCH
Cardiac fibrosis reversal by serelaxin: in vivo pharmacology in a transgenic cardiomyothy model

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Purpose: Fibrosis is a hallmark of cardiac disease and a therapeutic target. There is unmet need for drugs to reverse established fibrosis. Human recombinant relaxin (serelaxin) has been shown to reverse fibrosis in animal models, but its in vivo pharmacological feature is unclear. We studied fibrosis reversal by serelaxin therapy in a transgenic (TG) model of cardiac fibrosis.
Methods: The TG mouse model had cardiac overexpression of β2-adrenoeptor (β2-AR). Male TG and wild-type (WT) mice aged 5-6 months were used (n=7-8). Serelaxin was given s.c. via osmotic minipump. Myocardial fibrosis was determined by hydroxyproline assay and quantitative histology (picrosirus-red staining). Gene expression was determined by real-time RT-PCR.
Results: Collagen content was 2-fold higher in TG than WT mice ($P<0.001$). Treatment with serealxin at 0.15 and 0.5 mg/kg/day for 14 days reduced fibrosis by 23±3% and 42±2%, respectively, from TG control level (both $P<0.01$). This efficacy was largely lost after 4-week washout following 14-day serelaxin therapy (0.5 mg/kg/day) with collagen 16±3% lower than TG control (P=0.15). Serelaxin therapy (0.5 mg/kg/day) time-dependently reduced fibrosis that become statistically significant from day-3 after treatment (Fig. 1). Serelaxin therapy suppressed expression of α-smooth muscle actin at day-3, but pro-collagen expression was unaffected. Serelaxin had no effect on β2-AR mediated functional activation. In WT mice, serelaxin therapy (0.5 mg/kg/day for 14 days) did not change collagen content in various organs.

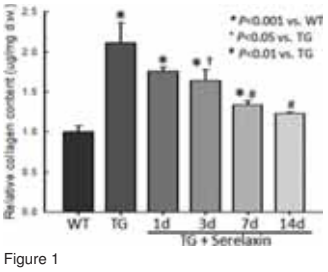

Figure 1

Conclusion: Serelaxin therapy does not affect collagen levels of healthy organs, but mediates a rapid cardiac fibrosis reversal that is dose- and time-dependent. Suppression of de novo collagen synthesis is not a major mechanism for this action in vivo.

3089 | BENCH
Involvement of fibroblast growth factor-21 in gestation-induced cardiac hypertrophy

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Purpose: During pregnancy, heart enlarges as a physiological adaptive process. The regulatory mechanisms eliciting this process, a model of non-pathological cardiac hypertrophy, are poorly known. Recently, the endocrine factor FGF21 has been identified as a protective agent against pathological cardiac hypertrophy. FGF21 is secreted by the heart and appears to act through endocrine/autocrine processes. The objective of our study has been to determine FGF21 involvement in gestation-induced cardiac hypertrophy.
Methods: We used a model of FGF21 knock out (KO) mice to determine the role of FGF21 in heart adaptations to pregnancy. Wild-type (Wt) and KO pregnant mice at day 18 of gestation were sacrificed, non-pregnant mice of the two genotypes at similar age served as controls. The same experimental procedure was used in a PPARalpha-null mice model.
Results: The systemic and cardiac FGF21 systems are profoundly altered during pregnancy: there is a significant increase in plasma levels of FGF21 and in FGF21 mRNA expression in heart. Cardiac expression of the FGF receptor-1 and co-receptor beta-Klotho also tended to increase due to pregnancy. The

induction of FGF21 expression in heart is totally dependent on PPARalpha, as PPARalpha-null pregnant mice did not exhibit enhanced FGF21 expression. Non-pregnant FGF21-null mice show signs of spontaneous cardiac hypertrophy, as evidenced by enhanced heart weight-to-tibia length. Whereas wild-type pregnant mice showed enhanced heart weight-to-tibia length ratio relative to non-pregnant female mice, FGF21-null pregnant mice did not show any significant induction. Gene expression of marker genes of adaptive lipid metabolism (medium chain acyl-CoA dehydrogenase, pyruvate dehydrogenase kinase-4, PGC-1alpha) was highly induced in heart due to pregnancy in wild-type mice, and such induction occurred similarly in FGF21-null pregnant mice. However, the expression of marker genes of pathologically induced cardiac hypertrophy, such as atrial natriuretic factor and alpha-actinin, were unaltered due to pregnancy, as expected. FGF21 gene invalidation did not alter the expression of these genes either in non-pregnant or pregnant mice.

Conclusions: We report for the first time that FGF21 changes are part of systemic and cardiac adaptations to pregnancy. PPARalpha controls pregnancy-induced FGF21 expression in pregnancy, and FGF21 is involved, at least in part, in adaptive cardiac hypertrophy during pregnancy. Further research is needed to determine the relative role of systemic FGF21 versus locally produced FGF21 in heart to modulate the hypertrophic response of heart to gestation.

3090 | BENCH
Novel insight in the mechanism of TGF-beta-mediated inflammatory-driven myocardial fibrogenesis in experimental autoimmune myocarditis and in systemic sclerosis

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Rationale: Previously, we showed that transition of inflammatory CD133+ progenitors and endogenous gp38+ heart fibroblasts into pathological myofibroblasts is a major process during myocardial fibrogenesis in experimental autoimmune myocarditis (EAM) model. TGF-b and Wnt signalling are important factors in the development of fibrosis. In the autoimmune disease systemic sclerosis (SSc), inflammatory dilated cardiomyopathy (iDCM) is as a major cause of death.
The interplay between TGF-b and Wnt signalling pathways during myofibroblast differentiation of inflammatory progenitors and cardiac fibroblasts has not been identified until now.
Methods and results: EAM was induced with alpha-MyHC/CFA immunization in BALB/c mice. CD133+ progenitors were isolated from inflamed hearts, gp38+ fibroblasts from adult healthy myocardium. Cells were expanded and treated with TGF-β, Wnt proteins or their inhibitors, or co-cultured with STF reporter cells expressing luciferase under the control of TCF/LEF transcriptional reporter element. CD45+/CD14+ monocytes were isolated from the blood of SSc patients and healthy subjects.
TGF-β initiated myofibroblast differentiation of inflammatory CD133+ progenitors and cardiac gp38+ fibroblasts via canonical SMAD2/3-dependent pathway. In both myofibroblast cell sources, TGF-β activated canonical Wnt pathway (Wnt-1, -10-b) that resulted in nuclear translocation of b-catenin, as well as the non-canonical pathway (Wnt-5a, -11) leading to JNK activation. Wnt pathways were activated in mouse myocardium during the EAM, and within the myocardium of patients with acute myocarditis.
We showed that TGF-β activated rapid secretion of Wnt proteins. Wnt secretion is crucial for myofibroblasts differentiation, and together with TGF-β controls Wnt(s) transcription. Wnt-1/5a stimulation failed to up-regulate TGF-β receptor 1 or 2, excluding activation of both receptors. Blocking of Wnt activity with Wnt inhibitors reduced myofibroblast differentiation of both cell types. Notably the formation of inflammatory-driven cardiac fibrosis was prevented by treatment with Wnt inhibitors. Finally, TGF-β induced myofibroblast differentiation of human blood-derived CD14+ monocytes via activation of canonical and non-canonical Wnt pathways.
Conclusions: We showed here a novel mechanistic insight of TGF-β in Wnt-dependent myofibroblast differentiation pathway. A better understanding of the mechanisms triggering inflammatory-driven cardiac fatal fibrosis in iDCM and SSc might be helpful in developing novel and effective therapies targeting a broad spectrum of pathologic and inflammatory-mediated processes.

CARDIOVASCULAR DISEASES: NO GEOGRAPHICAL BOUNDARIES?

3163 | BEDSIDE
The effect of hurricane sandy on cardiovascular events

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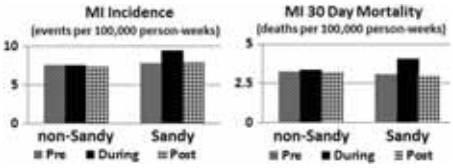
Purpose: Extreme weather conditions have been associated with increased rate of acute myocardial infarction (AMI). Hurricane Sandy was the largest Atlantic hurricane on record, a Category 2 storm off the coast of the Northeastern United States. High impact counties of New Jersey (NJ) were hit with high winds, torrential rain, destruction of property and infrastructure e.g. loss of electric power, heat and telephone for up to two weeks, while other counties were not severely affected (low impact). We examined the effect of Sandy on the incidence and mortality of AMI in high and low impact counties.
Methods: Counties were designated as high or low impact using data from the US Federal Emergency Management. The occurrence of AMI and of in-hospital or out-of-hospital death were ascertained using the Myocardial Infarction Data Acquisition System (MIDAS), a statewide, longitudinal database of all hospitalizations for cardiovascular diseases in NJ, and the NJ death certificate files. We compared the two Sandy weeks with the same two weeks in the five previous years and to the two weeks preceding and to the two weeks following Sandy using Poisson regression.
Results: In the high impact counties during the two Sandy weeks, there was a 23% increase in the number of AMI incidence (from the expected 273 events per 100,000 person-weeks to 335, 62 more, $p<0.0001$). In addition, the total number of AMI deaths (in-hospital plus out-of-hospital) increased by 28% (from the expected 120 to 154 deaths per 100,000 person-weeks, 34 more, $p<0.0001$). There was no rebound decrease in these effects in the two weeks after Sandy and the effects in low impact counties were not statistically significant.



Conclusions: Hurricane Sandy was associated with marked increase in AMI incidence and deaths.

3164 | SPOTLIGHT
Burden of myocardial infarction, atrial fibrillation and heart failure in Aboriginal Australians: more than a matter for cardiology

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Purpose: Cardiovascular diseases contribute 23% of the 11 year life expectancy gap between Aboriginal and non-Aboriginal Australians. We present disparities in incidence and outcomes of AMI, atrial fibrillation (AF) and heart failure (HF) in Western Australia and a framework to address these disparities.
Methods: In 3 separate analyses, first-ever AMI, HF and AF events (hospital-admitted patients or deaths; lookback period=15 years) were identified using person-based linked hospital and death data. Age-standardised rates (ASR) were calculated in two broad age groups, below and above 55 years. Comorbidities were identified using a 5-year lookback period and mortality outcomes compared, after multi-variable adjustment.
Results: In all age groups, Aboriginal rates were significantly higher than non-Aboriginal rates. In males under 55 years, the ASR was approximately 6, 4 and 10 times higher in the Aboriginal population for AMI, AF and HF respectively (Fig. 1). Disparities were larger in Aboriginal women and less at older ages. Aboriginal patients had much higher prevalence of diabetes, chronic kidney and lung

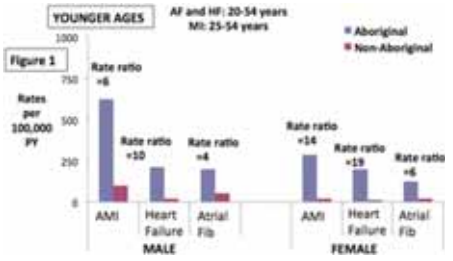

Figure 1. ASR for AMI, HF and AF <55 years

disease. Adjusted 1-month mortality was similar but 1-year (AF, HF) and 2-year (AMI) mortality in Aboriginal patients twice that of non-Aboriginals.
Conclusions: AMI, HF and AF in Aboriginal people are characterised by high rates, early onset and poorer survival, with comorbidities an important determinant of outcomes. The disparities can be understood by considering a hierarchical system of causes in which cardiology intervention is essential but insufficient, stressing the importance of social determinants of cardiac health. Our framework outlines that social, policy and systems change are needed across multiple sectors to reduce Aboriginal disparity.

3165 | SPOTLIGHT
Outdoor temperature, blood pressure and cardiovascular disease mortality among people with diagnosed cardiovascular diseases: findings from the China Kadoorie Biobank

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Introduction: Outdoor temperature has a negative association with blood pressure. Individuals with cardiovascular disease (CVD) may be particularly vulnerable to low temperatures, but little is known of the association between outdoor temperature, blood pressure and CVD mortality among them.
Methods: We analyzed cross-sectional and follow-up data of 23,000 individuals with a prior history of physician-diagnosed CVD who were recruited into China Kadoorie Biobank from 10 diverse regions across China during 2004-8, and measured whether blood pressure related to the season and the mean daily temperature as well as to the subsequent mortality from CVD.
Results: The overall mean adjusted SBP was 141 mmHg, much higher in winter than in summer (145 vs. 136 mmHg), with each 10℃ lower temperature associated with 6.21 mmHg higher SBP, at least above 5℃ in outdoor temperature. The strength of the association was stronger in older people (6.59 mmHg), current regular smokers (7.06 mmHg) and those with prior hypertension (6.43 mmHg) or diabetes (7.34 mmHg), but use of central heating tended to attenuate the effects significantly. Regardless of antihypertensive treatment (31%), higher blood pressure still independently predicted CVD mortality, with each 10mmHg higher SBP associated with 14% (95% CI: 11%-16%) higher CVD rate. Mirroring the seasonal variation of blood pressure, there was also a winter peak of CVD mortality, with the rate in winter being 45% greater than in summer.
Conclusion: Among people with prior CVD, lower outdoor temperature is associated with increased blood pressure, through it, to rise in CVD mortality, especially among those without effective central heating.

3166 | BEDSIDE
Epidemic of coronary heart disease and risk factors in rural communities of Pakistan, females dominate male

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Background: Major segment of Pakistani Population lives in rural areas and data regarding Coronary Heart Disease (CHD) and Risk Factors (RF) is scanty. Objectives: To determine the prevalence of CHD/RF among adults of rural areas of Pakistan.
Methods: Representative sample of 2000 subjects, age ≥30 years randomly selected using stratified sampling technique. Predesigned questionnaire used for interview. Physical examination, fasting blood sample and ECG recorded. RF were predefined using standard criteria. CHD defined on affirmative response to rose questionnaire, positive history and ECG changes.
Results: Overall prevalence of CHD was 9.2% significantly higher in females. RF detail is given in table. Prevalence of metabolic syndrome was 21.8% in females and 3.8% in males (p. value <0.001). Physical inactivity was higher in females. House wives were predominantly affected. Literacy has positive impact on the occurrence of CHD. Level of mental and physical stress at work & home is statistically associated with female CHD (p. value <0.01).

Risk factors distribution

Risk factors	Overall prevalence %	Male %	Female %	P value
Hyper tension	25.3	26.0	24.8	0.554
DM	12.7	11.6	13.4	0.239
Total cholesterol (≥240)	2.3	2.7	2.0	0.327
LDL-C (≥160)	1.3	1.1	1.4	0.601
HDL-C (>40)	18.6	17.2	19.5	0.199
TGs (>200)	18.8	46.6	53.3	0.001
BMI (≥25)	45.4	41.5	47.8	0.001
Smoking	19.8	37.2	8.3	0.001

Conclusion: This study discovered very high prevalence of CHD in rural women of Pakistan. The level of physical and mental stress in females, gender discrimination regarding utility of health care facilities, illiteracy in females are further contributors. Apart from conventional interventional strategies to control the modifiable RF, the educational and socioeconomic uplift in under privileged rural areas of Pakistan can halt this epidemic of CHD in women.

3167 | BENCH
The burden of cardiovascular disease in nomadic population: Mongolian study

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Introduction: Mongolia has only one cardiac center. It makes very challenging for people who lives in rural area. Patients with cardiovascular disease /CVD/ in nomadic population is never been explored and basically no data available. Therefore the study was aimed to find out the prevalence and clinical data of patients having CVD and related risk factors in forgotten population of Mongolia.
Method: A questionnaire interview and medical examination including ECG were conducted at local clinics of rural 3 provinces /3 portable ECG machines were donated from non-profit organization/. Total 1684 people were voluntarily participated from 2011 to 2013 at local health center.
Results: A total of 1684 (978 females) patients aged 23-81 years were enrolled in the study. The mean BMI was 27.6±3.0kg/m^2. Newly diagnosed CVD was 48% with complication of heart failure 9%. Rheumatic heart disease cases were most common (26%), followed by atrial fibrillation (19%), coronary artery syndrome (8%), pulmonary artery hypertension (5%) and congenital heart defect (3%). A hypertension 17% and diabetes mellitus 12% were diagnosed newly. About 45% of them were smoker and 36% were consuming alcohol regularly. The daily food was mainly consisted from fatty meat (98%) and carb (90%, mostly flour and rice), vegetables (5%) and basically no fruits are available. 74% of newly diagnosed patients never attended follow-up checkup. 61% of total patients rather apply to local healer or traditional medicine than moving urban area to see specialist physician.
Conclusion: Lack of financial resources, access to health services and nomadic life style make them very difficult to keep up with treatment and follow-up checkups. Most of the patients do not want to go to central hospital for further treatment and rather willing to apply to local healer. Majority of the patients are seen by general practitioners at local clinics who is not specialized in CVD. The study found that under-diagnosis of CVD is common due to lack of diagnostic knowledge, no long term availability of treatment and people's health education is lacking severely. Multidisciplinary actions and further studies should address these issues, especially on health education and guidelines of local health centers.

3168 | BENCH
Assessment of future trajectories in coronary heart disease mortality in the Czech Republic

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Purpose: The decrease in CHD mortality rates seen in the Czech Republic since the mid-1980s slowed in recent years. The aim of our analysis was to predict future CHD mortality in the Czech Republic based on main life-style related cardiovascular risk factor trends.
Methods: An updated IMPACT CHD Policy Model was used to predict changes in CHD mortality between 2007 and 2020 among the projected population of the Czech Republic aged 25–74 years. Calculations were based on (i) data on population numbers and projections, (ii) population risk factors levels and projections (Czech post MONICA Study), and (iii) effectiveness of specific risk factor reductions (meta-analyses). We evaluated a projection with CHD mortality remaining constant since around 2010. Three scenarios of improved risk factor control were modeled: a conservative one assumed changes in energy from saturated fats by 1%, in salt intake by 10%, and in absolute percentage of smokers and physically inactive individuals by 5%. An intermediate scenario assumed changes by 2%, 20% and 10%, and an optimistic one by 3%, 30% and 20%, respectively.
Results: In 2007, the number of CHD deaths was 8,039. Assuming no future changes in mortality, the number of CHD deaths in 2020 will be 10,598. The

Table 1. Forecasted decrease in number of deaths (N and %) due to changes in risk factors

Risk factor	Scenario					
	Conservative		Intermediate		Optimistic	
	N	%	N	%	N	%
All	1164	11%	2245	21%	3146	30%
Physical activity	174	2%	340	3%	500	5%
Salt intake	346	3%	650	6%	920	9%
Saturated fats	255	2%	478	5%	675	6%
Smoking	389	4%	777	7%	1051	10%

decreases in the predicted numbers of deaths under the three above scenarios are shown in Table 1. The biggest effect can be expected from a decrease in salt intake and smoking prevalence.
Conclusions: Only the optimistic scenario with substantial improvement in the control of risk factors can secure a further decrease in CHD mortality.
This study was part of the EUROHEART II Project, WP 6 and was partly supported by IGA, Ministry of Health, Czech Republic, grant No NT/13186

Poster Session 4

THE BODYWEIGHT BURDEN

P3182 | SPOTLIGHT
Weight reduction is associated with reduced risk for atrial fibrillation in apparently healthy middle-age men and women

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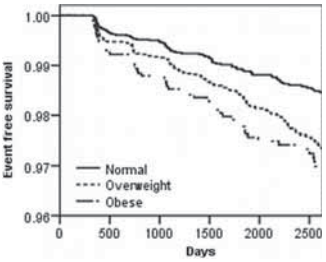
Background: Obesity is a strong predictor of atrial fibrillation (AF). The aim of the current study was to assess time-dependent association between body mass index (BMI) and new onset AF among middle aged apparently healthy men and women.
Methods: We investigated 18,468 men and women who were annually screened at the institute for medical screening of our medical center. All subjects were free of AF at baseline and had their BMI documented at each visit. Subjects were divided at baseline into three groups: normal weight (BMI<25; N=7,819), overweight (BMI≥25 and <30; N=8,067) and obese (BMI≥30 kg/m^2; N=2,582). The primary endpoint was the first occurrence of AF during follow-up.
Results: Mean age of study population was 49±11 years and 73% were men. A total of 371 (2.0%) incident events occurred during 6±4 years of follow-up. Kaplan Meier survival analysis showed that the cumulative probability of AF events at 6 years was highest among obese subjects, intermediate among overweight subjects and lowest among subjects with normal weight (2.6%, 2.0% and 1.3% respectively; Figure). Multivariate Cox regression analysis adjusted for multiple covariates including age, gender, diabetes mellitus and hypertension showed that overweight and obesity were associated increased risk of first AF event (HR 1.33 and 2.10; p=0.023 and <0.001, respectively). Multivariate Cox regression model adjusted for the same covariates with BMI as a time-dependent covariate showed that each 1 kg/m^2 reduction in BMI during follow up was associated with 7% reduction in the risk of first AF event (95% CI 0.87-0.99; p=0.016).



Kaplan-Meier analysis.

Conclusions: Overweight and obesity are independently associated with increased risk of first event of AF. Weight loss can significantly reduce AF disease burden.

P3183 | BEDSIDE
The effects of weight gain after smoking cessation on atherogenic alpha1-antitrypsin-low-density lipoprotein

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Background: Although cardiovascular risks decrease after quitting smoking, body weight often increases in the early period after smoking cessation. We have previously reported that the serum level of the α1-antitrypsin–low-density lipoprotein complex (AT-LDL)–an oxidatively modified low-density lipoprotein that accelerates atherosclerosis–is high in current smokers, and that the level rapidly decreases after smoking cessation. However, the effects of weight gain after smoking cessation on this cardiovascular marker are unknown.
Methods: We determined serum levels of AT-LDL by an enzyme-linked immunosorbent assay (ELISA) in 183 patients (134 males and 49 females) who visited our outpatient clinic for smoking cessation, and successfully achieved smoking abstinence. We measured AT-LDL both at baseline and at 12 weeks, and we also calculated BMI twice.
Results: Patients experienced an increase in BMI (p<0.001), LDL-C (p=0.042), HDL-C (p<0.001), and TG (p<0.001), whereas they had a decrease in systolic blood pressure (SBP) (p=0.012), AT-LDL (p<0.001), and the CO concentration in exhaled breath (p<0.001) after smoking cessation compared with their baseline values. Using the median BMI increase as the cutoff point, participants were divided into 2 groups. In the ΔBMI < median group, patients' BMI decreased after smoking cessation by an average of 0.4 kg/m^2 (p<0.01), whereas in the ΔBMI ≥ median group, the BMI increased after smoking cessation by 1.1 kg/m^2 (p<0.01). There was no significant change in serum LDL-C levels over 12 weeks in the ΔBMI < median group, whereas a significant increase (p=0.001) was found in the ΔBMI ≥ median group after smoking cessation. Conversely, although no significant change in the serum levels of AT-LDL was found in the ΔBMI ≥ median group, a significant decrease in AT-LDL levels (p<0.001) from before to after smoking cessation was identified in the ΔBMI < median group. Moreover, the degree of change in serum AT-LDL levels was significantly larger (p=0.041) in the ΔBMI < median group than in the ΔBMI ≥ median group. Other than LDL-C and AT-LDL levels, no significant differences were found among the ΔBMI groups regarding the changes in values before and after cessation.
Conclusions: Although the serum levels of AT-LDL after smoking cessation significantly decreased in the ΔBM < median group, the levels did not decrease in the ΔBMI ≥ median group. The findings suggest that the decrease in serum AT-LDL levels after quitting smoking is inhibited by weight gain after smoking cessation.

P3184 | BEDSIDE
Plasma glucagon-like-peptide 1 and body fat mass among young and healthy adults

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Purpose: Glucagon-like-peptide-1 (GLP-1) receptor agonists have been shown to reduce bodyweight in overweight and/or diabetic individuals. We aimed to evaluate the relationship between intrinsic GLP-1 levels and body fat mass in young and healthy adults.
Methods: Our population-based study in our country included healthy individuals aged 25 to 41 years. In the current analysis, we included 1540 individuals who had GLP-1 levels and body fat mass data available. Exclusion criteria were prevalent cardiovascular disease, diabetes or a body mass index (BMI) >35 kg/m^2. GLP-1 was determined with a research-use-only Single Molecule Counting technology assay. Body fat mass was obtained by bioelectrical impedance analysis using standardized methodology and a validated device. Multivariable linear regression analyses were used to model the relationship between GLP-1 and body fat mass.
Results: Median age of our population was 38 years. Median BMI was 24.18 kg/m^2, and median body fat was 25.11%. The results of the multivariable linear regression models are shown in the Table. After adjustment for each other, body fat mass but not BMI was strongly related to GLP-1 levels.
Conclusions: Plasma levels of GLP-1 show a significant positive linear relationship with body fat mass but not BMI among young and healthy adults. These results support the hypothesis that GLP-1 impacts body fat mass regulation.

Abstract P3184 – Table 1. GLP-1 and body fat mass/BMI relationship

	Continuous† (n=1540)	Quartile 1 (n=384)	Quartile 2 (n=385)	Quartile 3 (n=386)	Quartile 4 (n=385)	P for trend‡
Glucagon-like peptide 1 (GLP-1, Log) and body fat mass; β (95% CI)						
Sex, age adjusted	1.54 (1.00; 2.08) **	Ref.	0.37 (–0.33; 1.08)	1.09 (0.38; 1.80)	1.67 (0.96; 2.38)	<0.0001
Fully adjusted +	0.60 (0.20; 1.01) **	Ref.	0.08 (–0.45; 0.60)	0.51 (–0.01; 1.03)	0.83 (0.30; 1.36)	0.0006
	Continuous† (n=1568)	Quartile 1 (n=392)	Quartile 2 (n=391)	Quartile 3 (n=394)	Quartile 4 (n=391)	P for trend‡
Glucagon-like peptide 1 (GLP-1, Log) and BMI; β (95% CI)						
Sex, age adjusted	1.02 (0.64; 1.39) **	Ref.	0.34 (–0.15; 0.83)	0.55 (0.06; 1.04)	0.94 (0.45; 1.43)	0.0001
Fully adjusted+	0.02 (–0.25; 0.29)	Ref.	–0.04 (–0.39; 0.32)	–0.17 (–0.52; 0.18)	–0.19 (–0.55; 0.16)	0.21

+Adjusted for sex, age, smoking status, education level, systolic blood pressure, estimated glomerular filtration rate (CKD-EPI-formula), low density lipoprotein, high density lipoprotein, hemoglobin A1c, high sensitivity C-reactive protein, physical activity, alcohol consumption, fruit/vegetable consumption, BMI and/or body fat mass (n=1490). **P-value <0.01; †Log-transformed variable; ‡p for trend across quartiles of GLP-1.

P3185 | BEDSIDE
Impact of body mass index and visceral adipose tissue on cardiovascular risk factors and outcomes

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Background: The power of body mass index (BMI) as a cardiovascular risk factor is still controversial. Recent interest has focused on the heterogeneity of outcomes among overweight individuals. The aim of this study was to investigate whether adding visceral adipose tissue (VAT) measurements using computed tomography to BMI provides better cardiovascular risk assessment
Method: 369 consecutive patients without history of cardiovascular disease who underwent 64-slice computed tomography angiography (CTA) were recruited. %VAT was calculated as VAT/(VAT + subcutaneous adipose tissue) × 100, and its median value was 39.4%. Patients were divided into four groups based on BMI (<25 and 25≤) and %VAT (<39.4 and 39.4≤). The investigated cardiovascular risk factors were hypertension, hyperglycemia, and dyslipidemia. We analyzed the incidence of major adverse cardiac events (MACE), including cardiovascular death, myocardial infarction, and any revascularization.
Result: The rate of patients who have two or more concomitant risk factors ($p<0.0001$) and who underwent PCI or CABG after CTA (p=0.02) was significantly higher among BMI≥25 with higher %VAT group. During the median follow-up of 2020 days, 32 events occurred. MACE occurred more frequently in BMI≥25 with higher %VAT group than the other groups (log-rank p=0.003). In Cox analysis, the hazard ratio of BMI≥25 with higher %VAT for MACE was 4.38 (95% confident interval[CI] 1.58–12.18, p=0.005) compared to BMI<25 with lower %VAT, 2.74 (95%CI 1.18–6.35, p=0.02) compared to BMI<25 with higher %VAT, and 4.68 (95%CI 0.98-22.51 p=0.05) compared to BMI≥25 with lower %VAT, after adjustment for confounding factors.

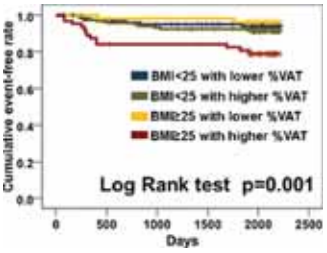

Figure 1

Conclusion: BMI in combination with VAT is a useful predictor of cardiovascular risk factors and outcomes.

P3186 | BEDSIDE
Left ventricular deformation properties in lean and obese children and adolescents after 3 year-follow-up

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Background and objectives: The increasing prevalence of obesity in childhood appears to precede the development of cardiovascular diseases. Childhood obesity is associated with significant changes in left ventricular geometry and function. However, less is known about longitudinal development of left-ventricular performance in children with obesity.
Aim of the present observational study was to assess geometric and functional left ventricular alterations after 3 year-follow-up in initially pubertal children with overweight or obesity compared to age-matched lean controls.
Methods: Eighteen obese (O) (Age 13.2±2.6, SDS-BMI 2.47±0.64, 39% male) and 30 lean control children (L) (Age 14.1±3.1, SDS-BMI -0.38±0.86, 53% male) were examined with a standardized transthoracic echocardiography at baseline and 3 year-follow-up (median 3.07 years [IQR 2.96-3.25]). 2-D Speckle Tracking was performed in all apical and parasternal short axis views to calculate longitudinal, circumferential and radial strain.
Results: At baseline, O showed in comparison to L a 38% higher left ventricular (LV) mass index, 18% higher LV end-diastolic volume and 38% higher left atrial volume index ($p<0.01$). Despite identical LV-EF, parameters of longitudinal and circumferential deformation were reduced in obese children compared to lean controls (longitudinal strain: –12%, $p<0.01$; circumferential strain: -13%, $p<0.01$). Radial strain was comparable between O and L.
After 3 year-follow-up, there was a mean weight gain of 11.7±18.6 kg in O and 11.3±7.9 kg in L (n.s.), SDS-BMI remained significantly different (-0.45±0.97 vs 2.11±0.83, $p<0.001$). Left ventricular (LV) mass index (+38%), LV end-diastolic volume (+21%) and left atrial volume index (+36%) continued to be significantly higher in O compared to L ($p<0.01$). Despite identical LV-EF, parameters of longitudinal and circumferential deformation were still reduced in obese children compared to lean controls (longitudinal strain: –10%, $p<0.05$; circumferential strain: -9%, $p<0.05$). Radial strain remained comparable between O and L.
Conclusion: Childhood obesity is associated with significant changes in left ventricular geometry and function, indicating an early onset of detrimental alterations in the myocardium. These changes remain present during the course from early to late adolescence.

P3187 | BEDSIDE
Overweight/obesity since adolescence and its impact on anthropometric indexes, blood pressure, adipokines, inflammation, and pulse wave velocity in Brazilian young adults. Rio de Janeiro Study

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Background: The impact of overweight/obesity (O/O) in adolescence on other cardiovascular risk factors in young adults is important for primary prevention.
Purpose: To evaluate anthropometric indexes, blood pressure (BP), metabolic and inflammatory variables, and pulse wave velocity (PWV) of youngsters stratified by their body mass index (BMI) in a 18 year-follow-up period, since adolescence. Population and Methods: 116 subjects (63 males) from the Rio de Janeiro Study (follow-up 17.76 +1.63 years) performed three assessments: A1 (12.40±1.49 years old), A2 (21.40±1.74 years old) and A3 (30.09±2.01 years old), and were divided into two groups: GN (n=80) with normal BMI in at least two of three assessments, and GO/O (n=36) with abnormal BMI in at least two of three assessments. BP and BMI were obtained in A1, A2 and A3. In A2 and A3, glucose (G), insulin (Ins), HOMA-IR, and lipids were included, and in A3, abdominal circumference (AC), PWV, Apolipoprotein A1, Apolipoprotein B 100, Lipoprotein (a), Adiponectin, Leptin, E-selectin, VCAM and ICAM, CRP, and fibrinogen were added.
Results: 1) Groups did not differ by age and sex; 2) In A1, A2 and A3, GO/O showed higher BMI, SBP, DBP means and higher prevalence of O/O ($p<0.0001$) and hypertension ($p<0.01$); 3) In A2, GO/O presented higher fasting glucose ($p<0.010$), Ins ($p<0.02$), HOMA -IR ($p<0.010$), total cholesterol ($p<0.02$), LDL cholesterol ($p<0.001$), triglycerides ($p<0.04$) means; 4) in A3, GO/O showed higher prevalences of increased AC ($p<0.001$), metabolic syndrome ($p<0.001$), hyperinsulinemia ($p<0.007$); and higher HOMA-IR ($p<0.02$), LDL cholesterol ($p<0.05$), leptin ($p<0.0001$), E- selectin ($p<0.001$), CRP ($p<0.0001$), fibrinogen ($p<0.004$), and PWV ($p<0.05$) means, and higher leptin / adiponectin ratio ($p<0.0001$). 5) In logistic regression analysis it was observed that BMI in A1 showed an odds ratio of 1.509 (CI 95% 1.247-1.821; $p<0.001$) for the occurrence of metabolic syndrome in A3.
Conclusion: In a 18 year-follow-up period, since adolescence, overweight/obesity was associated with higher anthropometric indexes, BP, PWV, a worse metabolic profile, with the presence of inflammatory markers, and a higher risk for metabolic syndrome in young adulthood. These results highlight that primary prevention measures should begin early in life.

P3188 | BEDSIDE
Influence of weight and height on echocardiographic parameters in healthy subjects

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Purpose: Indexing of echocardiographic parameters in chamber quantification is nowadays mandatory given the influence of body size on them. Individual influence of weight and height has not been previously assessed in a large cohort. We aim to report the normal reference ranges for cardiac chambers size index by weight and height in healthy subjects.
Methods: NORRE study is a multi-centre study involving accredited echocardiography laboratories of the EACVI studying echocardiographic parameters in a large cohort of healthy population (n=734; 45.8±13.3 years; 43.6% of male). All 2D parameters were indexed by height, weight and body surface area (BSA).
Results: There were significant differences between men and women regarding left ventricle (LV) volumes and right ventricle (RV) areas when indexing by the height or BSA (Table). By contrast, when indexing by the weight, the differences in LV volumes (LV end-diastolic volume 1.37 vs. 1.33 ml/kg; p=0.135) and RV areas were attenuated (RV end-diastolic area: 0.24 vs. 0.24 cm^2/kg; p=0.924). LA volume (LAV) was not different between men and women when indexing by BSA. However, when indexing by height, LAV were significantly higher in men (28.4 vs.

Table 1

Parameters	Male mean ± SD	Male 1st–3rd	Female mean ± SD	Female 1st–3rd	p-value
LV end-diastolic volume biplane, mL/m	59.2±13.7	52.2–64.5	50.5±11.0	44.9–54.3	<0.001
LV end-systolic volume biplane, mL/m	21.8±6.2	18.6–24.1	18.1±4.9	15.8–19.9	<0.001
End-diastolic RV area, cm^2/m	10.3±2.3	9.2–11.0	9.01±2.06	7.9–9.6	<0.001
End-systolic RV area, cm^2/m	5.9±1.5	4.6–5.9	4.4±1.4	3.7–4.9	<0.001
LA volume area-length biplane, mL/m	31.8±8.0	28.3–34.3	29.1±7.3	25.7–31.1	0.002
RA volume area-length, mL/m	26.3±7.8	22.9–27.9	20.8±7.3	17.2–22.4	<0.001

26.4 ml/m; p=0.008), whereas after indexing by weight, LAV was higher in women (0.65 vs 0.69 ml/kg; p=0.044). Regarding the influence of age in these parameters, there was a significant negative correlation between age and LV volumes and RV areas index by BSA, weight or height.
Conclusion: The height of the patient is the main factor influencing the cardiac chamber sizes. After normalization by weight, the differences between men and women are attenuated. Caution should be taken when indexing by the BSA in obese patients to avoid underestimation of volumes and areas. In these cases, normalization by the height should be advised.

P3189 | BEDSIDE
Novel sonographic indicators of body adiposity in relation to cardiometabolic risk factors

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Visceral adiposity is known to be associated with cardiovascular risk factors (RF) and CVD risk. Novel lipometric approach of ultrasonic measurement of subcutaneous and abdominal fat is proposed for assessment of body fat distribution. The correlates of ultrasonic lipometric indicators in a general population were not studied.
Purpose: We aimed to study the distribution and predictors of subcutaneous and premesenteric fat layer in a population based sample.
Methods: We used the data from a random population sample (n=163; men/women aged 18-64) examined in a city in the frame of EPOGH Project. Subcutaneous fat (subCF) thickness and preperitoneal fat (prePF) thickness and width were measured on transverse images with conventional ultrasound probes standing on the abdominal midline in subxiphoid region. Ultrasonic measurements were validated against CT (n=40). CVD RF and anthropometric measures (body mass index, BMI; waist-to-hip ratio, WHR; skin fold) were evaluated by standardized methods. Predictors of fat measures were assessed in multivariable linear regression; models did not include BMI, WHR and skin fold as covariates to avoid over-adjustment.
Results: Image acquisition and online measurements were feasible in 100% of participants. Both fat measures had normal distribution through studied sample and were positively associated with anthropometric indicators (BMI, WHR, and skin fold). Mean subCF thickness in our sample was of 1.25cm (SD 0.55). Mean value of prePF was of 1.52cm (SD 0.63). In multivariable regression, the determinants of subCF thickness were female sex (p=0.042), systolic blood pressure (SBP) (p=0.051), plasma insulin level (p=0.034). The determinants of prePF thickness were again SBP (p=0.001) and plasma insulin (p=0.03). Additionally, prePF depo thickness was positively associated with younger age (p=0.037), total cholesterol (p=0.037), and negatively associated with HDL-C (p=0.021). The variability of subCF were explained by RF on 20% and variability of prePF measures - on 32-38% depending on statistical model.
Conclusion: Ultrasonic lipometric indicators of subcutaneous and preperitoneal fat are associated with insulin, SBP, female sex (subcutaneous fat), and younger age (preperitonel fat) independently of other factors. Additionally, preperitoneal fat but not subcutaneous one was positively associated with total cholesterol and negatively related to HDL-C. The relationships between preperitoneal fat and cardiometabolic correlates were sex-independent. Prospective analysis is warranted to estimate predictive significance of novel indicators for CVD risk.

P3190 | BEDSIDE
Prevalence of obesity in men and women in Ryazan region (dynamics through 2002-2007)

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Aim: To assess the dynamics of overweight and obesity prevalence in men and women in Ryazan region in 2002-2007.
Materials and methods: As a part of Russian epidemiological "EPOCH" study, a representative sample of Ryazan region population was evaluated: in 2002 with 95.3% response rate - 2098 subjects, mean age 44.8±18.6 years, in 2007 with 83.7% response rate - 1760 subjects, mean age 48.5±17.0 years. Anthropometric evaluation included measurement of height (cm) and body weight (kg). Excessive body weight was diagnosed at BMI of 25-29 kg/m^2, obesity – at BMI ≥30 kg/m^2. In 2007 additional measurement of waist (WC) and hip circumference. Abdominal obesity (AO) was diagnosed in case of WC>102 in men, and WC>88 in women.
Results: In 2002 mean BMI in men was 25.3±1.5 kg/m^2, in women - 27.0±1.3 kg/m^2. Portion of overweight men was 36.9±1.6%, women - 33.0±1.4%, p=0.07. Obesity was diagnosed in 11.7±1.1% of men and 23.6±1.2% of women. The number of obese men increased from 3.4% at 20-29 years to 16.2% at 60-69 and later decreased to 9.1% at 80-89. The number of obese women was 3.8%, 40.7% and 21.5% at the same ages. Obesity was more frequently diagnosed in countryside residents comparing to townsmen (22.8% vs. 18.0%, p<0.05), in men (14.4% vs. 9.0% in town, p<0.05). Prevalence of obesity in women did not depend from residency (28.9% vs. 24.6% in Ryazan, p=0.09). In the assessed sample 1st grade of obesity was the most prevalent (16.9% women and 9.2% men). 2nd grade obesity was diagnosed in 5.3% of women and 2.4% of men, 3rd grade - in 1.5% and 0.1%, respectively.
The repeated evaluation in 2007 revealed increase of mean BMI from 25.9±0.1 kg/m^2 to 27.0±0.1 kg/m^2, p<0.001. The prevalence of overweight didn't significantly change and was 39.2% in men and 35.2% in women. The obesity prevalence increased from 18.8% to 22.6%, p<0.001, more notably in women - from 23.6% to 29.4%, p<0.001, than in men - 11.7% to 14.0%, p=0.68. There was a significant increase in number of patients with 3rd grade obesity - from 0.9% to 1.9%, p<0.05. The prevalence of 1st grade obesity didn't significantly change over 5 years and was 19.6% in women, 9.7% in men; 2nd grade - 6.5% and 3.4%, respectively. Mean WC in 2007 was 88.1±0.5 cm in men and 83.7±0.4 in women. The prevalence of AO was higher in women than in men (34.2±1.5% vs. 14.4±1.3%, p<0.001).
Conclusion: The number of overweight and obese patients in Ryazan region increased over 5 years from 53.3% to 59.4%, p<0.01. The obesity prevalence was higher in women than in men and over the assessed period it increased from 23.6% to 29.4%, p<0.001.

P3191 | BEDSIDE
Waist to high ratio better identified cardiovascular risk factors and increased cardiovascular risk in a chilean survey

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Purpose: Obesity is an important determinant of cardiovascular risk in Latin America. However, optimal obesity indicators and their cut-off points are not well determined. The study objectives were to assess the relationship between body mass index (BMI), waist circumference (WC) and waist-to-height ratio (WHtR) with prevalence of hypertension, diabetes, dyslipidemia, and 10- year coronary heart disease (CHD) risk >10% estimation, and to define optimal cut-off points.
Methods: 2200 men and 3216 women from the Chilean Health Survey 2009-10 were analyzed. Crude Odds Ratio (OR) were calculated for upper, compared with lower quartile of anthropometric measurements for risk factors prevalence and CHD risk and adjusted for gender, educational level, physical activity, alcohol intake and smoking. ROC curves were used to compare discrimination and estimate cut-off points.
Results: The prevalence of overweight and obesity in men were 45,3% and 19,2%, and in women were 33,6% and 30,7% respectively. WHtR had highest crude OR for prevalence of hypertension (7.2 in men, 7.6 in women), diabetes (7.8 in men and women) and CHD risk (9.1 in men, 6.2 in women) with adjusted OR of 3,6 (95% CI 2,8-4,5); 3,9 (2,6-5,8) and 3,1 (2,8-4,1). WHtR also had higher ROC area for hypertension (0,707), diabetes (0,707), dyslipidemia (0,694) and CHD risk (0,691). Male and female optimal cut-off points for CHD risk were: 26,5 and 27,5 kg/m^2 for BMI, 95 and 89 cm for WC and 0,55 and 0,59 for WHtR respectively. Optimal cut-off points for prevalence of hypertension, diabetes and dyslipidemia had similar values
Conclusion: WHtR demonstrated the strongest correlation and associations with CV risks factors and estimated risk. Optimal cut-points are over those recommended in the literature.

P3192 | BEDSIDE
Do BNP and its associated lipolytic effects lead to subsequent weight change in older adults?

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Purpose: Besides the hemodynamic effects, natriuretic peptides (NP) lead to augmented rates of lipolysis in the adipose tissue. There have been several reports of reduced NP levels in overweight and obese subjects. This leads to questioning about the role of low NP levels on the development and maintenance of obesity. We investigated whether B-type natriuretic peptide (BNP) is associated with subsequent weight change in the elderly over a 3 year follow-up period.
Methods: Older adults (≥60 years) of the Bambuí (Brazil) Cohort Study of Aging who had BNP measured at baseline (1997) and weight reassessed 3 years later were selected for the present analysis. Weight change (loss or gain) was based on a 5% variation. We performed multinomial logistic regression models with weight change as the outcome (stability as reference), in order to investigate whether BNP is a determinant of subsequent weight variation independently of conditions which lead to high BNP levels or weight change (age, sex, smoking, diabetes, hypertension, Chagas disease, physical activity, BMI, major ECG abnormalities and log-transformed creatinine and C-reactive protein).
Results: 1120 predominantly female participants (707; 63.2%) with mean age of 68 (SD 6.7) years at baseline entered the study. 684 (61%) of them remained with stable weight. Among the ones who presented weight loss (246; 22%), median weight variation was 5.3 kg (IQR 3.9-7.7) and 26 (5.2%) initially normal weight were reclassified as underweight, 82 (19.5%) initially overweight turned into normal weight and 31 (21.6%) of the obese turned into overweight. Among those who gained weight (190; 17%), median weight variation was 4.9 kg (IQR 3.5-6.6), and 16 (23.5%) initially underweight turned into normal weight, whereas 48 (9.9%) and 31 (7.4%) initially normal weight turned into overweight and obese,

respectively. Median BNP was 70 pg/mL (IQR 39-134), 93 pg/mL (48-158) and 81 pg/mL (47-140) among those with weight stability, loss and gain, respectively (p=0.002). After full adjustment, BNP was independently associated with weight loss (OR 1.30; 95% CI 1.10-1.55), but not with weight gain (OR 1.20; 95% CI 0.99- 1.46).
Conclusions: Older adults with higher BNP levels had an increased odds of losing weight subsequently. Unrecognized morbid conditions might explain this association. However, lower BNP levels were not significantly associated with weight gain during a 3-year follow-up. These results suggest that having low BNP levels is not a clinically important mechanism to the development of obesity.

P3193 | BEDSIDE
Inflammation is associated with subsequent weight loss and gain in older adults

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Purpose: Inflammation may be a mediator of the increased mortality associated with weight change in the elderly. Our aim was to examine whether high sensitivity C-reactive protein (hs-CRP) is associated with weight loss or gain over a 3 year follow-up period in older adults.
Methods: Participants aged 60 years or older of the Bambuí (Brazil) Cohort Study of Aging who had hs-CRP measured at baseline (1997) and weight reassessed 3 years later were selected. Weight change (loss or gain) was based on a 5% variation and weight stable was used as reference. Adjusted multinomial logistic regression was applied to investigate whether CRP is a determinant of subsequent weight variation independently of baseline characteristics traditionally associated with inflammation and/or weight variation (age, sex, smoking, diabetes, hypertension, Chagas disease, physical activity, BMI, major ECG abnormalities and log-transformed creatinine and B-type natriuretic peptide). We also tested whether BMI at baseline, smoking and physical activity modified the effect of hs-CRP on weight change.
Results: In total, 1120 participants (684, 61% with stable weight; 190, 17% with weight gain and 246, 22% with weight loss) entered the study. Female sex was predominant (707; 63.2%). At baseline, mean age was 68 (6.7) years. Median hs-CRP and BMI at baseline were 3.1 mg/L (IQR 1.4-6.2) and 25.1 kg/m^2 (21.9-28.0), respectively. As compared to participants whose weight was stable (2.9 mg/L; IQR 1.2-5.7), hs-CRP was higher both in those who lost (3.7 mg/L; IQR 1.7-6.9) and gained weight (3.1 mg/L; IQR 1.6-7.0; p=0.003). Hs-CRP was an independent determinant of both subsequent weight loss (OR 1.02; 95% CI 1.01-1.04) and gain (OR 1.02; 95% CI, 1.01- 1.04). Interaction between CRP and smoking (p for interaction=0.34 for weight loss and 0.47 for weight gain), BMI at baseline (p for interaction=0.59 for weight loss and 0.49 for weight gain) or physical activity (p for interaction=0.91 for weight loss and 0.21 for weight gain) was not significant.
Conclusions: Older adults with higher levels of baseline inflammation were more likely to have subsequent weight loss or gain during a 3-year follow-up as compared to participants whose weight remained stable. These results were present regardless of conditions associated with increased levels of inflammation, such as cardiovascular and metabolic diseases, as well as determinants of weight change, such as smoking. Thus, inflammation per se might lead to weight change in either direction and be a link between weight variation and increased mortality in the elderly.

ENVIRONMENT AND CARDIOVASCUALR DISEASES

P3195

ABSTRACT WITHDRAWN

P3196 | BEDSIDE
Influence of air pollution on the risk of acute myocardial infarction in Korea from the Korea Acute Myocardial Infarction Registry

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Purpose: Atmospheric pollution would increase the risk of acute myocardial infarction (AMI). However, conflicting findings in various regions make it difficult to draw uniform results. The aim of this study is to determine whether a relationship exists between air pollution and the occurrence of AMI in Korea.
Methods: From Korean AMI Registry, 4,168 Koreans admitted for AMI in four university hospital between January 2006 and October 2010 was included in this study. The dates for onset of cardiac symptoms were merged with atmospheric pollutants including atmospheric particulate matter with diameter of 10 micromeres or less (PM10), ozone (O3), nitrogen dioxide (NO2), carbon monoxide (CO), and sulfur dioxide (SO2). Concentrations of pollutants were obtained from the database of the Ministry of Environment. The data of 11 measuring stations were analyzed to calculate average concentrations. Poisson regression model was carried out.
Results: The mean number of occurrence of AMI was 2.4 persons per day, averaging 1.6 men (68.2%) and 0.75 women (31.6%). Of these, 1950 (46.7%) were below 65-years-old. There was a significant negative relation between daily occurrence of AMI and the mean concentration of NO2. A 1/1000 ppm decrease in mean concentration of NO2 was associated with a 2% increase of occurrence of AMI (β=-0.020, risk ratio=1.020, $p<0.0001$). This association was consistently observed regardless of gender (β=-0.0195, risk ratio=1.0196, $p<0.0001$ for males vs. β=-0.0211, risk ratio=1.0213, $p<0.0001$ for females) and age (β=-0.0210, risk ratio=1.0212, $p<0.0001$ for <65-years-old vs. β=-0.0192, risk ratio=1.0193, $p<0.0001$ for ≥65-years-old). There were significant positive relations between daily occurrence of AMI and the mean concentration of CO and SO2. A 1/10 ppm increase in mean concentration of CO (β=0.067, risk ratio=1.069, $p<0.0001$) and 1/1000 ppm increase in SO2 (β=0.026, risk ratio=1.026, p=0.0078) were associated with 6.9% and 2.6% increase of occurrence of AMI, respectively. This association, particularly in CO, was stronger in females (β=0.0943, risk ratio=1.099, $p<0.001$ for females vs. β=0.0529, risk ratio=1.054, p=0.0003 for males) and in the young (β=0.0703, risk ratio=1.073, $p<0.0001$ for <65-years-old vs. β=0.0627, risk ratio=1.065, p=0.0001 for ≥65-years-old). There were no significant associations between concentrations of PM10 (β=-0.0002, risk ratio=1.0002, p=0.68) and O3 (β=-0.0032, risk ratio=1.003, p=0.059) and occurrence of AMI.
Conclusions: These finding suggests that air pollution have a modest influence on the occurrence of AMI in Korea.

P3197 | BEDSIDE
Microvascular endothelial function and endothelial microparticles level under the extreme weather conditions

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Purpose: The effects of extreme weather factors on endothelial function in humans are unknown. The aim of this study was to examine the endothelial function in healthy volunteers in extreme climatic conditions.
Methods: 6 healthy male volunteers aged 24 to 44 years were placed for 30 days in a residential module MARS 500 with simulation of extreme conditions of July - August 2010 (daily temperature +30 ...+38°C at a relative humidity of 30-50% a night temperature +26...+31 °C at a relative humidity of 50-75%, the CO content 5-40 mg/m^3). Microvascular vasomotor endothelial function was studied by finger photopletismography in reactive hyperemia test (Angioskan-01) every 10 days (Fig. 1: P0 - baseline, P1 - 10 days, P2 - 20 days, P3 - 30 days). Apoptotic endothelial microparticles CD31+ CD41-, as early markers of endothelial damage were determined by flow cytometry (Cytomics FC 500, Beckman Coulter).
Results: The amplitude index (IA) reflecting an increase in the amplitude of photopletismographic curve during the test with reactive hyperemia as a functional marker of microvascular endothelial function decreased in 5 of 6 volunteers from 10 to 50%, (P1, $p<0.1$). To the end of the experiment (P3) all six healthy volunteers had vasomotor endothelial dysfunction of microvascular arteries. All volunteers demonstrated a significant increase of microparticles CD31 + CD41- level. Trend of vasomotor endothelial function (delta IA) and apoptotic endothelial mi-

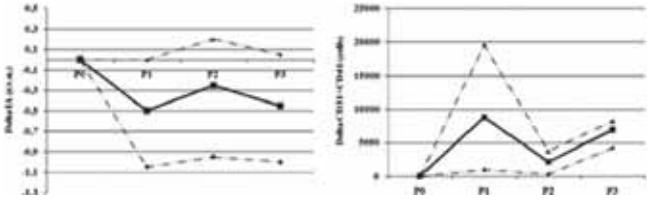

Figure 1

croparticles level (delta CD31 + CD41-) in experiment (median, 10 and 90 percentile) is presented in Fig. 1.
Conclusions: Extreme weather conditions are associated with functional and cellular markers of endothelial damage even in healthy volunteers.

P3198 | BEDSIDE
Severe adverse effects of nocturnal aircraft noise on endothelial function in patients with or being at risk for cardiovascular disease

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Purpose: Multiple epidemiological studies suggest a relationship between aircraft noise exposure and an increased risk for myocardial infarction and stroke. We recently demonstrated adverse effects of noise on endothelial function of healthy volunteers, the effects of nocturnal aircraft noise on endothelial function of patients with cardiovascular disease have never been studied.
Methods: 60 Patients with cardiovascular disease or at increased risk as determined by the Framingham score were in random and blinded order exposed to one night with aircraft noise and one night without noise. Aircraft noise was simulated in the patients bedroom at home and consisted of 60 noise events. Polygraphy was performed during study nights, endothelial function measurement via flow-mediated dilation of the brachial artery, questionnaires and blood sampling were performed on the morning after each study night.
Results: 60 patients (m:w = 44:16) with a mean age of 61 years were analyzed. The average calculated Framingham risk score was 26%. 50 patients carried a diagnosis of invasively established coronary artery disease (CAD). The measured averaged sound pressure levels Leq(3)were 46.9±2.0 dB(A) in the Noise60 nights and 39.2±3.1 dB(A) in the Control nights.
Subjective sleep quality on a visual analogue scale was markedly reduced by simulated aircraft noise from 5.83±2.02 to 3.7±2.20 ($p<0.001$). Flow mediated dilatation of the brachial artery was significantly reduced after night-time aircraft noise exposure (FMD 7.86% ± 3.71) compared to study nights without noise simulation (FMD 9.57% ± 0.56; $p<0.001$). Furthermore systolic blood pressure continuously measured during the night was increased from a mean of 129.5±16.5 mmHg to 133.6±18.1 mmHg (p=0.026) in nights with noise exposure.
Morning adrenaline levels in this patient population did not differ significantly between nights with (38.6±3.8) and without noise exposure (36.8±2.4; p=0.493). Similarly mean heart rate was not significantly different between control and noise nights (60.7±7.9 vs. 61.2±8.0; p=0.286).
Conclusions: The current study demonstrates that night-time aircraft noise substantially impairs endothelial function in in patients with or being at risk for cardiovascular disease.
These adverse effects on vascular function were observed despite the use of vascular protection via medication with statins and blood pressure lowering agents. These findings may explain at least in part, why high blood, myocardial infarction and stroke have been observed as a consequence of nocturnal aircraft noise

P3199 | SPOTLIGHT
Season and outdoor temperature in relation to detection and control of hypertension in a large rural Chinese population

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Objectives: In many Western populations, blood pressure varies moderately with season and outdoor temperature. Relatively little is known about effects of seasonal changes in blood pressure on the detection and control of hypertension in general populations, especially in low- and middle-income countries. We therefore performed this study in a large group of rural adults from China.
Methods: We analysed cross-sectional data of 57,375 (42% men) participants aged 30-79 years who were enrolled during 2004-8, as part of the China Kadoorie Biobank, from a rural county in a south-east costal Province. Analyses related daily mean outdoor temperature, obtained from local Meteorological Bureau, to mean systolic (SBP) and diastolic blood pressure (DBP), rate of newly detected hypertension and, among those with self-reported physician-diagnosed hypertension, rate of adequate blood pressure control, using multiple linear and logistic regression models.
Results: The overall mean blood pressure was 135.9 for SBP and 80.5 mmHg for DBP. Daily outdoor temperature ranged between -2.9 and 33.7℃, with July being the hottest month (29.4℃) and January the coldest (4.0℃). The adjusted SBP/DBP differences between the coldest and warmest month were 19.2/7.7 mmHg. Each 10℃ lower ambient temperature associated with 6.9/2.9 mmHg higher SBP/DBP, 14.1% higher prevalence of newly detected hypertension and, among those with pre-diagnosed hypertension, 13.0% lower hypertension control rate (Figure).
Conclusion: Lower outdoor temperature is associated with higher mean blood pressure and hypertension prevalence as well as poorer hypertension control, and should be considered when conducting and evaluating population-based hypertension survey and providing treatment for hypertensive patients.

P3200 | BEDSIDE
Effects of air pollution exposure reduction by filter mask on heart failure: a prospective randomized double-blind controlled trial

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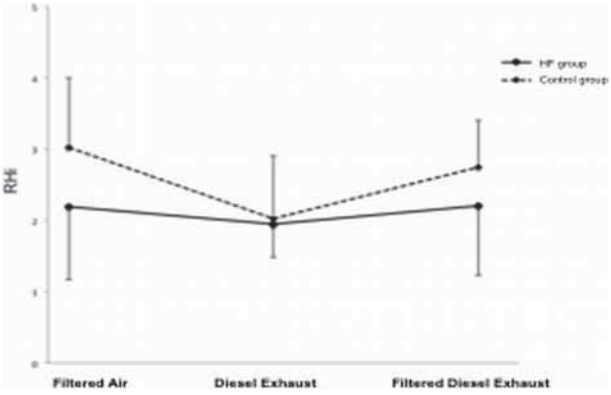
Short-term exposure to air pollution is associated with heart failure (HF) decompensation. A particle retention facemask has the potential to reduce these cardiovascular events. Our purpose is to investigate the effects of reducing diesel exhaust (DE) inhalation on endothelial function (non-invasive reactive hyperemia index - RHi), cardiopulmonar capacity (oxygen uptake-VO2; ventilatory efficiency-VE slope; 6 minute walking test-6mwt) and heart rate variability (HRV) in HF patients, by using a polypropylene filter-mask (FM). In a double-blind, randomized, crossover study, 19 HF patients (HF group) and 8 matched healthy volunteers (control group) were exposed to diluted DE (300 $\mu g/m^3$ particulate concentration), filtered DE or filtered air during 15 minutes of rest and 6 minutes stress testing in a controlled-exposure facility. Clinical and laboratory variables were normal in both groups. DE worsened RHi in both groups [2,5 vs. 1,9; 95%CI 0,01-1,04; (P=0,043)], and this effect was attenuated by the FM (P=0,012) (Figure). There was a significant worsening of VO2 [24,1 vs 14,3 ml/kg/min; 95%CI 16,9-31,3; (P=0,048)] and VE slope [27,5 vs. 38,3; 95%CI 1,7-19,9; (P=0,018)], also attenuated by the FM (P=0,007). However, these intervention significantly reduced both groups 6mwt's [265,9 vs. 211,3m; 95%CI 1,04-108,3; (P=0,045)]. Brief exposure to air pollution did not alter HRV in well-treated HF patients. We concluded that the FM could mitigate the DE inhalation effects on endothelial and cardiopulmonary function in HF patients and healthy volunteers, though it causes respiratory discomfort and reduces the walking distance.



DE inhalation and endothelial function.

Our results, although partial, provide some insight into the mechanisms involving particulate matter and cardiovascular diseases.

P3201 | BENCH
Effects of arsenic exposure and genetic polymorphisms in detoxification metabolism and DNA repair genes on subclinical atherosclerosis in high-exposed population of our country

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Background: Arsenic (As) exposure is an environmental risk factor for atherosclerosis. The individual susceptibility to arsenic-induced atherosclerosis might be associated to the presence of specific genetic polymorphisms in genes involved in arsenic metabolism or in DNA repair.
Aims: The purpose of this study was to evaluate the effect of interaction of As with the presence of common genetic variants in genes implicated in arsenic metabolism (ASIIIMT, GSTT1 and GSTM1) and DNA repair (hOGG1 and XRCC1) on early signs of subclinical atherosclerosis in populations living in four zones of Italy known to be affected by As exposure.
Methods: Two-hundred twenty-nine healthy individuals (112 male mean age=32.6±7.3years) who were residents in the high risk areas were recruited through advertisement in local media. Participants were administered a questionnaire about life habits, work, medical history, and diet in a face-to-face interview. Urinary inorganic As (iAs; including trivalent and pentavalent) and methylated metabolites (monomethylarsinic and dimethylarsinic acid, MMAVand DMA) were measured by mass spectrometry. Carotid intima-media thickness (cIMT) was evaluated by high-resolution B-mode ultrasound with automatic measurements. Genotyping was carried out by PCR-RFLP.
Results: As expected, IMT was correlated with age (ρ=0.50, $p<0.001$) and carotid diameter (ρ=0.49, $p<0.001$). Smokers did not have a significantly higher IMT (p=0.25). There was no correlation between carotid IMT and total As (ρ=0.02, p=0.83), iAs (ρ=0.02, p=0.83), the sum of iAs+MMA+DMA (ρ=0.01, p=0.85) Sub-

jects with a high urinary arsenic level (Asi≥3.86 μg/L) and OGG1 Cys allele had a significantly increased cIMT (0.58±0.1 vs. 0.51±0.1 mm, pintercation=0.004) than those with a low urinary arsenic level (Asi<3.86 μg/L) and OGG1 Ser–Ser genotype.
Subjects with a high urinary arsenic level and carriers of GSTT1-1 genotype also had increased IMT values than those with a low urinary arsenic level and the of GSTT1-0 genotype (0.56±0.09 vs 0.53±0.09 mm; pintercation =0.01)
Conclusions: GSTT1 and OGG1 polymorphisms may play an important role in the individual risk of arsenic-induced carotid atherosclerosis.

P3202 | BENCH
Subclinical carotid atherosclerosis and early vascular aging from chronic low-dose ionizing radiation exposure: a genetic, telomere and vascular ultrasound study in cardiac catheterization laboratory

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Background: There is growing evidence of an excess risk for cardiovascular disease at moderate doses of ionizing radiation exposure. We assessed the association between chronic radiation exposure in the cath-lab and early subclinical atherosclerosis.
Methods: In the Healthy Cath Lab study, 223 staff personal (141 male; age=45±8 years) and 222 unexposed subjects (113 male; age=44±10 years) were evaluated. Carotid intima-media thickness (CIMT) were assessed by high-resolution B-mode ultrasound. Leukocyte telomere length (LTL) was evaluated by qRT-PCR. The interaction between a functional variant Thr241Met in XRCC3 DNA repair gene and radiation exposure was evaluated.
Results: There was a positive linear relationship between left (p<0.0001), right (p<0.0001) and averaged CIMT (p<0.0001) and age. Exposed workers in younger age category (<45 years) had significantly greater values of left (p=0.01), right (p=0.0004) and averaged CIMT (p=0.003) than controls (Fig. 1).

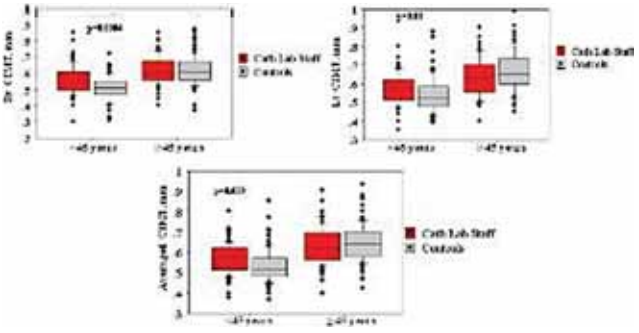

Figure 1

LTL was significantly reduced in exposed personnel compared to controls (0.98±0.2 vs 1.1±0.3, p=0.008). There was a significant correlation between estimated cumulative radiation dose and left (p=0.01), right (p=0.02), averaged CIMT (p=0.001) and LTL (p=0.008). Exposed carriers with XRCC3 Met241 allele had significant increased right (p=0.03), left (p=0.007) and averaged CIMT (p=0.006). XRCC3 Met241 allele presented a significant interaction with years of exposure (≥10) for right (pinteraction=0.0002), left (pinteraction <0. 0001) and averaged CIMT (pinteraction <0. 0001).
Conclusion: Chronic radiation exposure in cath-lab is associated with increased subclinical CIMT and TL shortening, suggesting evidence of early atherosclerosis. Thr241Met XRCC3 variant may alter DNA repair capacity leading to accelerated vascular aging.

P3203 | BEDSIDE
Perceived stress and 6-year incidence of high blood pressure in relation to sex and occupational status: the IPC cohort study

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Purpose: Contrary to lay beliefs, current perceived stress is not consistently associated with an increased incidence of high blood pressure (BP) in prospective studies, possibly because of modulating factors. The present prospective study examined the association between stress and high BP and explored the potential modulating effects of gender or occupational status.
Methods: 19,766 normotensive adults (13,652 men, mean age±standard deviation: 46.8±9.3 years), without history of cardiovascular and renal disease and not on either psychotropic or antihypertensive drugs were included in the Paris IPC cohort study. Perceived stress was assessed at baseline with a 4-item self-administered questionnaire (PSS-4 score, Cohen 1983). High BP was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or using antihypertensive drugs. Occupational status was categorized into 6 classes. Logistic multivariate regression models were used to determine risk of high BP (OR [95% CI]).
Results: After a mean follow-up of 5.8±2.1 years, 3,774 participants (19.1%) had high BP. There was a significant interaction between baseline perceived stress and gender (p=0.02) in relation to high BP at follow-up. After adjustment for potential confounders, baseline perceived stress was associated with high BP at follow-up in women (OR [CI]: 1.20 [1.03-1.38]; p=0.016). In addition, a significant interaction between perceived stress and occupational status was observed in women (p=0.02) but not in men (p>0.05). Baseline perceived stress was positively associated with high BP at follow-up among women of medium or low occupational status, with a linear trend suggesting a linear increase of the risk according to occupational status (p=0.005).
Conclusions: Perceived stress may be considered as a risk marker for hypertension in women of lower occupational status. Research addressing the relationships between stress and high BP should systematically look for possible interactions with gender and occupational status.

P3204 | BEDSIDE
Low vitamin d levels are associated with multimorbidity: the lifelines cohort study

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Purpose: Prevalence of multimorbidity (MM), >1 multifactorial disease within an individual, is rapidly increasing. So far, studies on the relationship between vitamin D (Vit-D) and multifactorial diseases have mainly focused on patients with single disease, while Vit-D exerts numerous effects throughout the human body. Therefore, we studied the association of Vit-D levels with MM and single morbidities.
Methods: LifeLines is a multi-disciplinary prospective population-based cohort study of 165,000 persons living in The Northern Netherlands. For this study, we obtained 25-hydroxyvitamin D levels (25-D) from 8562 subjects. Self-reported questionnaires and baseline assessment were used to define 12 morbidity categories, representing the cardiovascular, central nerve, dermal, endocrine, head & neck, locomotor, renal, respiratory, psychiatric, psychosocial and urogenital systems. Presence of morbidities was used to define MM severity: no MM (0-1), mild MM (2-3), moderate MM (4-5) and severe MM (>5). After seasonal adjustment of 25-D, 4 Vit-D subcategories were created: sufficient >80 nmol/L, hypovitaminosis 50-80 nmol/L, insufficient 25-50 nmol/L, deficient <25nmol/L. Univariate (OR) and multivariable (adjusted OR, corrected for age/gender/eGFR/drug use/BMI/waist hip ratio/smoking and other lifestyle factors) logistic regression analyses were performed to determine the association between MM/single morbidities and 25-D.
Results: Study subjects were aged between 18 - 91 (mean 45.0±12); 27% males with a median BMI of 25 kg/m^2 ((IQR) 23-28). Median 25-D was 58 nmol/L (43-73).
Each SD increase in 25-D was associated with lower MM severity: OR 0.93 (0.9-1.0); adjusted OR 0.94 (0.9-1.0), p<0.05. Subjects deficient for 25-D had more severe MM: OR 1.51 (1.2-1.9); adjusted OR 1.57 (1.3-2.0), p<0.000, compared to subjects sufficient for 25-D.
For single morbidities, the strongest association between deficient 25-D and disease was within the cardiovascular (OR 1.47 (1.2-1.9); adjusted OR 1.53 (1.2-2.0) p<0.001), psychiatric (OR 1.51 (1.1-2.0); adjusted OR 1.44 (1.1-1.9) p<0.05) and endocrine domains (OR 1.31 (1.0-1.8); adjusted OR 1.35 (1.0-1.8) p<0.05).
Conclusion: In this large cohort from the general population, we observed that severe Vit-D deficiency was weakly associated with single morbidities, whilst association with MM was outspoken. This underscores the potential role Vit-D might have for maintaining general health. We propose that future studies should address if Vit-D supplementation may prevent or retard progression of MM instead of focusing on single organ system outcomes.

P3205 | SPOTLIGHT
Birth prevalence and time trends of congenital heart defects in Norway 1994-2009 - a CVDNOR project

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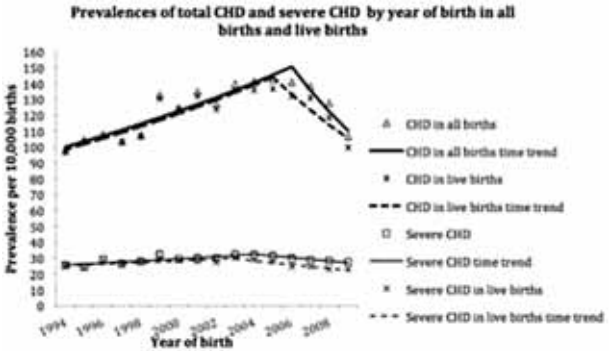
Purpose: In this study we present population-based birth prevalences and time trends of congenital heart defects (CHD) among live births, stillbirths, and terminated pregnancies during 16 years of follow-up.
Methods: CHD diagnoses among all births in Norway, 1994-2009, were ascer-

tained from national health registries and databases; the Medical Birth Registry of Norway, the hospitals' Patient Administrative System, the National Hospital's clinical database for children with heart disease, and the Cause of Death Registry. Using a hierarchical classification system, individuals were assigned specific cardiac phenotypes. Time trends were analyzed using Joinpoint Regression Program.
Results: Among 954,413 births 13,081 were identified with CHD (137.1 per 10,000 births). Live birth prevalence was 133.2 per 10,000. Excluding preterm PDA, CHD prevalence per 10,000 births was 123.4; per year, the prevalence increased with 3.5% (95% confidence interval 2.5, 4.4) in 1994-2005, and declined with 9.8% (-16.7, -2.4) from 2005 onwards. Severe CHD prevalence was 30.7 per 10,000; annual increase was 2.3% (1.1, 3.5) in 1994-2004, and annual decrease 3.4% (-6.6, -0.0) in 2004-2009. The prevalence of severe CHD in live births was 26.7 per 10,000; annual increase in 1994-2003 was 1.8% (0.2, 3.4), and annual decrease in 2003-2009 was 4.6% (-7.3, -1.8). Stillbirths and terminated pregnancies constituted an increasing proportion of births with severe heart defects; 3% in 1994-2007, and 16.9% in 2006-2009.



Conclusions: Although there has been a shift from diagnosing CHD in live births to prenatal diagnosis with the possibility for termination of pregnancy, this could not explain the decreasing live birth prevalence of total CHD and severe CHD from 2005 to 2009 in the present nation-wide study.

P3206 | BEDSIDE
Effect of smoking on the age at incidence of first acute coronary syndrome in patients from 58 European hospitals: the EURHOBOP study

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Purpose: To estimate the contemporary independent effect of smoking on the age at incidence of a first acute coronary syndrome (ACS).
Methods: We studied 13079 episodes of ACS cases consecutively discharged from 58 hospitals in the six participant countries: Finland, France, Germany, Greece, Portugal and Spain, in 2008-2010. The discharge notes and electronic/paper medical files were retrospectively reviewed by trained data extractors. Patients who had previous history of cardiovascular disease (including coronary heart disease, stroke, peripheral artery disease, percutaneous coronary intervention and coronary artery bypass grafting) were excluded from the analysis. Linear regression models were used to compute the age difference of the patients according to smoking status (current smokers vs non-current smokers), adjusting for other major cardiovascular risk factors (diabetes, hypertension, and obesity), in ST elevation acute myocardial infarction (STEMI) and non-ST elevation ACS (NSTE-ACS) patients, by sex.
Results: Of 7456 first ACS patients, 45% had a STEMI, 50% had an NSTE-ACS, 4% had a non-classifiable type of ACS and in 1% that information was not reported in clinical files. The median age of the patients was 64 years (range 19–99 years) and 70% were men. Thirty-five percent of the patients were current smokers (50% of men with STEMI, 25% of women with STEMI, 36% of men with NSTE-ACS and 15% of women with NSTE-ACS). Currently smoking men with STEMI had the first ACS event 10.4 years (95% confidence interval (95%CI): -11.3;-9.5) earlier than those who were non-smokers, independently of the presence of other major risk factors. The corresponding value in men with NSTE-ACS was -10.3 years (95%CI: -11.2;-9.4), in women with STEMI -16.4 years (95%CI: -18.2;-14.7) and in women with NSTE-ACS -14.1 years (95%CI: -15.8;-12.2).
Conclusions: The incidence of a first ACS in European patients occurs more than a decade earlier in smokers. Smoking is a well-established risk factor for ACS, but these results add the potential for delay of ACS with smoking prevention.

HEARTS AND MINDS

P3208 | BEDSIDE
Trajectories of depressive symptoms and aspirin adherence in the 9 months after acute coronary syndrome: an electronic monitoring study

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Purpose: To study objectively-assessed aspirin adherence among patients across 9 months after an Acute Coronary Syndrome (ACS) using an electronic monitoring device and to compare trajectories of aspirin adherence in patients with and without persistent depressive symptoms.
Methods: 97 post-ACS patients were given 9 month supplies of their prescribed aspirin dosage with a Medication Event Monitoring (MEMS) cap that stored the time opened. Patients were administered the Beck Depression Inventory at baseline and 3 months after the event, and their MEMS data was downloaded at 3, 5, 7 and 9 months. Persistently depressed (n=36; BDI score $\geq$10 at baseline and 3 months) patients were contrasted with remittent depressed (n=22 BDI score $\geq$10 at baseline and $<$10 after 3 months) and nondepressed (n=39; BDI $<$10 at both timepoints). Adherence was determined by the percentage of days aspirin was taken as prescribed.
Results: 42% of the patients (35% female, mean age 63$\pm$9.8) took their aspirin on less than 80% of the days across the 9-months period. Mean adherence was 69%, 75%, and 81% in the three groups, respectively, and was significantly lower in the persistently depressed patients compared to the non-depressed patients ($p<0.05$). Adherence did not significantly change across time in any of the three groups.
Conclusions: We found that adherence was poor in over a third of patients and remarkably stable over time. ACS patients with persistent depressive symptoms should be targeted for adherence interventions as they have sustained risk for poor adherence to risk reducing cardiovascular medications.

P3209 | BEDSIDE
Understanding the pathway of education status, clinical characteristics and 10-year incidence of cardiovascular disease: the attica study

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Objective: The pathway by which education affects cardiovascular disease (CVD) risk has not been clearly understood. The aim of this work was to explore the pathway by which education status interacts with medical history, on 10-year incidence of CVD.
Methods: From May 2001 to December 2002, 1514 men and 1528 women ($>$18 y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011-12, the 10-year follow-up was performed in 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria. Education status was measured in years of school; medical history of hypertension, hypercholesterolemia, diabetes at baseline, was evaluated through physical examination of the participants. Lifestyle behaviors and dietary habits were also recorded.
Results: The 10-year CVD incidence was 14.3% in men and 9% in women ($p<0.001$). Age-sex analysis revealed that the higher the education level, the lower the risk of CVD (Relative Risk per 1 additional year of school=0.94, 95%CI 0.92-0.99). Moreover, people in the basic education group ($<$9 yrs) had significantly higher prevalence of hypertension, diabetes, and hypercholesterolemia, were more likely to be sedentary and smokers, and adhere an unhealthier diet, as compared with high education group ($p<0.001$). From the clinical and dietary factors studied, history of diabetes was associated with 85% higher risk of CVD (95%CI 1.20-2.86), history of hypertension was associated with 21% higher risk of CVD (95%CI 0.89-1.63), and history of hypercholesterolemia was associated with 15% higher risk of CVD (95%CI 0.85-1.54). When all factors entered in the model, education status was not anymore associated with CVD risk. Path-analysis revealed that the pathway that mainly characterised those who developed a CVD event was: absence of diabetes $>$ education status below 9 yrs $>$ history of hypercholesterolemia (in that order) and was associated with 3.35-higher risk of CVD events as compared to the reverse categories.
Conclusions: Low education seems to increase CVD risk, an observation that was partially explained by baseline clinical characteristics of people belonging into this group. Public health strategies should focus on low educated people, especially under the prism of the financial crisis, since they seem to be prone for developing CVD more frequently than the others.

P3210 | BEDSIDE
Hostility as a psychosocial risk factor for coronary artery disease in open population aged 25-64 years

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Hostility is sustained negative attitude towards others including cognitive, emotional and behavioral aspects and frequently associated with increased risk factor for coronary artery disease (CAD).
Purpose: To study correlation between the prevalence of high hostility level in patients with and without CAD in open male population aged 25-64 years of Siberian urban city.
Methods: Single epidemiological study was carried out using a standard questionnaire of World Health Organization (WHO) MONICA project ("MOPSY" Hostility Scale). A representative sample of 1000 men was recruited from the voting lists of one of the administrative districts of Siberian urban city. The response rate to cardiac screening was 85.0% (n=850). Different forms of CAD ("definite" and "possible") were determined using standard epidemiological methods (WHO's questionnaire for angina, EGG at rest, Minnesota Code).
Results: The odds ratio (OR) in group with CAD according to extended epidemiological criteria and high hostility level in male population aged 25-64 years was 2.71 (95% CI=1.63±4.52, $p<0.05$). While analyzing the influence of high hostility level on definite and possible CAD the OR was detected as 4.65 (95% CI=2.14±10.12, $p<0.05$) and 1.36 (95% CI=0.69±2.66, $p>0.05$), respectively. Hostility reached its significant maximum in the group of subjects aged 55-64 years and was similar to population aged 25-64 years. Therefore, OR in group with CAD according to the extended epidemiological criteria and high hostility level aged 55-64 years was 5.42 (95% CI=2.32±12.66, $p<0.05$), vs 25.85 (95% CI=3.30±202.60, $p<0.05$) in group with "definite" CAD and high hostility level. Among subjects of age range 55-64 years OR in group with "definite" CAD and hostility was 5.6 times higher compared to population-based index, and in group with CAD according to the extended epidemiological criteria and hostility was twice higher. Male aged 55-64 years with "definite" CAD and high hostility level OR did not reach its statistical significance.
Conclusion: Male responders with CAD demonstrated high hostility level more frequently compared to patients without CAD. The increase of risk for "definite" CAD was observed in subjects with high hostility level. The increase of risk for CAD and "definite" CAD in association with high hostility level reached its significant maximum at 55-64 years.

P3211 | BEDSIDE
Symptoms of anxiety and depression: the impact of diagnostic angiography

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Purpose: Coronary angiography is the gold standard diagnostic test for coronary heart disease (CHD) and the diagnostic results can have an immediate effect on symptoms experienced. Little is known, about the effect of having the diagnostic results on symptoms of anxiety and depression, and in this study the effects of diagnostic angiography on these symptoms was explored.
Method: The study included 780 consecutive patients, with established or suspected CHD undergoing examination both with invasive and CT Angiography. The trial was approved by the regional board of ethics. Data were collected at baseline and after six months. Symptoms of anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). The HADS has a range from 0-21 and optimal cut-off scores above 8 on both scales identify possible cases with anxiety and depression.
Results: The sample comprised 508 men and 272 women with mean age of 63.6 years (SD 10.8). A total of 468 (59.7%) did not have previous CHD. The results indicated that 26% had normal vessels; 20% wall changes (20-49%); and 53% obstructive stenosis (≥50%). At baseline a total of 23.6% and 19.9% in the sample had a score above 8 in the HADS anxiety and depression scales, respectively. After six months these proportions were reduced to 16.5% and 14.6% correspondingly. Among those with and without previous CHD there were no significant differences in baseline mean HADS anxiety or depression scores. Women had a significant higher baseline anxiety score than men (5.5 vs 4.8 p=0.02), otherwise there were no gender differences in scores or changes.
From baseline to six months there were significant improvements in the entire sample ($p<0.001$), in both the anxiety (mean change 0.93) and depression (mean change 0.93) scores. Analysing those without previous CHD, there were significant improvements over time in both anxiety and depression in those diagnosed with normal vessels; mean change 0.77 (p=0.001) and 0.63 (p=0.016) respectively. Likewise, in those with stenosis there were significant improvements; mean change 1.38 ($p<0.001$) and 0.81 (p=0.001), correspondingly. In those with wall changes, there were non-significant smaller improvements (mean change 0.49 and 0.53).
Conclusion: Undergoing diagnostic angiography significantly reduces symptoms of anxiety and depression in both those with stenosis and those with normal coronary arteries. The group being diagnosed with non-obstructive stenosis i.e. 20 -49%, not eligible for revascularization, have a small however not significant improvements in symptoms of anxiety and depression.

P3212 | BEDSIDE
The relationship between inappropriate shock and psychological distress in Japanese implantable cardioverter-defibrillator patients: results from DEF-Chiba study

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Aim: We have designed this study to analyze the relationship between inappropriate shock therapy and the psychological distress of implantable cardioverter-defibrillator (ICD) patients.
Methods: Two hundred and fourteen patients were enrolled in DEF-Chiba Study which refelcts a multi-center prospective study. All patients completed the Florida Shock Anxiety Scale (FSAS), which represents a tool designed to provide a quantitative measure of ICD shock-related distress. We analyzed the difference in the amount of change scores of FSAS before and after shock therapy at 1 year of follow up.
Results: The survival rate was 94.3% a year. The rate of inappropriate and appropriate shock were 4.2% and 5.7% one year past ICD implantation, respectively. There was no significant difference in the change amount of FSAS score between inappropriate and appropriate shock group. (Figure)

The score of FSAS

Shock therapy	Before shock	After shock	Δ	
Inappropriate shock group	185±89	253±123	633±99	P=0.62
Appropriate shock group	185±54	235±74	52±51	P<0.01
Shock therapy	**registration**	**12M**	**Δ**	**P<0.001**
None	160±75	172±88	076±46	

The score of FSAS

Conclusions: Experience of any shock therapy reflects the most important determinant of psychological distress in ICD patients. Therefore, the main goal to reduce distress in ICD patients is to reduce shock delivery by programming the ICD properley, i.e. acitivating antitachycardia pacing and supraventricular tachycardia discriminators, change detection settings accorindg to recent trials.

P3213 | BEDSIDE
Neutrophil to lymphocyte ratio and severity of depression in patients with depressive disorder and its relation with cardiovascular risk factors

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Purpose: Chronic inflammation is associated with cardiovascular (CV) risk fac-

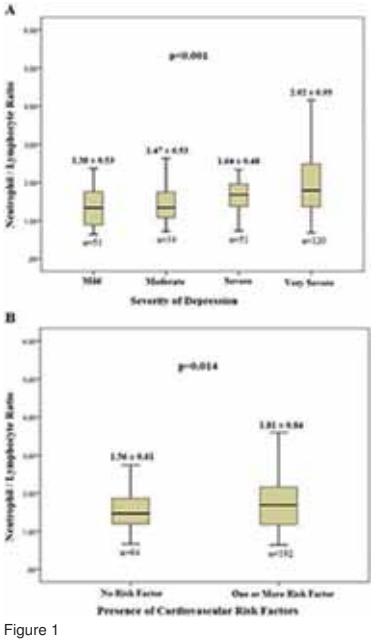

Figure 1

tors and psychiatric disorders. The neutrophil to lymphocyte ratio (NLR) has been investigated as a new predictor for systemic inflammatory response. The aim of this study was to explore the association between NLR and severity of depression and its relation with CV risk factors.
Methods: The study population consisted of 256 patients with depressive disorder. Patients were evaluated with the Hamilton Rating Scale for Depression (HAM-D). Patients were classified into four groups according to their HAM-D score such as mild, moderate, severe, and very severe depression. Patients were also evaluated in terms of CV risk factors.
Results: Patients with higher HAM-D score had significantly higher NLR levels compared to patients with lower HAM-D score (Fig. 1A). Correlation analysis revealed that severity of depression was associated with NLR ($r=0.333$, $p<0.001$) in depressive patients with. Patients with one or more CV risk factors have significantly higher NLR levels (Fig. 1B). Correlation analysis revealed that CV risk factors associated with NLR in depressive patients ($r=0.132$, $p=0.034$). In logistic regression analyses, NLR level was independent predictor of severe or very severe depression (Odds ratio: 3.02, 95% Confidence Interval: 1.867–4.884, $p<0.001$). A NLR of 1.57 or higher predicted severe or very severe depression with a sensitivity of 61.4% and specificity of 61.2%.
Conclusion: Higher HAM-D scores are associated with higher NLR levels in depressive patients. NLR more than 1.57 was independent predictor of severe or very severe depression. A simple, cheap white blood cell count may also give idea about severity of depression.

P3214 | BEDSIDE
Delirium, subsyndromal delirium, and cognitive changes in patients undergoing cardiac surgery

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Purpose: To evaluate incident postoperative delirium (POD) and subsyndromal delirium (SSD) and their risk factors and cognitive impact after cardiac surgery.
Methods: This prospective study enrolled consecutive patients scheduled for cardiac surgery at a tertiary medical center in Taiwan. Patients were excluded if they had symptoms of delirium prior to surgery. Delirium was assessed daily for 10 days after surgery using the Confusion Assessment Method. The SSD was defined as presenting with any core symptom that below diagnostic threshold for delirium. Cognitive function was assessed by the Mini-Mental State Examination.
Results: For this on-going study, 120 participants have been enrolled with a mean age of 62.9 years and 65.8% were males. Surgery type involved isolated valve surgery in 34.2%, isolated coronary surgery in 35.0%, combined coronary and valve in 7.5%, aorta and others in 23.3%. Incident POD was 26.6% while incident SSD was 34.2%. Three major risk factors were identified. Notably, the frequencies of these risk factors for SSD were intermediate between those of risk factors in groups with and without POD. Participants with POD had longest length of stay and lowest cognitive scores, SSD was intermediate, than those without delirium one month after surgery.
Conclusion: Delirium and SSD after cardiac surgery is common. Increasing number and severity of risk factors for delirium may predict increasingly poor outcomes and SSD is intermediate between no symptoms and full delirium. Intervention trials, particularly for patients with increasing number and severity of predisposing and precipitating risk factors are indicated.

P3215 | BEDSIDE
Living with recurrent atrial fibrillation: searching for control and appropriate support

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Background: Living with recurrent atrial fibrillation is often characterized by the unpredictability of incidence, symptom intensity and duration which may have major impact on patients' perception of control in daily life. In addition, patients may experience periods of high disease activity and frequent hospitalizations. However, little is known about how recurrent atrial fibrillation may influence patients' experience of control in daily life. Furthermore, studies examining patients' perception of support from healthcare professionals still seem to be sparse.
Purpose: To describe 1) how recurrent atrial fibrillation may influence patients' experience of control in daily life and 2) how patients perceive support from healthcare professionals.
Methods: A descriptive and explorative qualitative design, including semi-structured interviews with nine patients (eight men and one woman) living with recurrent atrial fibrillation, was used. The participants' mean age was 63 years and the duration of recurrent atrial fibrillation varied from 2-27 years. The interviews were audiotaped, transcribed verbatim and the data were analysed using Systematic Text Condensation.
Results: Two main themes were identified. The first theme "losing control in everyday life" was based on two subthemes: 1) living with unpredictability and 2) living with uncertainty. The second theme "seeking adequate support" was illustrated by the following subthemes: 1) need for consistent information and 2) need for assurance and emotional feedback.
Conclusion: Patients with recurrent atrial fibrillation experience loss of control in everyday life. The diminished control seems to be contributed by the unpredictability and uncertainty associated with the disease. Support from healthcare professionals is perceived insufficient and inconsistent. The patients therefore need to be provided with more adapted information and an individualized schedule for treatment. Also, various psychosocial and emotional aspects associated with the disease must be addressed.

P3216 | SPOTLIGHT
Does treatment experience impact on patients illness perception and behavioural changes in myocardial infarction?

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Background: Treatment for acute myocardial infarction (AMI) differs according to presentation, and there are claims in the literature that this may impact on patients' understanding of their diagnosis, illness perception (IP) and subsequent behavioural changes.
Aim: To determine if the treatment modality (TM) had an impact on IP and secondary prevention outcomes (SPO) across 3 different TM –
ST-Elevation AMI treated by PPCI,
STEMI treated by thrombolytic therapy (THROMB),
Non ST-Elevation AMI (NSTEMI) treated by medication.
Methods: A mixed-methods, repeated-measure design was used to collect data from a cross-sectional sample of patients during hospitalisation and 6 months later. Standardised instruments were used to measure IP, anxiety and depression (AD), coping behaviour and SPO. Qualitative interviews (n=14) were transcribed and thematically analysed.
Results: A total of 186 patients completed questionnaires at both time points. There were no significant differences in IP, AD at baseline. Those treated with THROMB had significantly higher cognitive approach coping scores (p=0.001), and PPCI had significantly higher (p=0.001) quality of life scores compared to the other groups at baseline.
At 6-month follow-up, PPCI patients had Sig. lower personal control (p=0.02), and higher perception of treatment control (p=0.001) and illness coherence (p=0.03) compared to baseline. However, there were no Sig. changes in the other four IP factors, AD, coping factors, or general health.
Examining the SPO change on follow up showed that THROMB patients had significantly higher control of cholesterol (p=0.02), PPCI patients had lower control of blood pressure (p=0.01), and all groups had significantly lower smoking status (p=0.05). Analysis shows THROMB patients had significantly higher activity levels (p=0.001). However, there were no significant changes in body mass index and low density lipoprotein in any group. The qualitative thematic analysis at both baseline and follow-up confirmed the link between IP and motivation to change lifestyle, but did not demonstrate differences in IP between the TMs.
Conclusion: The findings from this study demonstrate a lack of evidence to support the hypothesis that TM impacts on Illness perception, coping and subsequent behavior change across time. Cognitive and behavioural changes did occur, but with no set pattern across TM. PPCI patients had lower personal control and higher treatment control and illness coherence, but these did not impact on SPO at 6 months. Further research with longer follow up is required.

PREDICTING PROGNOSIS AND BLEEDING RISK IN MI AND ATRIAL FIBRILLATION

P3218 | BEDSIDE
Could simple cluster of risk factors, PARADOCS (Pressure of ARtery Abnormality, Diabetes, Obesity, Cholesterol, Smoking) score, predict clinical outcome in patients with acute myocardial infarction?

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Purpose: Conventional risk factors are differently contributed to short-term prognosis of acute myocardial infarction (AMI); hypertension and diabetes increase adverse outcome, whereas hyperlipidemia, smoking, and obesity are paradoxically decrease adverse outcome of post-MI patients. The aim of this study is to assess whether simple cluster of conventional risk factors, PARADOCS (Pressure of ARtery Abnormality, Diabetes, Obesity, Cholesterol, Smoking) score, would improve the ability to predict major adverse cardiac events (MACEs) in patients with AMI.
Methods: Between November 2005 and July 2011, 24,020 patients (17,232 men; mean age = 63.0 ± 12.8 year-old) with a diagnosis of AMI were analyzed in this study from Korean AMI registry. PARADOCS score was calculated on the basis of number of five modifiable risk factors; [number of non-paradoxical risk factors (NRF) – number of paradoxical risk factors (PRF)] + 3 in which non-paradoxical risk factors are hypertension and diabetes, and paradoxical risk factors are hyper-

lipidemia, smoking, and obesity. The 1-year MACEs were defined as death and non-fatal MI.
Results: NRF including hypertension and diabetes were present in 49.6% (n=11,918) and 27.0% (n=6,475), whereas PRF including hyperlipidemia, smoking, and obesity were present in 12.3% (n=2,955), 43.0% (n=10,271), and 34.6% (n=8315), respectively. During the study periods, the number of NRF ($p<0.001$) and PRF (p=0.003) significantly increased over time. During the follow-up, 1,409 (5.9%) MACEs occurred. PARADOCS score was significantly higher in patients with 1-year MACEs (3.38±1.03 versus 2.81±1.08, $p<0.001$). In Cox proportional hazards model, PARADOCS score was an independent predictor of 1-year MACEs (hazards ratio [HR] 1.26, 95% confidence interval [CI] 1.18–1.34; $p<0.001$) after adjusting for confounding variables. Patients were categorized into 3 groups according to the PARADOCS score; PARADOCS-LOW (0-1, n=2,446), PARADOCS-MID (2-3, n=14,594), and PARADOCS-HIGH (4-5, n=6,980). Kaplan-Meier survival curve showed that there were significant differences in the 1-year MACEs among three groups including 3.5% in PARADOCS-LOW, 8.5% in PARADOCS-MID, and 16.4% in PARADOCS-HIGH, respectively (long-rank $p<0.001$). Adjusted HRs for 1-year MACEs were 1 (PARADOCS-LOW, reference), 1.52 (PARADOCS-MID, p=0.23), and 2.07 (PARADOCS-HIGH, $p<0.001$), respectively.
Conclusions: In post-MI patients, conventional risk factors were differently associated with short-term prognosis, and simple cluster score of these risk factors, PARADOCS score, could provide useful prognostic information to clinicians.

P3219 | BEDSIDE
An index for the prediction of in-hospital and 30-day mortality of patients with an acute coronary syndrome

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Aim: To develop a simple index for the risk assessment of 30-day outcome of patients who had had an ACS, using clinical and biological measurements at hospital admission.
Methods: Six national hospitals were enrolled and almost all consecutive ACS patients from October 2003 to September 2004, were recruited (n=2172 patients). Socio-demographic, biochemical, clinical and lifestyle characteristics were recorded. Using as components: age, systolic blood pressure, white blood cells count, CPK-MB, creatinine levels at the time of admission, and the time between the onset of symptoms and presentation at hospital, a risk score (range 6-36) was developed, and tested against in-hospital and 30-day outcome of the patients.
Results: The index demonstrated a strong discriminating ability for in-hospital mortality (AUC=0.812, $p<0.001$) and 30-day after hospitalization death rate (AUC=0.720, $p<0.001$). The score's ability remained significant among several subgroups of patients (i.e., men or women, type of ACS, and diabetes status). Cut-off point analysis revealed that the optimal value of the score, which discriminates those who will die in-hospital from survivors, is 24 and for those who will die at 30-day after discharge is 22.
Conclusion: The proposed index seems to have high discriminating ability, irrespective of sex, type of ACS and diabetes mellitus history. It can be easily applied and will be a useful tool for clinicians to take decisions regarding therapeutic interventions and allocation of clinical resources.

P3220 | BEDSIDE
A prediction model for 30-day unscheduled cardiovascular rehospitalisation following acute myocardial infarction: estimating the risk of readmission in an international registry

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Purpose: Readmission after acute myocardial infarction (AMI) is common and costly. There is a paucity of data that define characteristics associated with AMI readmission. We performed an analysis of the Global Registry of Acute Coronary Events (GRACE) registry to identify predictors of readmission after AMI.
Methods: Data were analyzed from 31649 patients with AMI enrolled in GRACE between 1999 and 2007. Patients with an unscheduled hospitalisation for cardiovascular disease within 1 month of discharge were identified. Stepwise logistic regression analysis was performed to evaluate for independent predictors of 30-day readmission. All univariate predictors of readmission with p values <0.25 were considered for the final model.
Results: 1856 patients (5.9%) were readmitted for a cardiovascular cause within 30 days. The following variables were predictive of readmission: elevated initial serum creatinine level; recurrent ischemic symptoms in-hospital; history of CABG; not having in-hospital catheterization, CABG, or PCI; no in-hospital stress test; history of AMI; in-hospital CHF or pulmonary edema; prescription of insulin at discharge; female gender; increased pulse rate at presentation; and older age. The c-statistic was 0.62. Though the addition of participating hospital to the final model improved the c-statistic to 0.70, this GRACE-specific variable was not included.

Table 1
Predictors of 30-day rehospitalisation

Predictor	Odds ratio (95% CI)	Wald Chi-squared
Initial creatinine level (0.2 mg/dL increase)	1.03 (1.02 to 1.04)	39.9
Recurrent ischemic symptoms in-hospital	1.38 (1.22 to 1.55)	27.1
History of coronary artery bypass grafting	1.41 (1.20 to 1.65)	18.0
No in-hospital cardiac catheterization/coronary artery bypass grafting/percutaneous coronary intervention	1.29 (1.15 to 1.45)	17.8
No in-hospital stress test	1.40 (1.19 to 1.65)	16.5
History of myocardial infarction	1.25 (1.11 to 1.41)	13.0
In-hospital congestive heart failure or pulmonary edema	1.27 (1.11 to 1.46)	11.5
Insulin prescribed at discharge	1.32 (1.12 to 1.55)	11.1
Female gender	1.20 (1.07 to 1.34)	9.5
Pulse at presentation (10 bpm increase)	1.03 (1.01 to 1.06)	7.2
Age (10y increase)	1.05 (1.01 to 1.10)	4.8

CI, confidence interval.

Conclusions: This prediction model identifies the risk of 30-day readmission for cardiovascular causes following AMI.

P3221 | BEDSIDE
Prediction of long-term outcomes in patient with myocardial infarction using locus 9p21.3 risk genotypes

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Background: The identification of 9p21 locus in coronary artery disease (CAD) has been a milestone discovery in cardiovascular genetics. The association between 9p21.3 locus variants and severity of coronary atheromatous burden is well known. However clinical implementation of 9p21 remains unclear. Our study was aimed at investigating association between 9p21.3 locus single nucleotide polymorphisms (SNP) and long-term outcomes in patients with myocardial infarction (MI) didn't underwent of percutaneous coronary intervention (PCI) and treated invasively during hospitalization.
Methods: A total of 500 patients (411 male, 89 female) with MI age younger 65 old (mean 53,35±7,79 years) were recruited in study. All participants gave written informed consent to participation. This investigation was approved by an ethic committee of a state medical university and conformed to the declaration of Helsinki. Genomic DNA was extracted from blood samples by phenol-chloroform method. One SNP (rs1333049) was selected for genotyping on strength of association in previous studies. Genotyping was carried out by real time PCR and subsequent analysis (TaqMan, AB 7900HT). All discharged patients were divided on two groups: patients underwent PCI were included in group 1, patients received conservative treatment (incl. thrombolytic) were joined in group 2. Follow-up prospective period lasted two years.
Results: We revealed a direct strong association of the locus 9p21.3 rs1333049 with worse outcomes (hospitalization due to acute coronary syndrome (ACS) and recurrent MI) in group 2 during follow-up period (12, 24 months). In group 2 patients who carried of risk allele C rs1333049 had significant higher odds ratio of recurrent MI [OR=1,13; 95% CI: 1,07-1,19] and hospitalization due to ACS [OR=1,32; 95% CI: 1,15-1,51] during 1 year after MI. These differences saved after two years follow up for recurrent MI [OR=1,26; 95% CI: 1,12-1,63] and hospitalization due to ACS [OR=1,46; 95% CI: 1,21-1,78]. There were not association in group 1.
Conclusion: For the first time, genotype CC rs1333049 demonstrated a direct strong association with high risk of recurrent MI and ACS duiring 2-years postMI period in patients didn't underwent of PCI. This findings could potentially be applied into clinical practice.

P3222 | BEDSIDE
Cystatin C as a risk factor of thrombotic and bleeding events after elective PCI in patients without severely decreased kidney function: the results of 3 years follow-up

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Cystatin C has been proposed to improve the estimation of glomerular filtration rate (eGFR) and subsequent thrombotic and bleeding risk stratification. The aim of the study was to investigate the role of cystatin C as a predictor of adverse prognosis after elective percutaneous coronary intervention (PCI) in patients without severely decreased kidney function.
Methods: Cystatin C concentrations were measured after successful elective PCI in 254 pts (male 205, mean age 58 yrs) without severe kidney impairment according to creatinine-based eGFR. The frequency of clinical factors with potential impact on renal function was: heart failure – 6%, diabetes – 18%, hypertension – 85%, history of acute coronary syndrome (ACS) – 57%.
Results: The composite end point of thrombotic and bleeding events (vascular death, ACS, stroke/transient ischemic attack, any bleeds) occurred in 24% of pts during a median follow-up of 3.2 years. Relative risk (RR) of events increased with cystatin C level >1500 umol/L: age-adjusted RR 2.8 (95% CI 1.0-7.4, p=0.03), age- and clinical-adjusted RR 2.3 (95% CI 0.9-6.2, p=0.07). No significant associations were found between creatinine-based eGFR and events. Reclassifica-

tion with a combination of creatinine and cystatin revealed reverse J – shaped association with elevated risk at highest (>92 ml/min/1.73m^2) and lowest (<65 ml/min/1.73m^2) quintiles of eGFR distribution. Age- and clinical-adjusted RR were 1.8 (95% CI 0.9-3.2, p=0.07) and 2.1 (95% CI 1.1-4.1, p=0.04) respectively.
Conclusion: Cystatin C is a predictor of thrombotic and bleeding events beyond clinical risk factors and creatinine-based eGFR in patients without severely reduced kidney function.

P3223 | BEDSIDE
Five-year cardiovascular event rates in patients with post-procedural myocardial injury after elective stent implantation

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Background: The prognostic value of troponin-T (TnT) elevation after elective stent implantation is remain controversial and in most studies, a follow-up period is less than two years. The aim of this study was to evaluate the impact of post-procedural TnT elevation on cardiovascular events rate during longer follow-up period in patients with stable coronary artery disease (CAD).
Methods: Among 270 consecutive patients who underwent elective percutaneous coronary intervention (PCI) in our hospital from September 2005 to August 2007, 14 patients with elevated pre-procedural cardiac biomarkers were excluded. Finally, 256 patients were included in this study. TnT was analyzed at baseline and 18 hours after the procedure. Post-procedural TnT levels higher than three times the 99th percentile were defined as post-procedural myocardial injury (PMI). Patients were divided into 2 groups based on the presence or absence of PMI after PCI. The end point of this study was the composite of cardiovascular death and nonfatal myocardial infarction.
Results: In this study, PMI were observed in 28 patients (10.9%), while the remaining 228 patients represented the control group. During the median follow-up period of 5.3 years, 15 events occurred. Event-free survival was significantly lower in patients with PMI (85.7%) as compared to the other group (95.2%) during follow-up period (Log rank p=0.042). In cox analyses, patients with PMI (hazard ratio 3.73; 95% confidence interval 1.09 to 12.78; p=0.036), Age (hazard ratio 1.14; 95% confidence interval 1.04 to 1.24; p=0.004), male (hazard ratio 4.91; 95% confidence interval 1.26 to 19.07; p=0.022) were proven to be independent predictors of cardiovascular death or nonfatal myocardial infarction even after adjustment of confounding factors.
Conclusions: In patients with stable CAD who underwent elective stents implantation, post-procedural TnT elevation was significantly associated with five-years worse clinical outcomes.

P3224 | BEDSIDE
Stroke or systemic embolism in atrial fibrillation with renal insufficiency: from the Fushimi AF registry

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Purpose: Renal Insufficiency (RI) and atrial fibrillation (AF) were both reported to increase the risk of stroke or systemic embolism, however, the effect of RI on that in patients with AF was not fully evaluated.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll AF patients in Fushimi-ku, Kyoto. We have enrolled 3,821 patients from March 2011. RI was defined as estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73m^2 at the index laboratory data. One-year follow-up was completed in 2,966 patients as of December 2013. After excluding 197 patients without laboratory data, 2769 patients finally made up the study population to assess the impact of RI on stroke or systemic embolism in patients with AF.
Results: RI was observed in 1352 patients (48.8%), and stroke or systemic embolism occurred in 76 patients (2.7%) during 12 months follow-up. We added 5 components of stroke predicting index, CHADS2, such as congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, and prior cerebral ischemia into a multiple logistic-regression model. After adjustment of these 6 factors including the status of oral anticoagulant consumption, RI was not independently associated with stroke or systemic embolism in patients with AF [odds ratio (OR): 1.27, 95% confidence interval (CI): 0.78-2.10, p=0.3]. Sensitivity analysis confirmed this result by using the criteria "severe RI" defined as eGFR less than 30 mL/min/1.73m^2 [OR: 1.71, 95% CI: 0.84-3.20, p=0.13].
Conclusions: RI was observed in approximately one-half of patients with AF, and was not associated with stroke or systemic embolism at 1-year follow-up in our study population.

Adjusted multivariate risk factors

Variables	Odds ratio	95% Confidence Interval (lower, upper)	P value
Renal insufficiency	1.27	0.78 to 2.10	0.3
Congestive heart failure	1.34	0.81 to 2.18	0.2
Hypertension	1.35	0.82 to 2.27	0.2
Age ≥75 (elderly)	2.09	1.24 to 3.66	0.005
Diabetes mellitus	1.06	0.61 to 1.76	0.8
Prior cerebral ischemia	2.39	1.47 to 3.84	0.0006
Oral anticoagulant consumption	0.77	0.48 to 1.23	0.3

P3225 | BEDSIDE
Risk-prediction scores and bleeding events in atrial fibrillation: data from the PREFER in AF registry

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Purpose: Despite the clear net clinical benefit of oral anticoagulation (OAC) for the prevention of thromboembolic events in patients with atrial fibrillation (AF), the occurrence of major bleeding may be devastating. Therefore we evaluated bleeding risk scores and the frequency of these events.
Methods: The PREvention oF thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF) prospectively enrolled 7243 unselected patients with AF in Austria, France, Germany, Italy, Spain, Switzerland and the United Kingdom from Jan 2012 to Jan 2013 in 461 centres. The mean age was 71.5±11 years, and 60.1% were male. The mean CHA2DS2-VASc score at baseline was 3.4±1.8 and the mean HAS-BLED score 2.0±1.2, with 30% of patients presenting a score ≥3. Frequency of the factors that determined the HAS-BLED score were: age >65 years 75%, hypertension 56.4%, drug use 27.3%, labile INRs 13.5%, prior stroke 8.9%, prior bleeding 4.9%, alcohol abuse 2.5%, abnormal renal function 13.7% and abnormal liver function 2.0%. 85.6% of patients with CHA2DS2-VASc score ≥2 received OACs (4793 of 5600), and 70.1% of those with CHA2DS2-VASc score of 1 (468 of 668). Most frequent contraindications for OAC were bleeding predisposition (4.5%), active cancer (3.2%), lack of compliance (2.6%) and a previous bleeding event (2.3%).
Results: Both thromboembolic and bleeding risk were considered to be high in the population included in this registry as assessed at baseline. Subsequently 135 (2.5%) major bleeds that required hospitalization occurred during 1-year follow-up. 14 were intracranial haemorrhages, 36 bleeds appeared in critical organs different than the brain and 109 were major bleeds of other location. HAS-BLED score was significantly higher in patients receiving Vitamin K antagonists (VKA) + antiplatelet (AP) treatment, or AP alone (2.6 and 2.4 respectively) than those receiving VKA only, a new oral anticoagulant (NOAC) or with no preventive treatment (1.7, 1.9 and 1.3 respectively). The corresponding unadjusted bleeding rates in patients with VKA + AP, AP therapy alone or OAC (VKA only or NOAC) were 4.4, 1.8 and 2.4 bleeds per 100 patient-years, respectively. Interestingly, patients with no antithrombotic treatment presented an unexpectedly high 2.7% of annual bleeds.
Conclusions: Bleeding events are relatively frequent in patients with AF. The combined use of OAC and AP therapy entailed the highest bleeding rates as predicted by HAS-BLED, whereas the group of patients without antithrombotic treatment also presented a higher than expected bleeding rate, which was not adequately predicted by HAS-BLED.

P3226 | BEDSIDE
Usefulness of combined syntax and has-bled score for predicting major bleeding in patients with atrial fibrillation undergoing percutaneous coronary intervention

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Background: Oral anticoagulant therapy (OAC) with dual antiplatelet therapy increases the risk of hemorrhagic complications in patients with AF undergoing percutaneous coronary intervention (PCI). The HAS-BLED score has simply assessed the risk of major bleeding in patients with AF and OAC. On the other hand, the SYNTAX Score, reflecting coronary lesion complexity, predict clinical outcomes in patients undergoing PCI, it remains unclear whether the SYNTAX score can predict major bleeding events in patients with AF after PCI. We investigated whether the combination of SYNTAX and HAS-BLED score could im-

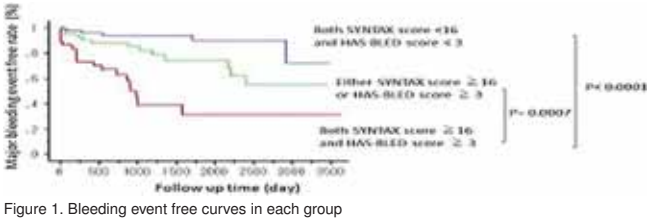

Figure 1. Bleeding event free curves in each group

prove the prediction of major bleeding events in patients with AF undergoing PCI.
Methods and results: We studied 158 consecutive patients (72.8% men, mean age 73±9 yrs) with AF undergoing PCI. We evaluated clinical data, laboratory finding, the phase of diagnostic coronary angiography, and obtained SYNTAX and HAS-BLED score. We respectively defined high risk as SYNTAX score ≥16 and HAS-BLED score ≥3, according to median value (SYNTAX score: 15, HAS-BLED score: 2). During the follow-up period of 1309±974 days, 37 patients had major bleeding events. Kaplan-Meier analysis revealed that patients with both risk factors had significantly higher risk of major bleeding events than those with either (p=0.0007) and without (P<0.0001) risk factors.
Conclusion: The Combination of SYNTAX and HAS-BLED score is useful for predicting major bleeding events in patients with AF undergoing PCI.

P3227 | BEDSIDE
Is the decision to anticoagulate elderly patients with atrial fibrillation driven by stroke or bleeding risk? results from the registry of atrial fibrillation to investigate new guidelines (RAFTING)

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Purpose: According to current guidelines, patients with atrial fibrillation (AF) at high thromboembolic risk as assessed by the proposed CHA2DS2VASc score should be treated with oral anticoagulants (OAC). By definition, all patients ≥75 year old have a score that dictates OAC. In this report, we recorded the anticoagulation attitudes of treating physicians in elderly AF patients and tried to assess whether the clinical decision is driven mainly by stroke or bleeding risk.
Methods: RAFTING was a country-wide prospective observational study of the Hellenic Cardiological Society that enrolled 1127 patients with AF diagnosis during their admission for any reason in the Emergency Departments of 31 representative hospitals in Greece; 807 pts had known AF and of those, 342 were ≥75 year old. We recorded the current anticoagulation treatment and associated it with clinical characteristics.
Results: Patients on OAC (207; 61%) in comparison with pts not on OAC (135; 40%) were younger (81±4 vs 83±5; p<0.001) and tended to have less frequently paroxysmal AF (31% vs 40%; p=0.098) and fewer previous bleeding episodes (11% vs 19%; p=0.098). Otherwise, there were no significant differences in clinical variables including prior stroke, renal dysfunction, peptic ulcer, alcohol consumption, tendency to fall and mean CHA2DS2VASc or modified HASBLED scores. OAC had been prescribed more frequently in patients with CHA2DS2VASc score >4 compared to score 2-4 (65% vs 55%; p=0.065) and equally in patients with low (0-2) or higher (>2) modified HASBLED score (61% vs 59%; p=0.78). The interaction between CHA2DS2VASc and modified HAS-BLED score was significant (p<0.001) in patients receiving OAC. Patients with a lower bleeding risk received OAC in 58% vs 64%, if CHA2DS2VASc score was lower or higher, respectively (ns); patients with a higher bleeding risk received OAC in 43% vs 66% if CHA2DS2VASc score was lower or higher (p=0.087).
Conclusion: In this representative country-wide registry of AF, 61% of elderly pts with AF received OAC. The decision to use OAC was driven more by stroke than bleeding risk. At national level, a wider application of bleeding scores could increase the overall use of OAC if low risk is ascertained.

BIOMARKERS: INFLAMMATION, OXIDATIVE STRESS AND VASCULAR FUNCTION

P3229 | BEDSIDE
The association of oxidative stress biomarkers with cardiovascular risk: prospective results from the HAPIEE cohorts

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Purpose: Oxidative stress leads to cellular and tissue damage and it has been proposed that it is associated with increased rates of age-related conditions, including cardiovascular diseases (CVD). We examined the association between fatal and non-fatal CVD and plasma biomarkers of (i) oxidative stress (assessed by derivates of reactive oxygen metabolites [d-ROM], (ii) biological antioxidant activity (BAP), and (iii) redox control status (assessed by total thiol levels [TTL]).
Methods: We conducted a case-control study nested in the Health, Alcohol and Psychosocial factors In Eastern Europe (HAPIEE) prospective cohorts based in Krakow (Poland), Kaunas (Lithuania) and 6 Czech towns. The cohorts were established in 2002-06; after median follow up of 6.5 years, plasma samples from 495 new cases of CVD (including 198 deaths) and 4,884 controls aged 45-69 years at baseline were analysed in a central laboratory. Subjects with previous history of CVD were excluded. Odds ratios for cohort-specific quartiles and continuous measures of d-ROM, BAP and TTL were estimated by logistic regression models controlling for potential confounders.
Results: After controlling for age, sex, study centre, smoking, education and material deprivation, the odds ratios of CVD death per 1 SD increase in biomarkers were 1.32 (95% CI 1.19-1.47) for d-ROM, 1.17 (1.00-1.6) for BAP and 0.75 (0.65-0.87) for TTL. For non-fatal CVD, the adjusted odds ratios per 1 SD deviation were 1.08 (0.98-1.20), 0.87 (0.75-1.01) and 0.91 (0.79-1.05), respectively; the odds ratio for fatal and non-fatal CVD combined were 1.20 (1.11-1.29), 1.00 (0.89-1.12) and 0.82 (0.74-0.92), respectively. Results were consistent across cohorts. For total and fatal CVD, the odds ratios by quartile of d-ROM and TTL followed a dose-response pattern. Excluding first 2 years of follow up did not affect the results. As expected, among the used covariates, smoking made the largest contribution to attenuation of odds ratios.
Conclusions: These results suggest strong and significant association between fatal CVD and biomarkers of oxidative stress and redox control status in the predicted direction. The absence of a significant association of any of the biomarkers with non-fatal disease may reflect incomplete case recruitment or less severe disease; alternatively, oxidative status may also be implicated in case-fatality of CVD events. The role of oxidative stress markers in CVD requires further investigation.

P3230 | SPOTLIGHT
Plasma endothelin-1 and risk of obstructive sleep apnea among young and healthy adults

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Introduction: Recently, obstructive sleep apnea (OSA) has been linked to endothelial dysfunction, a major precursor of cardiovascular disease. The aim of this study was therefore to assess the relationship between plasma levels of endothelin-1 (ET-1) and OSA among young and healthy adults.
Methods: We performed a population-based study among 882 healthy adults aged between 25 and 41 years in the Principality of Liechtenstein. Individuals with prevalent cardiovascular disease, diabetes or a body mass index >35 kg/m^2 were excluded. ET-1 was measured from plasma samples using a novel single-molecule counting technology (research-use-only). All individuals underwent nighttime pulsoximetry with nasal flow measurement. OSA was defined as apnea-hypopnea index (AHI) ≥5 (n=96). Multivariable logistic regression analyses with elevated AHI as outcome variable were used to assess the relationship between ET-1 and OSA.
Results: Median age of our population was 36 years. 11% of participants met criteria for OSA. Median ET-1 levels in subjects with OSA were 3.0 pg/ml (interquartile range [IQR]: 2.6, 3.8) and without OSA 2.5 pg/ml (IQR: 2.0, 3.0; p<.0001), respectively. In multivariable logistic regression models, log-transformed ET-1 was significantly associated with an increased risk of OSA (odds ratio: 5.8 [95% confidence interval: 2.7, 12.6]) (Table).

Plasma endothelin-1 and risk of OSA

	Obstructive sleep apnea	
n=882	OR (95% CI)	P value
Crude model	7.0 (3.6, 13.8)	<0.0001
Age- and sex-adjusted model	5.5 (2.8, 11.2)	<0.0001
Multivariable model †	5.8 (2.7, 12.6)	<0.0001

Logistic regression analysis. CI, confidence interval; OR, odds ratio. Endothelin-1 was log-transformed. †Additional adjustment for body mass index, estimated glomerular filtration rate (CKD-EPI-formula), smoking, systolic and diastolic blood pressure, low density lipoprotein, high density lipoprotein, triglycerides, HbA1c, and high sensitive C-reactive protein. The models were based on data of 882 participants.

Conclusions: Elevated plasma levels of ET-1 are strongly associated with an increased risk of OSA among young and healthy adults. These findings underscore the potential adverse effects of OSA on endothelial function, which may be one mechanism by which OSA is associated with future cardiovascular events.

P3231 | BEDSIDE
Reduction of C-reactive protein is associated with reduced risk of myocardial infarction. A meta-analysis of 16 randomized trials

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Purpose: The association between C-reactive protein (CRP) levels and risk of cardiovascular (CV) events has been reported in several studies. However, it is unclear whether a reduction in CRP is associated with an equal reduction in risk of clinical events. Therefore we sought to investigate, in a meta-regression analysis of randomized studies enrolling patients treated by statins, whether changes in CRP are associated with changes in risk of myocardial infarction (MI) and stroke.

Methods: MEDLINE, ISI Web of Science, Cochrane Database and Scopus were searched for randomized trials enrolling patients treated by statins, reporting CRP at baseline and at end of follow-up and CV events [MI and stroke].
Results: Sixteen trials enrolling 49,407 participants were included in the analysis. Meta-analysis showed that active treatment significantly reduced the risk of myocardial infarction by 10.1% (RR: 0.899; 95% Confidence Interval [CI]: 0.851 to 0.949; p<0.001) and the risk of stroke by 9.6% (RR: 0.904; CI: 0.824 to 0.992; p=0.033). Meta-regression analysis revealed that reduction of CRP was significantly associated with reduction of MI (Regression Coefficient [RC]: 0.016; CI: 0.001 to 0.031; p=0.036), whereas no relationship was identified between changes in CRP and risk of stroke (RC: 0.008; CI: -0.037 to 0.054; p=0.703).
Conclusions: These findings demonstrate a significant correlation between the reduction of CRP and the risk of MI in high-risk patients enrolled in randomized clinical trials, reinforcing the concept that CRP represents a valid surrogate for coronary risk.

P3232 | BEDSIDE
Body mass index significantly modulates the power of C-reactive protein to predict cardiovascular event risk among angiographied coronary patients

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Purpose: Epidemiological studies in various populations show that obesity is associated with inflammation and with increased cardiovascular risk, and that the inflammatory marker C-reactive protein (CRP) strongly predicts the incidence of cardiovascular events. Whether CRP is equally predictive of cardiovascular event risk in obese patients and in non-obese subjects is not known and is addressed in the present study.
Methods: Cardiovascular events were recorded over a follow-up period of 10 years in a large high-risk population of 1731 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Obesity was defined as BMI ≥30kg/m^2.
Results: At baseline, CRP surprisingly was significantly higher in non-obese subjects (n=452) than obese individuals (0.6±1.5 vs. 0.5±0.8 mg/dl; p<0.001). Prospectively, 27.8% of our patients suffered vascular events. CRP proved to be a strong and independent predictor of vascular events in non-obese subjects (HR 1.13 [1.06-1.20]; p<0.001) but not in obese subjects (HR 1.08 [0.94-1.235]; p=0.262). An interaction term BMI x CRP was significant (p<0.001), indicating that the body mass index significantly modulated the power of CRP to predict vascular events.
Conclusions: From the results of this large 10-year prospective cohort study we conclude that obesity significantly modulates the power of CRP to predict cardiovascular event risk among angiographied coronary patients.

P3233 | BEDSIDE
Creatinine, eGFR and association with myocardial infarction, ischemic heart disease and early death in the general population

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Aim: We tested the hypothesis that moderately elevated plasma creatinine levels and decreased levels of estimated glomerular filtration rate (eGFR) are associated with increased risk of myocardial infarction, ischemic heart disease, and early death in the general population.
Methods: We studied 10,489 individuals with a plasma creatinine measurement and calculated eGFR from the Danish general population, of which 1,498 developed myocardial infarction, 3,001 ischemic heart disease, and 7,573 died during 32 years follow-up.
Results: Cumulative incidences of myocardial infarction and ischemic heart disease as a function of age increased with increasing levels of creatinine, and survival decreased (log-rank trends: <0.001). The median survival age was 78.7 (95%CI: 78.0-79.2) years for persons with creatinine levels <90th percentile, 78.1 (76.3-79.5) years for 90th-94th percentiles, and 74.8 (72.8-76.7) years for ≥95th percentile. Hazard ratios for plasma creatinine levels of 90th-94th percentiles and ≥95th percentile versus <50th percentile were 2.06 (95%CI: 1.67-2.56) and 1.90 (1.56-2.31) adjusted for gender and age, and 1.35 (1.09-1.68) and 1.11 (0.90-1.36) adjusted multifactorially, respectively. Corresponding estimates for creatinine and ischemic heart disease were 1.57 (1.33-1.85) and 1.64 (1.42-1.89) adjusted for age and gender, and 1.16 (0.98-1.37) and 1.11 (0.95-1.29) adjusted multifactorially. Finally, corresponding values for early death were 1.18 (1.06-1.32) and 1.43 (1.30-1.57), and 0.97 (0.87-1.09) and 1.13 (1.02-1.24), respectively. Low eGFR did not associate consistently with increased risk of either endpoint.
Conclusions: In the general population, moderately elevated plasma creatinine was associated with increased risk of myocardial infarction, ischemic heart disease, and early death, while low eGFR was not.

P3234 | BEDSIDE
Adiponectin, adiponectin/leptin ratio, arterial stiffness, hypertension and obesity related disorders in adolescents girls with obesity

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Obesity is associated with numerous comorbidities. The dysregulation of adipokines production by the adipose tissue may promote obesity related disorders and CVD. Adiponectin in women predicts hypertension (HT) and pulse wave velocity (PWV). However, have not been fully clarified relationships between adipokines and obesity related comorbidities in young females.
The aim of the study was to compare levels of adiponectin, adiponectin/leptin in obese adolescent girls with and without HT and to evaluate association of adipokines with obesity related disorders and arterial stiffness in obese adolescent girls.
Methods: 75 adolescent girls (16,6±1,95, range 14-20 years) with obesity (BMI 35,2±4,2, range 30-42 kg/m^2) were included: 34 untreated hypertensive and 41 normotensive. Serum levels of lipids, fasting glucose, insulin, total adiponectin, leptin, HbA1C; HOMA-IR were measured. Arterial stiffness was assessed with carotid-femoral PWV. 24-hour ABPM was performed.
Results: Age, BMI, waist circumference (WC), total cholesterol, LDL, HDL, triglycerides (TG), glucose, insulin, HOMA-IR, leptin, PWV were similar in both groups. Levels of adiponectin (8,09±5,42 vs 25,7±25,5μg/ml, p=0,02), adiponectin/leptin ratio (0,16±0,11 vs 0,71±0,55, p=0,01) were lower, HbA1C (6,12±0,64 vs 5,31±0,53%, p<0,01), dyslipidemias (82% vs 50% p<0,01) were higher in pts with HT than in normotensive. All pts were categorized according to tertiles of adipokines levels. Pts from low tertile of adiponectin had higher TG, HOMA-IR, PWV and presence of HT than pts from higher tertiles. Pts from upper tertile of leptin had higher WC and TG only. In total group adiponectin levels correlated with WC, TG, HOMA-IR, PWV, HT, mean SBP (day, night, 24-h). Leptin levels correlated with age, WC, TG, mean nightSBP. Adiponectin/leptin ratio correlated with WC, TG, PWV, HT, mean daySBP. Multiple regression analysis among age, BMI, WC, HOMA-IR, HT, dyslipidemia revealed that determinants for adiponectin were HOMA-IR (beta=-0,55), HT (beta =-0,85), presence of dyslipidemia (beta =-0,74, p<0.05), and no indepent predictors for leptin and adiponectin/leptin ratio. In multivariate analysis, the independent predictors for PWV were age (beta=0,44) and levels of adiponectin (beta=-0,57).
Conclusion: Hypertension in obese adolescent girls is associated with dyslipidemia, higher levels of HbA1C, lower levels of adiponectin and adiponectin/leptin ratio. Low levels of adiponectin could prove beneficial for early identification of adolescent girls with obesity related comorbidities (hypertension, insulinresistance, dyslipidemia) and arterial stiffness.

P3235 | BEDSIDE
A comparison of nitroglycerine-induced vasodilation with flow-mediated vasodilation as a cardiovascular risk marker

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Objective: Nitroglycerine-induced vasodilation, a response to a sublingually-administered 75 μg nitroglycerine tablet in the brachial artery, has been used as a control test for flow-mediated vasodilation (FMD) to differentiate endothelium-dependent from endothelium-independent response when evaluating endothelial function in humans. Recently, nitroglycerine-induced vasodilation has also been reported to be impaired in patients with atherosclerosis. The purpose of this study was to determine the relationships between nitroglycerine-induced vasodilation and cardiovascular risk factors.
Methods and results: We measured nitroglycerine-induced vasodilation and FMD in 436 subjects who underwent health examinations (mean age, 53±19 years; age range, 19 to 86 years), including patients with cardiovascular diseases. There was a significant relationship between nitroglycerine-induced vasodilation and FMD (r=0.42, P<0.001). Univariate regression analysis revealed that nitroglycerine-induced vasodilation correlated with age (r=-0.34, P<0.001), systolic blood pressure (r=-0.32, P<0.001), diastolic blood pressure (r=-0.24, P<0.001), heart rate (r=-0.21, P<0.001), glucose (r=-0.23, P<0.001), and smoking pack year (r=-0.12, P=0.01) as well as Framingham risk score (r=-0.30, P<0.001). We categorized subjects into 4 groups: no risk group (n=30), at-low risk group (subjects with 1 risk factor, n=146), at-high risk group (subjects with ≥2 risk factors, n=148), and CVD group (subjects with established cardiovascular disease, n=106). Both nitroglycerine-induced vasodilation (15.3±4.3% vs. 15.1±5.6% vs. 12.4±4.9% vs. 10.5±5.6%, P<0.001) and FMD (7.5±2.4% vs. 5.2±2.7% vs. 3.8±2.6% vs. 3.2±2.3%, P<0.001) were gradually impaired according to the severity of atherosclerosis. There was a significant difference between the no risk group and at-low risk group in FMD (P<0.001), but not in nitroglycerine-induced vasodilation (P=0.84). In contrast, there was a significant difference between the at-high risk group and CVD group in nitroglycerine-induced vasodilation (P=0.006), but not in FMD (P=0.08).

Conclusions: These findings suggest that nitroglycerine-induced vasodilation may be a marker of the grade of atherosclerosis. Nitroglycerine-induced vasodilation is a useful marker for identifying subjects with advanced atherosclerosis, whereas FMD is an appropriate marker for detecting asymptomatic subjects at an early stage of atherosclerosis.

P3236 | BEDSIDE
Effects of highly specific lipoprotein(a) reduction on the soluble markers of atherosclerosis and inflammation

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Aim: There are no interventional studies evaluating the association between specific lipoprotein(a) (Lp(a)) removal and soluble markers of atherosclerosis and inflammation in patients with Lp(a) excess.
Methods: We recruited 43 stable CHD patients (mean age 53.9±14.7 years, 65% male) with Lp(a) level ≥50 mg/dL and LDL-C level ≤2.6 mmol/L on atorvastatin therapy. Fifteen patients from active group were also treated with weekly Lp(a) apheresis using highly specific "Lp(a) Lipopak"® columns. Measurements of high sensitivity C-reactive protein (hsCRP), lipoprotein-associated phospholipase A2 (Lp-PLA2), and oxidized LDL (oxLDL) were performed at baseline and after 18-month period. Blinded quantitative coronary angiography was carried out at baseline and follow-up.
Results: Initially groups were comparable according to traditional risk factors distribution. At baseline Lp(a) and LDL-C levels were as follows: 107±27 mg/dL and 2.2±0.2 mmol/L in Lp(a) apheresis group, and 95±46 mg/dL and 2.3±0.3 mmol/L in control group. Acute effects of specific Lp(a) apheresis (difference before and immediately after procedure) resulted in a 73±5% reduction in Lp(a), producing a final mean of 29±16 mg/dL; corrected for Lp(a) LDL-C was decreased by 7±3% to 1.9±0.2 mmol/L. In atorvastatin-only group no significant changes in lipid parameters were obtained by the end of the study. After 18-month follow-up in specific Lp(a) apheresis regimen, Lp-PLA2 concentration was reduced by an average of -41% (-52% to -22%, p=0.0005), hsCRP levels were also decreased significantly: -38% (-54% to -20%, p=0.003), whereas no relevant changes were seen in oxLDL levels -13% (-29% to 26%, p=0.26). Over the study period there were no significant changes in biomarkers in control group. Addition of Lp(a) apheresis resulted in significant coronary atherosclerosis regression. The mean change in angiographic percent diameter stenosis had positive correlation only with relative changes in Lp(a) levels (r=0.33, p<0.05).
Conclusion: In a prospective clinical study we demonstrated a relationship between isolated Lp(a) decrease and reduction in hsCRP and Lp-PLA2 levels, implicating Lp(a) in proinflammatory pathways of atherogenesis. There was no association between Lp(a) and analyzed form of oxidized LDL.

P3237 | BEDSIDE
Cardiac biomarkers pmmp-9, il-6, and et-1 are elevated in asymptomatic patients at risk for heart failure and associate with disease severity

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Purpose: Current ACC/AHA guidelines recommend measuring the cardiac biomarker BNP to inform clinical decisions in ambulatory heart failure patients. Other biomarkers that reflect inflammation or endothelial function may help diagnose, assess severity, and prognosticate heart failure. This study tested the association of the novel biomarkers Interleukin-6 (IL-6), endothelin-1 (ET-1), and matrix metalloproteinase-9 (pMMP-9) with ACC/AHA stages of heart failure.
Methods: 200 patients (age 54±15 yrs) were selected from our institution's registry according to the following ACC/AHA stages: A (cardiac risk factors without disease), B (structural disease without symptoms), C (structural disease with current or past symptoms), D (refractory heart failure). Plasma IL-6, ET-1, and pMMP-9 were measured using high sensitivity single-molecule counting technology. The upper limit of normal values are 4.5 pg/mL, 3.7 pg/mL and 13 ng/mL for IL-6, ET-1 and pMMP9 respectively.
Results: IL-6, ET-1, and pMMP-9 were elevated in all stages of heart failure, including stage A, where patients are asymptomatic and have no structural disease, but are at risk (Table). The levels of IL-6 and ET-1 increased progressively according to ACC/AHA stage, but pMMP9 only increased significantly with stage D heart failure (Table). Using a 75th percentile cut-off, the ordinal odds ratios for predicting an elevated ACC/AHA stage were 3.8 (2.0,7.2), 3.2 (1.7,6.1), and 3.6 (1.9,6.7) for IL-6, ET-1 and pMMP-9 respectively. In aggregate, the odds ratio for IL-6, ET-1, and pMMP-9 was 9.0 (2.0,39.7). All odds ratio models remained statistically significant after adjustment for age and sex.

Plasma biomarker levels across HF stages

	Stage A (n=26)	Stage B (n=43)	Stage C (n=66)	Stage D (n=65)	P value for trend
IL-6 (pg/mL)	5.6 (2.9,8.5)	7.9 (4.9,12.1)	8.2 (4.6,12.0)	17.4 (10.1,43.0)	P<0.0001
ET-1 (pg/mL)	3.9 (3.1,5.3)	4.4 (3.6,5.6)	4.5 (3.8,5.7)	5.6 (4.5,7.8)	P<0.0001
pMMP-9 (ng/mL)	15.1 (8.2,27.2)	14.3 (8.0,25.9)	13.4 (8.1,20.9)	31.1 (12.8,63.1)	P=0.0008

Values are median, interquartile range.

Conclusion: The novel biomarkers of inflammation and endothelial function pMMP-9, IL-6, and ET-1 are elevated in heart failure and increase progressively with higher ACC/AHA stage. These biomarkers are elevated early (stage A or B), prior to the development of symptoms. Future analysis of this cohort will determine whether a multi-marker panel can be used early to identify individuals at risk for disease progression, morbidity, and mortality.

BLOOD PRESSURE TREATMENT

P3239 | BEDSIDE
Clinical effectiveness of combined antihypertensive therapy in patients with diabetic nephropathy and different salt sensitivity of blood pressure

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Purpose: Assess the clinical effectiveness of combined antihypertensive therapy depending on the salt sensitivity of BP in patients with diabetic nephropathy.
Methods: 40 Patients with NIDDM (avg. age 63.2±1.2 years) and diabetic nephropathy combined with diabetic nephropathy and hypertension were examined. The patients were randomized into 2 groups (20 patients in each group) comparable in terms of age, sex, duration of disease. Patients of the first group were on a fixed combination of 2 drugs, perindopril 5 mg and indapamide 1.25 mg, patients of the second group – on free combination of valsartan 80 mg and indapamide SR 1.5 mg for 2 months. 24-Hour BP monitoring was conducted in patients twice using ABPM 04 (Hungary) apparatus. Dynamics of GFR (by MDRD) and 24-hour microalbuminuria were identified. Salt sensitivity of BP was evaluated by the (Weinberger MN, 1986) method. Patients with office-measured SBP reduction by 10 mm Hg and more when switching over from a diet with a high salt content (250 mmol) to a low salt (50 mmol) diet were considered to be salt sensitive.
Results: After 2 months of therapy, avg. SBP in patients of the first group decreased from 152.75±1.5 to 128.4±0.9 mmHg (p<0.01), avg. DBP - from 88.95±1.9 to 75.45±0.7 mm Hg (p<0.05); in patients of group 2 from 153.2±1.3 mm Hg to 133.7±0.9 (p<0.05) and from 89.15±1.9 to 77.85±0.9 mm Hg (p<0,05), respectively. Both combinations of drugs were most effective in patients with salt-sensitive type of hypertension: administration of perindopril and indapamide in salt-sensitive patients resulted in absolute reduction of avg. SBP by 27.8±0.7 mm Hg vs 18.3±0.4 mm Hg in salt-resistant ones, p<0.01, avg. DBP decreased by 13.7±1.5 mm Hg vs 9.0±1.08 mm Hg, p<0.05, respectively; administration of valsartan and indapamide in salt-sensitive patients resulted in avg. SBP decrease by 18.4±0.7 mm Hg vs 12.2±0.5 mm Hg in salt-resistant ones, p<0.01, avg. DBP – by 10.3±1.2 mm Hg vs 6.7±0.9 mm Hg p<0.05, respectively. After 2 months of therapy, the patients in first group demonstrated an increase of GFR by 10.0±0.16 ml/min/1.73 m^2 and reduction of microalbuminuria from 25.7±0.64 to 20.4±1.0 mg/day, p<0.05 regardless of salt sensitivity of BP, indicating the improvement of renal function.
Conclusions: 1. Both combinations of drugs showed a comparable antihypertensive effect, which was significantly more pronounced in salt-sensitive patients, with perindopril and indapamide having demonstrated a nephroprotective effect. 2. Determination of salt sensitivity of BP allows optimizing individual antihypertensive therapy.

P3240

ABSTRACT WITHDRAWN

P3241 | BEDSIDE

Association between insomnia and use of BP-lowering drugs in hypertensive patients: a cross-sectional cohort study

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Purpose: Insomnia and short sleep duration have been associated with increased prevalence, incidence and severity of hypertension. However, the relationship between insomnia and use of different antihypertensive drug classes has not been ascertained yet.
Methods: 371 hypertensive patients at their first visit in a tertiary Hypertension Outpatient Unit were enrolled. Insomnia Severity Index (ISI), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAY-Y2) were administered. Insomnia was defined as ISI>8, depressive symptoms as BDI>10, trait anxiety as STAI -Y2>40. Patients with self-reported sleep apneas or snoring (n=29) or with incomplete data (n=12) were excluded.
Results: Data from 330 patients were analyzed (males 51%, mean age 57±13 years, antihypertensive treatment 84%, previous CV events 9%, diabetes 7%, obesity 24%, smoking 13%, hypercholesterolemia 67%). Insomniacs (n=70, 21%) were older than non-insomniacs (60±11 vs 56±13 years, p=0.02); female gender (62 vs 46%, p=0.01), anxiety (68 vs 34%, p<0.0001) and depressive symptoms (30 vs 6%, p<0.0001) were more prevalent in insomniacs. Insomniacs were treated with higher number of antihypertensive drugs (1.8±1.0 vs 1.5±1.0, p=0.04) and more frequently with angiotensin-receptor-blockers (ARBs, 49 vs 31%, p=0.009) and diuretics (50 vs 28%, p=0.0007), whereas the use of other drug classes was similar.
In a multiple logistic regression analysis, adjusted for cardiovascular and psychiatric variables, ARBs use (OR 2.4, CL95% 1.1-5.2), depressive symptoms (OR 3.2, CL95%1.2-8.7) and anxiety (OR 2.9, CL95%1.4-6.1) were associated with a higher probability of insomnia.
Conclusions: This cross-sectional analysis suggests that ARBs use may be associated with insomnia in a cohort of hypertensive patients.

P3242 | BEDSIDE

Comparative efficacy of valsartan and LCZ696, an angiotensin receptor neprilysin inhibitor (ARNI), in hypertensive individuals: effects of gender

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Purpose: To better characterize the blood pressure (BP) lowering efficacy of the first-in-class angiotensin receptor neprilysin inhibitor (ARNI), LCZ696 (Japanese Adopted Name [JAN]: Sucabitril Valsartan Sodium Hydrate), was compared to valsartan in female and male patients with hypertension (HTN).
Methods: Data were pooled from two 8-week, multicenter, randomized, double-blind, placebo- and active-controlled studies in female and male patients with HTN to evaluate reductions in mean sitting (ms) BP, ms pulse pressure (PP), mean ambulatory (ma) BP and maPP in response to daily therapy with either LCZ696 400 mg, valsartan 320 mg or placebo.
Results: Overall, 377 (44.5%) female and 471 (55.5%) male patients were randomized. Baseline characteristics of females (mean age, 58.1 yrs, 32% ≥65 yrs; body mass index (BMI), 30.3 kg/m^2; mean duration of HTN, 7.7 yrs; baseline ms systolic BP (SBP)/ms diastolic BP (DBP)/ms pulse pressure (PP), 157.1/95.1/62.0 mmHg) and males (mean age, 54.8 yrs, 22% ≥65 yrs; BMI, 29.7 kg/m^2; mean duration of HTN, 6.7 yrs; baseline msSBP/msDBP/msPP, 158.5/97.0/61.6 mmHg) treated with LCZ696 were similar. After 8 weeks of treatment, LCZ696 lowered msSBP by 5.8 mmHg (p<0.01) and msPP by 3.3 mmHg (p<0.05) more than valsartan in female HTN patients, and by 5.8 mmHg (p=0.0001) and 3.4 mmHg (p<0.05) more than valsartan in male HTN patients (Table 1).

Table 1. LSM change in BP from baseline to Week 8

LSM (±SE), mmHg	Female			Male		
	Placebo	LCZ696 400 mg	Valsartan 320 mg	Placebo	LCZ696 400 mg	Valsartan 320 mg
N	106	145	125	123	167	181
msSBP	–7.4±1.5	–21.6±1.2*#	–15.8±1.3*	–7.3±1.3	–19.7±1.1*#	–14.0±1.0*
msDBP	–6.7±0.9	–13.1±0.7*#	–10.5±0.8†	–3.7±0.9	–11.0±0.7*#	–8.6±0.7*
msPP	–0.6±1.1	–8.6±0.9*#	–5.3±1.0†	–3.6±0.9	–8.7±0.8*#	–5.3±0.8
N	43	60	62	49	83	85
maSBP	–2.3±1.1	–13.4±1.0*	–11.0±0.9*	–2.2±1.0	–13.8±0.7*‡	–9.1±0.7*
maDBP	–0.8±0.7	–6.4±0.6*	–6.2±0.5*	–0.3±0.6	–7.2±0.5*	–5.9±0.5*
maPP	–1.6±0.6	–6.9±0.5*#	–4.7±0.5*	–1.7±0.5	–6.7±0.4*‡	–3.3±0.4†

LSM, least squares mean; SE, standard error. *p<0.0001 vs placebo; #p<0.05 vs valsartan; †p<0.05 vs placebo; ‡p<0.0001 vs valsartan.

Conclusion: LCZ696 was superior to valsartan in reducing SBP and PP in female and male patients. Thus, ARNI is an effective antihypertensive treatment in patients with HTN, regardless of gender.

P3243 | BEDSIDE

Effectiveness of ivabradine in combined therapy in hypertensive patients with coronary artery disease and type 2 diabetes mellitus

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Purpose: The purpose of study was investigation of efficacy and safety of If inhibitor ivabradine in hypertensive patients with coronary artery disease (CAD), moderate heart failure and type 2 diabetes mellitus (DM) who received selective beta-adrenoblocker bisoprolol and ACE inhibitor ramipril, as well as assessment of its administration as medication for prevention of complications in such patients.
Methods: Thirty five patients (20 men and 15 women, average age 47,2±1,5 years) with arterial hypertension (AH) I and II stage (WHO classification, 1999) and CAD stable angina I-II functional classes (classification of Canadian Cardiologist's Association), with moderate heart failure (NYHA class II-III) and type 2 diabetes were divided into 2 groups. All patients had sinus rhythm >70 bpm. Patients of group I (n=18) received bisoprolol 5 mg daily and ramipril 10 mg daily, patients of group II (n=17) received same treatment, after 2 weeks 7,5 mg ivabradine twice a day was added. Echocardiographic parameters (end systolic volume (ESV), ejection fraction (EF), left ventricular mass index (LVMI)) and total cholesterol (TC), low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), triglycerides (TG) and level of fasting glucose in blood serum were determined. All patients received antidiabetic per oral Gliclazide in 30mg daily.
Results: Statistically significant decrease of BP up to purposed level <130/80 mm was achieved in all patients after 12 months of treatment. Statistically significant decrease of angina pectoris attacks and need in sublingual use of Nitroglycerine on 54% were revealed in patients of group I and in all patients of group II. Decrease of ESV by 6,1% (p<0,05) in group I and by 9,2% (p<0,05) in group II, increase of EF by 8,5% (p<0,05) – in group I and by 11,3% (p<0,05)in group II were accompanied with decrease of LVMI by 12,2% (p<0,05). After 12-weeks treatment TG level had statistically significant decrease by 12,9% and 13,2% respectively (p<0,05), that became correspondent to recommended level for patients without type 2 diabetes - 1,80 mmol/l.
Conclusions: Hypotensive effect of bisoprolol and ramipril in hypertensive patients with CAD, moderate heart failure and type 2 DM accompanies with regression of left ventricular hypertrophy, decrease of numbers of angina pectoris attacks and need in sublingual use of Nitroglycerine. Addition of ivabradine to bisoprolol and ramipril very early decreases of numbers of angina pectoris attacks. The negative chronotrope effect of ivabradine causes improvement myocardium contraction and decrease of functional class of heart failure.

P3244 | SPOTLIGHT

Possibilities of the pharmacological correction of moderate cognitive disorders in patients with arterial hypertension

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The purpose of the study was to estimate efficacy and safety of dopamine agonist piribedil in patients with arterial hypertension and cognitive disorders.
Methods: 115 patients with arterial hypertension and moderate cognitive disorders at the age from 52 till 70 years (mean age – 67,3±2,9 y.o., m-52%, f.-48%) were included into the study. All patients have been divided into 4 groups: 1st group (n=30) received base therapy of arterial hypertension and piribedil in total daily dose 50 mg, 2nd group (n=27) received base therapy of arterial hypertension, piribedil and different vasoactive drugs, 3st group (n=28) received base therapy of arterial hypertension and different vasoactive drugs and 4st group (n=30) received only base therapy of arterial hypertension during 12 weeks. Intensity Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCa) were estimated before and after the treatment. Diagnostic criteria of CD: MMSE 25-27 points and MoCa <26 points.
Results: The mean score of MMSE was 25,8±1,0, 25,7±0,8 and 25,9±1,1 in patients 1st, 2nd and 3st groups, respectively. The mean score of MoCa was 24,9±0,7, 24,5±0,4 and 24,7±0,3 in patients 1st, 2nd and 3st groups, respectively. The Patients in 4st group has mean score of MMSE 25,4±0,9, of MoCa-24,8±0,4. After 12 weeks of treatment of P in 1st and 2st group authentic changes of the psychological status are noted. After 12 weeks of treatment of piribedil the increase of mean score of MMSE up 7 and 9% (p<0,05, p<0,05) was revealed in patients 1st and 2st group respectively. Also the increase of mean score of MoCa up 9 and 9,5% (p<0,05, p<0,05) was revealed in patients 1st and 2st group respectively. There were no founded such changes in patients 3 nd group and 4 nd group (p>0,05, p>0,05).The tolerance of piribedil was satisfactory, adverse event (headache, vertigo, sleepiness, dyspepsia) were non-seriously and not required the cancel of piribedil.
Conclusion: Piribedil in total daily dose 50 mg authentically improves cognitive functions of patients with arterial hypertension.

P3245 | BEDSIDE

Effectiveness of perindopril/amlodipine fixed dose combination in high cardiovascular risk patients. A PanHellenic prospective non-interventional study

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Introduction: Arterial hypertension represents a major modifiable risk factor for cardiovascular disease and mortality. Early detection and treatment are crucial. Despite of the availability of effective therapies, hypertension remains poorly controlled. Drug regiment used, as well as compliance and adherence to treatment represent probably the main reasons.
Purpose: To assess the effectiveness of Perindopril/Amlodipine fixed dose combination on blood pressure control during a 6-month treatment of hypertensive patients. To record patient's compliance, and to identify comorbidities, co-existing risk factors. To record the total cardiovascular risk of patients and the effectiveness of this fixed combination on blood pressure control in High/Very high risk patients.
Methods: In this multicenter, non-interventional study, 2,300 patients were prospectively studied from 230 private cabinets, coordinated by 3 Cardiology departments. The data were recorded at baseline, 3 and 6 months. In all patients comorbidities, coexisting risk factors, and total cardiovascular risk were recorded. Compliance to treatment was evaluated using a 5 score scale, at the 2nd and 3rd visit.
Results: From 2.300 hypertensive patients participated in the study, 52 patients (2.3% of the sample) discontinued treatment. 73.1% of patients were of "Moderate" or "High/Very high added risk". Mean SBP values decreased from 157.0 mmHg (1st visit), to 129.0 mmHg (3rd visit) ($p<0.001$). Mean DBP values decreased from 91.5 mmHg (1st visit), to 78.8 mmHg (3rd visit) ($p<0.001$). Patients with higher SBP and DBP values on the 1st Visit showed greater SBP and DBP decrease respectively ($p<0.001$). Patients with higher cardiovascular risk showed greater SBP and DBP decrease ($p<0.001$). In patients with High/Very high cardiovascular risk (1.009 patients), mean SBP values decreased from 159 mmHg (1st visit) to 130 mmHg (3rd visit) ($p<0.001$), while mean DBP values decreased from 92 mmHg (1st visit) to 79 mmHg (3rd visit) ($p<0.001$). Compliance to treatment was high. 97.1% of the sample was taking their treatment "every day" or "quite often" during the study. In 1.927 patients (83.9% of the sample) was administered constant dosage of Perindopril/Amlodipine fixed dose combination during the whole study, while in 51.3% of those the patients was administrated the lower dose (5/5 mg).
Conclusions: Perindopril/Amlodipine fixed dose combination significantly and promptly reduces blood pressure levels, with high compliance to treatment. The degree of blood pressure reduction depends from baseline blood pressure levels and total cardiovascular risk.

P3246 | BENCH

The COMmon control of hypErtenSion and Therapeutic Attitudes in Belglum and Luxenbourg study

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Introduction: Despite overwhelming evidence that hypertension (HT) is a major cardiovascular risk (CVR) factor, a noticeable proportion remain unaware of this condition and normal blood pressure (BP) levels are seldom achieved. As a result, hypertension remains a leading cause of cardiovascular death in Europe and elsewhere in the world.
Aim of the study and methods: To characterise hypertension control in Belgium and Luxembourg in 2013 in 516 general physicians who enrolled 20 consecutive HT patients. All used the same definitions to assess global CVR.
Results: Office Systolic BP, Diastolic BP and heart rate were respectively 139±19 mmHg (mean ± SD, n: 100078), 80±11 mmHg (n:10061) and 73±10 bpm (n:9786). Age was 64±13 years and body mass index 28±5 kg/m^2. 86% of the consultations did not result in changes in antihypertensive therapy, although 34% of these 6847 patients had a SBP >140 mmHg. 10% were on no medication, 43% on monotherapy and 46% on >2 medications (n=7961). 58% of the patients were at high CVR, received more frequently >2 anti HT medications (59% vs. 23% in those at lower risk, p χ^2 <0.0001) but underwent less treatment intensification (66% vs. 72% in those at lower risk, p χ^2 <0.0001). BP was higher when treatment was intensified (156±14/88±11 mmHg vs. 149±13/81±9 mmHg, P<0.0001). In those with a SBP >140 mmHg, therapy was intensified in 24% after 70 years (n:1335) vs. in 33% before 70 years (n:1971, p χ^2 <0.0001). After 80 years, BP was 153±16/81±10 mmHg Treatment intensification occurred in 17% when SBP was between 140 and 159 mmHg (n=365) vs. 57% when SBP was >160 mmHg (n=130, p χ^2 <0.0001) after 80 yrs.
Conclusion: In 2013, 8 out of 10 consultations for hypertension did not result in antihypertensive therapy changes despite 1/3 were still hypertensive and <50% received <2 antihypertensive medications. Higher BP, and CVR with <2 medications, resulted in therapy intensifications. The higher threshold for BP control after 70 years is consistent with the 2013 ESC/ESC guidelines for the management of arterial hypertension.

P3247 | BEDSIDE

Fixed-combination olmesartan/amlodipine (OLM/AML) was superior to perindopril + amlodipine (PER/AML) in reducing central systolic blood pressure (CSBP) in hypertensive patients with diabetes

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Purpose: The SEVITENSION study showed that the absolute decrease in CSBP after 24 weeks' treatment with OLM/AML 40/10mg was non-inferior to PER/AML 8/10mg. Further, a pre-planned analysis showed that the reduction in CSBP with OLM/AML was superior to PER/AML (Adv Ther 2013;30:1086–99). The present analysis looks at changes in central and seated blood pressure (BP) in the diabetic subgroup.
Methods: SEVITENSION enrolled Caucasians aged 40–80 years with hypertension and ≥3 additional risk factors. At the end of the run-in, all pts had received AML 10mg for ≥2 weeks. Diabetic pts with inadequate BP control (≥130/80mmHg) were randomised to a fixed-dose combination of OLM/AML 40/10mg or PER/AML 8/10mg for 24 weeks. Hydrochlorothiazide was added at Weeks 4, 8, or 12 in pts with inadequate BP control. The primary variable was the absolute change in CSBP from baseline to week 24 in the per-protocol set (PPS). If the upper 95% confidence interval (CI) limit for the least squares mean difference in CSBP between the groups was <2mmHg, OLM/AML was non-inferior to PER/AML. If it was <0mmHg in the FAS (all randomised pts who took ≥1 dose of medication and had a baseline and ≥1 post-baseline CSBP measurement), then OLM/AML was considered superior. Changes in seated systolic and diastolic BP (SBP and DBP) in the FAS were also assessed.
Results: In the PPS, mean baseline CSBP was similar for OLM/AML (133.5±11.90mmHg, n=91) and PER/AML (134.7±11.16mmHg, n=96). A larger mean decrease in CSBP at week 24 (Table) established non-inferiority of OLM/AML over PER/AML. Analysis of the FAS showed that the mean CSBP reduction with OLM/AML (n=101) was even superior to PER/AML (n=110). For seated SBP and DBP, the decreases at week 24 were also significantly greater with OLM/AML.

Table 1. Changes from baseline to week 24 in CSBP and seated BP (mmHg)

	OLM/AML, mean (SD)	PER/AML, mean (SD)	Estimated difference (95% CI)
CSBP	−13.4 (12.21)	−10.5 (12.18)	−3.51 (−6.66, −0.36), p=0.0007 (non-inferiority test)
	−14.0 (12.30)	−10.2 (12.82)	−4.49 (−7.54, −1.44), p=0.0041 (superiority test)
Seated SBP	−15.3 (12.31)	−11.9 (12.29)	−3.83 (−6.97, −0.70), p=0.0168 (superiority test)
Seated DBP	−7.1 (7.73)	−4.5 (7.4)	−2.47 (−4.35, −0.60), p=0.0098 (superiority test)

SD, standard deviation.

Conclusions: OLM/AML was non-inferior, and even proved to be superior, to PER/AML for the mean reduction in CSBP from baseline to week 24 in pts with hypertension and diabetes. Also, OLM/AML was shown to be superior to PER/AML for the reductions in seated SBP and DBP.

BLOOD PRESSURE MONITORING AND HAEMODYNAMICS

P3249 | BEDSIDE

Agreement of systolic blood pressure measurement between standard sphygmomanometer and home based blood pressure monitoring devices

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Background: Hypertension poses a major health issue with no symptoms in early phases. Systolic blood pressure (SBP) has been in cardiovascular disease risk calculators. Accurate SBP measurement therefore is crucial for risk stratification and guiding treatment. However, considerable discrepancies in true value of SBP might be present between standard sphygmomanometer and home based BP monitoring devices. In this prospective study, we examined for potential discrepancies between 21 arm models and 6 wrists models of home based BP self-measuring devices commonly available in the market.
Methods: A total of 1,002 patients (540 male & 462 female, mean age 62 [range 30–94]) were studied from July 2010 to late 2013, according to the International Protocol of the European Society of Hypertension. Enrolment criteria included hypertensive patients in sinus rhythm; those with significant arrhythmia were excluded. Each patient received 9 sequential same-arm measurements of systolic and diastolic blood pressure; 7 of these readings were used for analysis. Limits of agreement were assessed by Bland-Altman method. A BP measuring team with 4 members experienced in BP measurements, including 2 observers, a registered nurse and a doctor conducted the study, with ethics committee approval & written informed consent obtained.
Results: In the 1,002 participants, 888 (88.6%) had BP measured by arm models

(Arm group) & 114 (11.4%) by wrist models (Wrist group). Individual device was separately compared to the sphygmomanometer. Overall, patients in the 2 groups showed no difference in the true SBP as measured by the reference sphygmomanometer (Arm 137.3±22.8 vs Wrist 138.6±20.8mmHg). Arm devices showed no difference in mean SBP readings (sphygmomanometer 137.3±22.8 vs Arm 136.9±23.0mmHg, p=0.20). While significant differences were observed in the diastolic BP readings, there was also no difference of SBP readings in the Wrist devices (sphygmomanometer 138.6±20.8 vs Wrist 136.5±20.9mmHg, p=0.139). Using the Bland and Altman analysis, the mean difference of Arm devices and sphygmomanometer was 0.382 (limits of agreement: 3.552 to -6.723) and Wrist device 1.978 (limits of agreement: 6.642 to -2.687).
Conclusions: Both Arm and Wrist home based BP monitoring devices performed equally well for "systolic" BP monitoring in patients with sinus rhythm. The agreement between the standard sphygmomanometer and the home based BP monitoring devices under test in this study* was confirmed by Bland and Altman method. *(Models to be enlisted at presentation as appropriate).

P3250 | BEDSIDE
Unsatisfactory blood pressure control in patients with established coronary heart disease. The Czech EUROASPIRE I - IV Surveys

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Objectives: Effective control of hypertension is one of cornerstones of secondary CHD prevention. We analyzed in detail blood pressure (BP) control in patients with established CHD in the Czech Republic as documented by the EURASPIRE (EA) I – IV surveys.
Methods: Four independent descriptive surveys were undertaken in 1996, 2000, 2006 and 2012. Consecutive patients <71 years of age hospitalized for an acute coronary event and/or revascularization procedure were identified and examined at least 6 months later following a standard protocol. Data collection was based on a review of medical records and an interview. BP was measured by automated sphygmomanometers, with the mean of the first two measurements evaluated.
Results: The study population included 4 series of 331, 410, 421, and 372 patients. A comparison of EA I and EA IV revealed, that systolic and diastolic BP decreased from 144.1/87.5 mmHg to 135.5/82.3 mmHg. Uptake of beta-blockers increased from 56.7 to 86.8%, of ACEIs or ARBs from 23.88 to 80.6%, of CCBs from 9 to 25.4%, and the uptake of any antihypertensive drug from 79.9 to 94.5%. Prevalence of BP in the hypertension range (≥140/90 mmHg) in the study populations decreased from 63.7 to 39.5%, prevalence of grade III hypertension (BP >180/110 mmHg) from 18.4 to 5.1%. In the EA IV survey population, a combination of at least 2 antihypertensive drugs was used in 84.6%, but the doses were unsatisfactory in 38.5% with beta-blockers, 56% with ACEIs, 36.6%with ARBs, and in 48% with CCBs.
Conclusions: Due to the stricter criteria for hypertension control, extensive use of antihypertensive drugs and the secular decrease in BP, hypertension control improved in patients with established CHD. However, antihypertensive drugs are prescribed at insufficient doses and control of hypertension remains rather unsatisfactory. This study was supported by IGA, Ministry of Health, Czech Republic, grant No NT/13186

P3251 | BEDSIDE
A comparison of office blood pressure, telemedical home blood pressure and ambulatory blood pressure monitoring

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Objective: Telemonitoring of home blood pressure is a new advance in blood pressure monitoring (HBPM). The aim of this study was to compare the accuracy of office blood pressure and telemedical home blood pressure with 24-h ambulatory blood pressure (AMPM).
Design and methods: 102 patients were consecutively recruited from a Renal Outpatient Clinic. Office blood pressure was measured three times with the HBPM equipment. Next patients used HBPM with telemonitoring three measurements three times daily for four consecutive days and finally ABPM on the following day.
Results: There was a significant difference between office blood pressure and ABPM (24-h and daytime); and between HBPM and daytime ABPM; HBPM was lower (-4.1 mmHg/-1.6 mmHg) than daytime ABPM ($p<0.05$). The strongest correlations were seen between all HBPM readings day 2-4 and ABPM (24-h and daytime). There was no significant difference between the different HBPM schedules (three measures three times daily for four days or three measures twice daily for three days). There was no significant difference between HBPM and 24-h ABPM.
Conclusion: The telemedical HBPM reflected more accurately 24-h ABPM than office readings. No significant difference between the different HBPM schedules.

P3252 | BEDSIDE
Effects of percutaneous transluminal renal angioplasty on blood pressure evaluated with 24-hour monitoring

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Background: Percutaneous transluminal renal angioplasty (PTRA) improves patency in atherosclerotic renal artery stenosis (ARAS). However, OFFICE blood pressure (BP) improvement as primary purpose was achieved in only 20-40% of patients performed PTRA. The purpose of this study was to clarify the effects of PTRA on BP response by 24-hour BP monitoring, and identify preoperative features that predict a sufficient BP response to PTRA.
Methods and results: Out of 1753 consecutive patients underwent coronary angiography, 706 patients with hypertension were followed by abdominal aortography for etiological screening of hypertension. Among patients with angiographically significant stenosis, 31 patients with more than 20 mmHg translesional pressure gradient at renal artery under hyperemic condition were underwent PTRA. Ambulatory blood pressure monitoring (ABPM) was performed before and 1 month after PTRA, and patients were categorized as "Responders" depending on average systolic BP decrease more than 10 mmHg. As results, although there was no significant difference in BP at admission between 13 Responders and 18 Non-responders (148±18 vs. 144±18 mmHg, p=0.47), baseline BP on ABPM was significantly higher in Responders (148±10 vs. 126±16 mmHg, $p<0.01$). Even in-hospital spot BP 2 days after PTRA was not different between the groups (130±19 vs. 132±17 mmHg, p=0.71), Responders achieved significant decreases in systolic BP on ABPM 1 month after PTRA (16±6.7 vs. -7.0±13 mmHg, $p<0.01$). Although there was no obvious relationship between spot BP and ABPM (r2=0.072, p=0.15), baseline BP and BP decrease on ABPM had a significant correlation (r2=0.48, $p<0.01$). Patients who achieved systolic BP decrease more than 10 mmHg showed higher baseline BP than 147 mmHg on ABPM. Translesional pressure gradient at hyperemic condition was not statistically different between the groups (36±32 vs. 30±24 mmHg, p=0.60). In terms of echorenographic parameters, acceleration time (AT) at baseline was significantly LOWER in Responders (72±19 vs. 94±26 msec., p=0.012), yet other parameters including renal/aorta ratio, peak systolic velocity or resistive index was not significantly different between the groups. Moreover, assessments of hormonal parameters suggested that either plasma renin activity, aldosterone concentration or BNP was not preoperative predictor for BP response to PTRA.
Conclusion: The present study demonstrated that office BP did not represent patients' daily hemodynamic status, and high 24-hour BP was a potent predictor for sufficient BP response to PTRA.

P3253 | BEDSIDE
Automated office blood pressure (AOBP) is better predictor of arterial stiffness then manual office blood pressure (MOBP)

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Introduction and aim: AOBP monitors allow measuring of blood pressure (BP) in ambulant setting without presence of medical staff with the accuracy near to 24h ambulatory blood pressure monitoring. The recommended cut-off point for defining hypertension using AOBP is the same as for awake ambulatory BP or home BP. Arterial stiffness is one of the markers of cardiovascular health and reflects subclinical target organ damage. Our aim was to compare the automated and manual BP values with measured equivalent of arterial stiffness.
Methods: During 11 months we investigated 1101 people (47% male) aged 25-65 years (47.3±11.4). We measured BP using sphygmomanometer according to the guidelines (10 minutes rest, average of 2nd and 3rd measurement), measurement was performed by a trained nurse. Then the volunteer was sent to a separate quiet room, where after 10 minutes of sitting, BP was measured automatically 5 times in 1 minute interval by AOBP monitor, during the measurement, the volunteer was resting alone on a chair. Equivalent of arterial stiffness (cardio-ankle vascular index) was measured using vascular screening system.
Results: According to AOBP, resp. to MOBP there was 14.7%, resp. 12.4% hypertensive volunteers (BP>135/85 mmHg, resp. BP>140/90 mmHg). There was a significant difference between AOBP and MOBP ($p<0.001$). AOBP was lower than MOBP in the majority of people. Arterial stiffness correlated with systolic blood pressure in both AOBP and MOBP (R=0.415, $p<0.001$ resp. R=0.306, $p<0.001$), the relationship with diastolic blood pressure was weak (R=0.280, $p<0.001$, resp. R=0.217 $p<0.001$).
Discussion and conclusion: There was a significant difference between AOBP and MOBP, which confirms, that any interaction with medical staff makes the volunteer's BP higher, known as the white coat effect. CAVI correlates slightly stronger with AOBP then with MOBP, suggesting that AOBP is better predictor of arterial stiffness.

P3254 | BEDSIDE

Comparative assessment of office blood pressure control and its home monitoring results in uncomplicated hypertension patients: focus on masked and white coat hypertension

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Purpose: Purpose of our study was to compare both target office (<140/90 mmHg) and "normal" home (<135/85 mmHg) BP attainment after 6 month (M) of standardized algorithmic treatment and home BP monitoring (HBPM) of uncomplicated hypertensives (UH) in longitudinal real-life program of BP control optimization (PERFECT-BP).
Methods: Intention-to-treat cohort of PERFECT-BP prospective observational study (No. ISRCTN75706523) included 501 patients (pts) aged 58,0±0,4 years, 44,1% male, 16,1% with type 2 diabetes with new diagnosed (15,3%) or treated but uncontrolled UH (BP <200/120 mmHg). Pts and MDs were provided with standardized automatic devices for BP measurements with individually selected and universal cuff correspondingly. At visit 1, after training in the use of BP device, pts were prescribed or switched to 1 FDC tab pd of perindopril/amlodipine (doses at discretion of MDs – 54 city ambulatory cardiologists) and instructed to perform HBPM twice per day (before breakfast and going to bed) minimum 7 consecutive days a week before each next visit, and record it in a log. Step 2 of target office BP attainment was uptitration to the highest tolerated FDC dose, step 3 – plus indapamid-R, step 4 – spironolactone 25 mg pd, step 5 – moxonidine or doxasosine.
Results: 60 pts (12%) dropped out for unspecified reasons and 10 (2%) – because of side effects (leg edema, cough). Per protocol cohort included 431 pts aged 57,6±0,5 years, 43,9% male, 17,2% with type 2 diabetes. In 6 months office systolic BP lowered from 165,7±0,7 to 131,1±0,5 mmHg, diastolic BP from 96,9±0,5 to 79,1±0,3 mmHg (p<0,001). This was achieved with triple therapy in 29,9% patients, and ≥4 drugs in 2,3%. At 6M home BP as a mean of 14±0,2 consecutive measurements was 129,5±0,4 mmHg and 77,9±0,3 mmHg. Target office BP was attained by 1M in 182 (42,2%), 2M – 250 (58%), 3M – 310 (71,9%), 6M – 245 (81,4%) pts, "normal" home BP – in 128 (29,7%), 282 (44,6%), 247 (57,3%), 284 (65,9%) pts. Corresponding both target office and "normal" home BP attainment rates were 45 (10,4%), 109 (25,3%), 177 (54,3%), 272 (63,1%), while masked hypertension had 73 (16,9%), 73 (16,9%), 75 (17,4%), 85 (19,7%) of pts and white coat one – 19 (4,4%), 15 (3,5), 13 (3%), 12 (2,8%).
Conclusion: Though target office BP attainment rate after 6 months algorithmized treatment of UH was 81,4%, it was associated with "normal" home BP in 63,1% of whole cohort. While rate of white coat hypertension was only 2,8%, while masked one was 19,7% and the rates of both stayed unchanged since 6M of treatment. Clinical significance of masked hypertension has to be validated.

PREGNANCY IN CONGENITAL HEART DISEASE

P3256 | SPOTLIGHT

Angiogenic imbalance and residual myocardial injury in women with peripartum cardiomyopathy and left ventricular function recovery

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Purpose: Recent studies suggest that angiogenic imbalance during the peripartum period may lead to acute periparum cardiomyopathy (PPCM). We propose that women recovering from PPCM may still have altered plasma concentrations of pro- and anti-angiogenic factors and an associated residual myocardial dysfunction.
Methods: We evaluated 34 women with PPCM (mean age 36±6 years), at least 6 months after the acute event 28 of whom exhibited LVEF recovery (LVEF≥50%). The number of circulating endothelial progenitor cells EPCs (CD34 and CD34/KDR), plasma levels pro-angiogenic endothelial growth factor growth (VEGF) and of VEGF inhibitor soluble Flt1 (sFlt1) were measured. Cardiac function assessment including, tissue Doppler imaging (TDI) and 2D strain echo techniques, was available in 13 patients. All measures where compared to age- and parity-matched controls.
Results: VEGF levels were significantly higher in PPCM group (244±71 vs. 169±30 pg/ml, p=0.04), as well as sFlt1 (149±70 vs. 46±8 pg/ml, p=0.006) compared to controls, with no significant differences in circulating EPC levels. When compared to healthy controls, patients with PPCM had a trend for lower systolic velocities (S') on TDI (7.9±2.0 vs. 9.5±1.9, p=0.07) and decreased global longitudinal strain (-20.5±2.3% vs. 22.8±2.2%, p=0.07).
Conclusions: The inappropriately low circulating EPC levels with concomitantly high VEGF concentrations shown here for the first time in patients recovering from PPCM may suggest that 'angiogenic imbalance' could predispose to this disease. Further studies should be taken to further support this finding that may pave for novel and preventive therapeutic measures in patients with PPCM

P3257 | BEDSIDE

Cardiac function one year after pregnancy in women with congenital heart disease

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Purpose: Little is known about long term cardiovascular outcome after pregnancy in women with congenital heart disease. We, 1) observed the incidence of late cardiovascular complications and 2) compared cardiac function prior to and one year after pregnancy in women with congenital heart disease.
Methods: We compared systemic ventricular ejection fraction, tricuspid annular plane systolic excursion (TAPSE), systemic ventricular end diastolic diameter (LVEDD), subpulmonary ventricular end diastolic diameter (sPVEDD), grade of valvular regurgitation or valvular stenosis prior to and one year after pregnancy. Late cardiovascular complications (CVC) were defined as need for urgent invasive cardiovascular procedure, episodes of heart failure, arrhythmia, tromboembolic events, myocardial infarction, cardiac arrest, cardiac death, endocarditis and NYHA class deterioration occurring >6 months after delivery.
Results: We observed 213 pregnancies in 203 women with CHD; 12 women were again pregnant <6 months after delivery, 18 women were lost to follow up, rendering 183 pregnancies in 173 women available for follow up. Late CVC were observed after 12 pregnancies (6.6%). Women with CVC during pregnancy were at risk for late CVC (HR 7.1, 95% CI 2.2-23.2,p=0.001,figure 1). In women with CVC during pregnancy, sPVEDD had significantly increased one year postpartum (38.5 (36.0-44.0) – 44.0 (38.0-55.0), p=0.022). No other significant differences were found in cardiac function or size one year after pregnancy compared to preconception values.

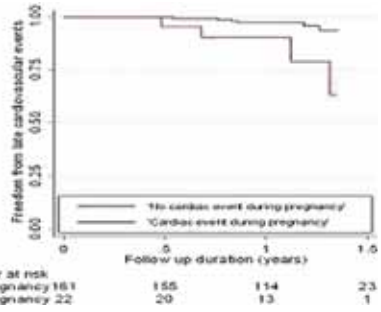

Figure 1

Conclusion: Pregnancy does not cause permanent damage to cardiac function in women with congenital heart disease. Women with cardiovascular complications during pregnancy are prone to develop late cardiovascular coplications and dilatation of the subpulmonary ventricle.

P3258 | BEDSIDE

Impact of atrial fibrillation/flutter during pregnancy on maternal mortality in patients with heart disease; analysis from the ROPAC registry

A.M.F. Salam[1], R. Hall[2], M.R. Johnson[3], E. Ertekin[4], I. Van Hagen[4], J. Al-Suwaidi[1], J.W. Roos-Hesselink[4] on behalf of the ROPAC investigators. *[1]Hamad Medical Corporation, Doha, Qatar; [2]University of East Anglia, Norwich, United Kingdom; [3]Imperial College London, London, United Kingdom; [4]Erasmus Medical Center, Rotterdam, Netherlands*

Objective: There is lack of contemporary data on atrial fibrillation or flutter (AF/Afl) occurring during pregnancy in patients with heart disease and its effect on maternal outcomes. The aim of the current study was to examine the impact of AF/Afl on maternal mortality in a multicenter multinational registry.
Methods: Retrospective analysis of patients prospectively enrolled in the European Registry on Pregnancy and Cardiac disease (ROPAC) between 2007 and 2011. Patients that developed AF/Afl were selected and maternal mortality was examined.
Results: Among 1321 pregnant women enrolled, 17 women (1.3%) developed AF/Afl during pregnancy. Hospitalization during pregnancy was needed for 12 patients (70.6%). Maternal mortality was significantly higher in women with AF/Afl than in women without AF/Afl (11.8% vs. 0.9%, p=0.01).
Conclusions: AF/Afl during pregnancy in patients with heart disease is associated with a significant increase in maternal mortality. Further research is warranted to explore possible associated characteristics and measures to reduce the high mortality observed in these patients.

P3259 | BEDSIDE
Clinical and echocardiographic study of pregnant women with bicuspid aortic valve- maternal and fetal outcome

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Background: The physiological changes occuring in pregnancy have a profound impact on pregnant women with valvular heart diseases, so their understanding is essential for the management of those patients during pregnancy, labour and childbirth.
Material and methods: 89 pregnant patients with bicuspid aortic valve (BAV), aged 18-42, mean 26.8±4.6 years, were observed. There were 52 patients with aortic stenosis (SA): 22 with mild SA (AVA 1.6-2.0 cm^2), 30 with moderate to severe SA (AVA 0.5-1.5 cm^2) and 37 patients with aortic insufficiency (IA). Medical history and physical examination, NYHA class assessment, ECG and echocardiography were performed during each trimester (TR) of pregnancy and 8-12 weeks after delivery.
Results: During pregnancy all patients with mild SA remained in NYHA functional class I. Echocardiographic monitoring - LVEDD,LVESD, EDV, ESV, SV, CO, RV, LA, LV mass, peak and mean aortic gradients increased significantly between I and II TR, II and III TR, I and III TR, and decreased after delivery. All of them delivered vaginally healthy babies, mean birth weight 3.700±480g. Patients with moderate to severe SA in the I TR remained in NYHA class I-II, in 6 patients a clinical deterioration was observed within III TR. Echocardiography revealed the maximum pressure gradient ranging from 56 to 152 mmHg, which was greater by 20 to 42 mmHg comparing to the post-delivery values ($p<0.001$). In this group of patients, there was no significant increase of LVEDD, EDV, CO, SV between II and III TR. Seventeen women with severe SA delivered by cesarean section, the remaining vaginally. All patients delivered healthy babies with normal birth-weight 3.560±380g. In the group of IA patients - the significant increase of LVEDD, LVESD, EDV, ESV, CO, RV, LA was notified during pregnancy. There were no statistical differences of SV values between II and III TR. Additionally, a significant increase of EF and FS postpartum comparing to pregnancy period was noted. Six of them delivered by cesarean section due to obstetric indications, the remaining vaginally. The mean birth-weight was 3.860±340g. The ascending aorta diameters (28-44 mm) didn't change during pregnancy.
Conclusions: Among the patients with BAV patients with mild SA tolerate well the increased cardiovascular demand of pregnancy. In patients with severe SA pregnancy intensifies the hemodynamic disorders. Volume overload of pregnancy is well tolerated in patients with mild and moderate IA. Our findings suggest that complication risk increases with severe IA, LV enlargemnet, impaired systolic function and/or the enlargement of ascending aorta.

P3260 | BEDSIDE
Risk score for predicting maternal complications in pregnancy: which is the most suitable for a spanish tertiary centre population?

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Background and objectives: Several cardiac and obstetric complications have been described in patients with congenital and acquired heart disease during pregnancy and postpartum period. Different risk scores have been developed to predict complications. CARPREG risk score has three categories (0, 1 and 2) with expected cardiac complications being 2.7%, 27% and 67% respectively. Recent European Society of Cardiology guidelines publication, suggest the use of modified World Health Organization (WHO) risk score in order to classify patients in 4 categories, considering 1: no risk, 2: low risk for complications, 3: significant risk for complications and 4: contraindication for pregnancy. The aim of this study is to report cardiac complications during pregnancy and postpartum period in a population of pregnant patients with heart disease and to evaluate suitability and applicability of several risk scores (CARPREG and WHO modified classification) to estimate risk and predict complications.
Methods and results: 179 patients (mean age 32 years) were referred to a high risk pregnancy and heart disease clinic of a tertiary referral centre from January 2007 until March 2012. Baseline cardiological (NYHA classification, type of heart disease, use of medication) and obstetrical characteristics were evaluated as well as cardiac and obstetric complications during pregnancy, delivery, postpartum and after one year of follow up. Patients were classified according to CARPREG score risk at the time of first assessment pre-pregnancy or in the first visit during pregnancy. Modified WHO classification was applied according to pre-pregnancy assessment. 14% of cardiac complications were described. 69% have been previously classified into CARPREG 0, 25% into CARPREG 1 and 6% into CARPREG 2. Regarding modified WHO classification 22% were considered WHO 1, 58% WHO 2, 15% WHO 3 and 4% WHO 4. In our population, observed cardiac complications according to CARPREG score were the following: 8.9% for CARPREG 0, 22% for CARPREG 1, and 40% for CARPREG 2. According to WHO modified classification were: 5% for WHO 1, 9.6% for WHO 2, 22% for WHO 3 and 100% for WHO 4.
Conclusions: Modified WHO risk score is better adjusted to predict cardiac complications than CARPREG in our population of pregnant patients with heart disease.

P3261 | BEDSIDE
Predictors of atrial fibrillation during pregnancy in patients with heart disease; analysis from the ROPAC registry

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Objective: There is lack of contemporary data on predictors of atrial fibrillation or flutter (AF/Afl) occurring during pregnancy in patients with heart disease. The aim of the current study was to examine that in a multicenter multinational registry.
Methods: Retrospective analysis of patients prospectively enrolled in the European Registry on Pregnancy and Cardiac disease (ROPAC) between 2007 and 2011. Patients that developed AF/Afl were selected. Univariable regression analysis of AF/Afl predictors was performed.
Results: Among 1321 pregnant women enrolled, 17 women (1.3%) developed AF/Afl during pregnancy mainly in the second trimester (61.5%). Pre-pregnancy risk factors for AF/Afl were AF/Afl before pregnancy (OR 7.1, 95% CI 1.5-32.8), valvular heart disease (OR 4.3, 95% CI 1.6-11.4), pulmonary hypertension (OR 3.3, 95% CI 1.1-9.4), beta-blocker use (OR 3.3, 95% CI 1.2-9), and left sided lesions (OR 2.9, 95% CI 1.0-8.3).
Conclusions: Our study identified pre-pregnancy risk factors that predict AF/Afl during pregnancy in patients with heart disease. These patients should be monitored closely for the development of this arrhythmia particularly in the second trimester.

P3262 | BEDSIDE
Syncope and arrythmias during pregnancy 10 years experience

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During the last 10 years, we have encountered with 123 pregnant women and 188 pregnancies of women who visited our cardiac problems of pregnancy clinic for cardiac causes. Mean age 26.8 years. Out of the 188 pregnancies, 50 of them (26.6%) visited our clinic for syncope and arrhythmia. Analyzing this group of syncope and arrhythmia-13 pregnancies (26%) were with recurrent supraventricular tachycardia during pregnancy treated with beta blockers according to the freguency of the episodes and with intravenous adenosine during the episode.10 of these pregnancies were delivered spontaneously at term,2 delivered preterm with cesarean section and one ended at 11 weeks for anencephallus.No maternal complications were noticed.10 pregnancies (20%) were with recurrent syncope-8 of them with reflex mediated syncope, 1 with orthostatic hypotension and 1 with postural orthostatic tachycardia syndrome. All of them were conducted how to behave during pregnancy and all of them successfully completed pregnancy with spontaneous delivery and without any maternal complications. 10 pregnancies (20%) were with wolf Parkinson white syndrome during pregnancy -7 of them delivered spontaneously and 3 with cesarean section, all of them at term and no maternal complications observed. 6 pregnancies (12%) were with multiple ventricular premature complexes-all of them deliveres spontaneously without maternal complication.4 pregnancies (8%) were with pacemakers for complete atrioventricular block – 2 of them deliverd with cesarean section and 2 with vacuum without any complications.2 pregnancies (4%) were with implantable defibrillators for long QT syndrome – Both deliverd spontaneously at term and without any complications.2 pregnancies (4%) were with paroxysmal atrial tachycardia who deliverd spontaneously at term without complications and 2 other (4%) were with suspected Brugada syndrome who deliverd at term without complications.
Most of the maternal arrhythmias were abolished with beta blockade without deleterious effect to the fetus.
In a minority of the arrhythmias there was a need for class 1c antiarrythmic drugs such as Flecainide and for sotalol in order to abolish the arrhythmia.
Conclusion: Based on our observation, Pregnant women with syncope and arrhythmias can safely complete pregnancy if they desire to do so.

P3263 | BEDSIDE
Pregnancy outcomes in women with coarctation of aorta - a five-year experience from a tertiary joint cardiac obstetric clinic

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Purpose: To assess pregnancy outcome in women with CoA managed within our multidisciplinary joint cardiac-obstetric clinic from 2008-14.
Methods: Clinic records were retrospectively reviewed to identify women with CoA. Pregnancy outcome was described in the whole cohort (A) and a case control study was carried out for the subset of the women delivering at our institution, either because we were their local hospital or they needed tertiary care (B).
Results: (A) Women with CoA form 12% of referrals. There were 44 pregnancies in 36 women with CoA. In the 36 pregnant women with CoA, the commonest additional cardiac defect was bicuspid aortic valve (52.7%). Three had unrepaired coarctation. Four repaired cases had significant pressure gradients across the coarctation and one underwent repair between her first and second pregnancies. Three had significant dilation of the ascending aorta. Ten (22.7%) had pre-existing or pregnancy induced treated hypertension. There were 4 cases of preeclampsia

(9.1%). The live-birth rate was 96%. All pregnancies had specialist fetal echocardiography. There were 4 fetal cardiac defects (9.1%) of which 3 were left-sided. There were no cases of stroke, cardiac failure, dissection, arrhythmia or maternal death.
(B) There were 25 pregnancies (1 ongoing) in 19 women with CoA delivering in our unit (see Table 1).

Outcome	Pregnancies in women with CoA N=24	Controls (healthy women, low risk at booking) N=72
Live birth, n (%)	22 (92)	72 (100)
Gestation age at delivery in weeks, median (IQR)	39 (37–40)	39 (38–40)
Birth weight in grams, median (IQR)	3125 (2725–3360)	3240 (2908–3643)
Caesarean section, n (%)	7 (31.8)	17 (23.6)
Preeclampsia, n (%)	2 (8.3)	3 (4.2)
Preexisting/pregnancy induced hypertension (treated), n (%)	6 (25)*	2 (1.4)
Other medical co-morbidities, n (%)	5 (20.8)*	3 (4.2)

Conclusion: Women with repaired CoA have successful pregnancies, although fetal cardiac defects are common. In our case control study, pregnancy outcomes of women with CoA are comparable to the controls. This is despite additional co-morbidites and hypertensive disorders. Dedicated multidisciplinary care in pregnancy is helpful in assessing high-risk cases that will need delivery in a tertiary setting and in improving overall maternal and fetal outcome.

P3264 | BEDSIDE
Changes in aortic root diameter throughout normal pregnancy

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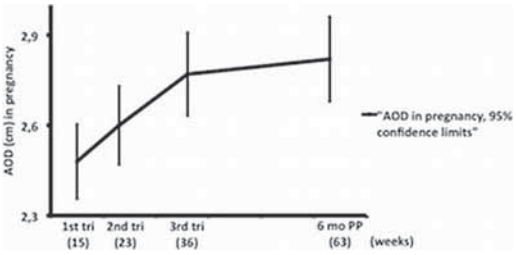
Purpose: During normal pregnancies in healthy women (HW) physiological changes facilitate the adaptations of the cardiovascular system. The aortic root diameter (AOD) may increase during pregnancy in patients with aortic pathology. The aim of this study was to investigate the AOD throughout pregnancy in HW.
Method: HW were examined using echocardiography with Doppler (GE Vingmed Vivid 7) at gestational weeks 14-16, 22-24, 36, and 6 months postpartum (PP). AOD was measured from parasternal longs axis 2D views at the sinus Valsalva in systole using "inner-egde-to-inner-egde" technique.
Results: (presented as mean±SD): Study included 50 HW, aged 32±5 years, 58% nullipara. AOD showed statistical significant increase through pregnancy: from 2.5±0.3cm in the 1st trimester, 2.6±0.3cm by 2nd trimester, to 2.8±0.2cm in the 3rd trimester ($p<0.05$). There was a statistical non-significant increase in AOD from the 3rd trimester to 2.80±0.3 cm by 6 months PP (figure). Parity was a significant covariant factor ($p<0.05$) with multipara women exhibiting a larger AOD in the 3rd trimester, but not by the 1st trimester. End-diastolic ventricular diameter and cardiac output changed significantly throughout pregnancy with normalization to 1st trimester values at control 6 months PP. Systolic blood pressure (mmHg), however, changed during pregnancy: 108±1, 104±1, 109±1 and further on to PP 112±1 ($p<0.01$).



AOD throughout normal pregnancy

Conclusion: Our data demonstrate an increase in the AOD by approximately 3mm in HW during pregnancy. The AOD does not normalize the first six months PP. This is an important finding with implications for interpretation of the AOD in pregnant women.

P3265 | BEDSIDE
Comparison of aortopathy in pregnancy related to bicuspid aortic valve disease and Marfans syndrome

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Purpose: pregnancy is high risk for patients with aortopathy.Haemodynamic and hormonal changes increase dissection risk.Bicuspid aortic valve (BAV) and Marfan syndrome (MFS) are associated with aortopathy.Ascending aortic (AA) dilatation is more frequent in BAV and dilatation at sinuses of Valsalva (SoV)more frequent in MFS.We evaluated the need for surgery and change in aortic size during pregnancy in BAV and MFS.
Methods: We reviewed medical records from BAV and MFS patients seen in cardiac antenatal clinic from 1999-2013.Age and presence of valve disease were recorded.Aortic size at SoV, sinotubular junction (STJ) and AA was taken from echocardiography performed pre-pregnancy and in the third trimester.Surgery performed during pregnancy or within six months post-partum were recorded.Patients were excluded if echo data were not available.Student's t- test was used to compare means.
Results: 47 patients had 57 pregnancies.12 patients were excluded.35 patients (age 27±6 years) and 45 pregnancies were then studied (11 MFS and 24 BAV). Three women had at least moderate aortic stenosis pre-pregnancy.Aortic measurements (mean±SD in mm) are shown in the Table.No cases of dissection occurred.Three patients with MFS (27.3%) underwent valve-sparing aortic root replacement for aortic dilatation, two post-partum and one during pregnancy.Three women with BAV (12.5%) underwent aortic valve surgery post-partum.At baseline, SoV measurements were significantly bigger in MFS than BAV (p 0.0003).Increase in aortic size during pregnancy was not significant in MFS (p 0.34, p 0.59 and p 0.49 for SoV, STJ and AA respectively) nor in BAV (p 0.55 p 0.64 and p 0.70 for SoV, STJ and AA respectively).

	SoV	STJ	AA
Baseline MFS	36.8±4.6	30.2±2.6	31.6±5.2
3rd trimester MFS	38.9±6.0	30.9±2.4	30.3±2.2
Baseline BAV	30.0±4.6	28.3±3.6	34.9±5.1
3rd trimester BAV	30.9±2.6	29.0±2.6	35.0±5.6

Conclusions: MFS is associated with a high risk of requiring aortic surgery related to pregnancy. Patients with BAV-related aortopathy are unlikely to require aortic surgery related to pregnancy but need for valve surgery is not uncommon.Progressive aortic dilatation in MFS may occur in pregnancy but is unlikely in BAV-related aortopathy.

P3266 | BEDSIDE
Peripartum cardiomyopathy in teen-age pregnancy

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Introduction: Peripartum cardiomyopathy is defined as a cardiomyopathy manifesting between the last month of pregnancy and 6 months post partum.Peripartum cardiomyopathy is common in African descent. but also is manifested in low income population worldwide. Older maternal age is defined as a risk factor for this kind of cardiomyopathy, PPCM can also occur in a young woman who is pregnant with her first child.
Methods: In this study we followed 18 teenage pregnant women with diagnosis of peripartum cardiomyopathy who was refferd from obstetrics clinic in our hospital (2011-2013), during pregnancy and till six month post delivery
Results: 18 patients with age range of 14 to 19 years old enrolled in study. They all were from poor income and did not completed public high school education. Three of patients (16%) were in their second pregnancy. Symptoms of heart failure developed from 31 to 38 th weeks of gestation. They were all small sized women with mean hight =145cm,mean weight=51kg (at third trimester), and mean estimated BMI at beginning of pregnancy was 17. In lab data there was mild increased in WBC count with lymph dominancy (60% of patients) in blood smear, Non of the patients had HIV or HBV infection. All (100%) had anemia (mean HB level=7.8 mg/dl). Active urine sediment was in 57% of patients. Mean left ventricular EF was 35%, with lowest 10% and highest was 40%. The maternal mortality rate was 11 percent, one patient died post delivery and another after 2months, other 16 patients completely recovered afer six months. The frequency of premature delivery was higher (90 percent), and perinatal infant mortality rate was high (30%).
Conclusion: Peripartum cardiomyopathy is usally seen in older women but in teenage mothers who are from low income with low educations, malnourished & anemic you must suspect it

P3267 | BEDSIDE
Impact of atrial fibrillation/flutter during pregnancy in patients with heart disease on fetal outcomes; analysis from the ROPAC registry

A.M.F. Salam[1], R. Hall[2], M. Johnson[3], E. Ertekin[4], I. Van Hagen[4], J. Al-Suwaidi[1], J.W. Roos-Hesselink[4] on behalf of the ROPAC investigators. *[1]Hamad Medical Corporation, Doha, Qatar; [2]University of East Anglia, Norwich, United Kingdom; [3]Imperial College London, London, United Kingdom; [4]Erasmus Medical Center, Rotterdam, Netherlands*

Objective: There is lack of contemporary data on fetal effects of atrial fibrillation or flutter (AF/Afl) occurring during pregnancy in patients with heart disease. The aim of the current study was to examine the impact of AF/Afl on fetal outcomes in a multicenter multinational registry.
Methods: Retrospective analysis of patients prospectively enrolled in the Euro-

pean Registry on Pregnancy and Cardiac disease (ROPAC) between 2007 and 2011. Patients that developed AF/Afl were selected and fetal outcomes were examined.
Results: Among 1321 pregnant women enrolled, 17 women (1.3%) developed AF/Afl during pregnancy. Mean duration of pregnancy was 37.5 weeks for patients with AF/Afl and 38.0 weeks for patients without AF/Afl (p=0.25). Mode of delivery in AF/Afl patients was by elective caesarean section (CS) in 7 (41.2%) and by emergency caesarean section in one patient while the rest delivered vaginally. CS was for cardiac reasons in all but one patient who needed CS for an obstetric reason. Low birth weight (<2500 gram) occurred more often in patients with AF/Afl (35% vs. 14%, p=0.02). Stillbirth did not occur in any patients with AF/Afl. Early/spontaneous abortion occurred once.
Conclusions: Low birth weight was more common in patients with AF/Afl due primarily to the higher preterm delivery rate. We did not find any increase in rates of stillbirth in women with AF/Afl.

LONG-TERM PROGNOSIS AT CONGENITAL HEART DISEASE

P3269 | BEDSIDE
How common is stroke in young adults with congenital heart disease

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Purpose: Stroke is one of the most common causes of death and a leading cause of adult disability in developed countries. Patients with congenital heart disease are presumed to be at increased risk of stroke due to shunts, arrhythmias and other vascular abnormalities. Nevertheless, a research gap exists in adults with congenital heart disease. The aim of this study was to investigate retrospectively the frequency of stroke in young adults with congenital heart disease.
Methods: Data from our country hospital discharge register and death register was used to investigate all patients between 18 and 41 years of age (mean age 20.1 years, mean follow-up 9.7 years), with congenital heart disease and a stroke diagnosis according to the International Classification of Diseases (8th, 9th and 10th edition) during 1970 - 2010
Results: Altogether, 26713 young adults (51.3% men, 48.7% women) had been hospitalized at any time since 1970 with congenital heart disease. Of those, 414 patients (1.6%) developed stroke, mainly ischemic stroke (1.4%, n=363). Among patients with isolated atrial septal defect (n=1301), 95 (7.3%) were subsequently diagnosed with ischemic stroke, representing 26.2% (95/363) of all cases of ischemic stroke. There were 51 haemorrhagic stroke cases, 23.5% (13/51) of which occurred in patients with coartation of aorta (1%, n=1170).
Conclusions: In this large registry study of young adults with congenital heart disease, young adults with isolated atrial septal defect had a markedly high risk of subsequent ischemic stroke. Likewise, patients with coartation of the aorta had a risk of haemorrhagic stroke. Further research is needed for stroke mechanisms and prevention in patients with congenital heart disease.

P3270 | BEDSIDE
The risk of type B aortic dissection in Marfan syndrome

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Aim: Aortic complications beyond the ascending aorta have become a major clinical problem in patients with Marfan syndrome. The aim of our study was to identify clinical parameters associated with type B aortic dissection and to develop a risk model to predict type B aortic dissection in Marfan syndrome.
Methods: All adults with Marfan syndrome attending a Dutch university Marfan screening clinic were recruited. Starting point of the study was defined as the date of first available aortic images. Association of type B aortic dissection with demographics, medicinal treatment, FBN1 mutation, surgical history, aortic diameter, dilatation rate and distensibility was assessed.
Results: Between 1998 and 2013, 54 type B aortic dissections occurred in 600 Marfan patients (36±14 years, 52% male). Mean diameter of the proximal descending aorta before type B aortic dissection was 31±7 mm. Independent variables associated with type B aortic dissection were (A) prior prophylactic aortic surgery (HR: 2.1; 95%CI: 1.2-3.8; p=0.010), and (B) proximal descending aorta ≥27mm (HR: 2.2; 95%CI: 1.1-4.3; p=0.020). In the risk model, the 10 years occurrence of type B aortic dissection in the low, moderate, and high risk patients was 6%, 19%, and 34%, respectively. Angiotensin-II receptor blocker therapy was associated with less type B aortic dissections (HR: 0.3; 95%CI: 0.1-0.9; p=0.030).
Conclusion: Marfan patients with prior prophylactic aortic surgery are at substantial risk for type B aortic dissection when the descending aorta is only slightly dilated. Angiotensin-II receptor blocker therapy seems to be protective in the prevention of type B aortic dissections.

P3271 | BEDSIDE
Tricuspid regurgitation predicts adverse events in tetralogy of Fallot

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Purpose: Tetralogy of Fallot (TOF) patients may develop tricuspid regurgitation (TR) due to annulus dilation or leaflet abnormalities. Our objective was to determine outcome of patients undergoing pulmonary valve replacement (PVR) and the effect of pre-operative TR.
Methods: Our retrospective, multicenter cohort consisted of 157 TOF patients who had undergone PVR between 1986 and 2013. 129 TOF patients (61% male, mean age at PVR 32.9±10.4 years, follow-up 8.4±4.2 years after PVR) with pre-operative echocardiographic derived TR grade available were included. Pre- and post-operative imaging and clinical data were collected.
Results: Thirteen (10%) patients had severe (grade III) pre-operative TR compared to 28 (22%) patients with moderate TR (grade II) and 88 (68%) patients with no or mild TR (grade 0 or I). In patients with no or mild TR, immediate post-operative TR remained limited (0.8±0.5). Twelve (92%) patients with severe TR and 10 (36%) patients with moderate TR underwent concomitant TV repair. Immediate post-operative TR grade was similar in patients with moderate or severe pre-operative TR (respectively: 1.2±0.7 and 1.2±0.6). However, TR was more likely to increase (respectively: 1.1±0.6 and 1.6±0.8 at 4.5±0.7 years after PVR, p=0.08) during follow-up in patients with severe pre-operative TR. Adverse events occurred in 39 patients (5 death, 6 sustained VT, 7 heart failure, 21 supraventricular tachycardia). Patients with severe pre-operative TR were at high risk for adverse events (HR: 3.73, 95% C.I.1.69-8.21, p=0.001) despite successful TV repair.

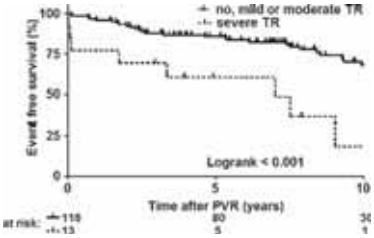

Figure 1. Event-free survival.

Conclusion: In TOF patients with severe TR undergoing PVR, TV repair resulted in a pronounced decrease of TR grade. However, those patients remained at high risk for adverse events and were prone for recurrent TR during follow-up.

P3272 | BEDSIDE
Right ventricular parameters are superior to clinical events for prognosis of adult patients with pulmonary hypertension due to congenital heart disease: long term outcome of a prospective study

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Purpose: Patients with pulmonary arterial hypertension (PAH) due to congenital heart disease (CHD) have a limited prognosis. In daily practice, combination therapy is often initiated after a clinical event. Although clinical events have been associated with a poor prognosis in idiopathic PAH, data on this association are limited in CHD-PAH. The aim of this study was to determine whether baseline characteristics and clinical events associate with mortality in patients with CHD-PAH.
Methods: In total 91 consecutive adults (42±14 year) with CHD-PAH were referred for therapy between January 2005 and June 2013. Cox proportional hazard analysis was performed to identify determinants of mortality, including clinical events as time dependent covariates.
Results: Twenty-four patients (nine with Down) died during the study period of 4.7 (range 0.1 – 7.9) years. The one and eight year mortality rates were 7.3% and 37.3%, respectively. Clinical events included admission for heart failure (n=9), arrhythmias (n=9), haemoptysis (n=5), change to a worse NYHA class (n=16), vascular events (n=1), syncope (n=1) and need for red blood cell depletion (n=4). In univariate analysis, both baseline characteristics and clinical events were associated with mortality. In multivariate analysis, only baseline NT-pro-BNP serum level ≥500 ng/L and TAPSE <15 mm at echocardiography were significant determinants of mortality. None of the clinical events remained significant. Patients with both a NT-pro-BNP serum level ≥500 ng/L and TAPSE <15 mm at echocardiography have a nine fold higher mortality rate than patients without both risk factors.
Conclusion: Prognosis is still poor in contemporary patients with CHD-PAH. Both baseline NT-pro-BNP serum level and right ventricular function are superior to

clinical events in prognostication. These two baseline characteristics should have a major impact on therapeutic management in patients with CHD-PAH, such as initiation of combination therapy.

P3273 | BEDSIDE
Enhanced beneficial outcome of losartan therapy in Marfan patients with FBN1 haploinsufficiency mutations

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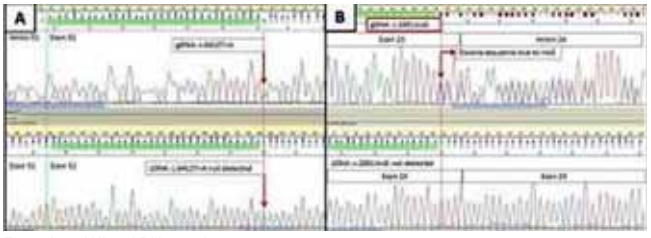
Background: Patients with Marfan syndrome (MFS) – mostly caused by FBN1 mutations – have an increased risk of life-threatening aortic complications. Classification of mutations based on biochemical effects of fibrillin-1 protein production, may predict clinical phenotype and response to medicinal therapy with β-blockers and losartan.
Methods: In this predefined sub-study of the COMPARE trial, we classified FBN1 mutations into: 1) mutations leading to normal fibrillin-1 abundance with mutant fibrillin-1 incorporated in the extracellular matrix, "dominant negative" (DN), 2) mutations leading to a decreased amount of normal fibrillin-1 without mutant fibrillin-1, "haploinsufficiency" (HI). The phenotype and the response to losartan and β-blocker therapy based on aortic root dilatation rate were compared between the two groups.
Findings: A pathogenic FBN1 mutation was found in 190 patients (85%). Patients with HI (n=67, 35%) displayed an equally severe MFS phenotype compared to DN mutations (n=123, 65%), with the exception of less frequently ectopia lentis (respectively 36% vs. 55%, p=0.015) and more often dural ectasia (respectively 60% vs. 38%, p=0·006). The inhibitory effect of losartan on the aortic root dilatation rate was most prominent in patients with HI no losartan: 1.8 versus losartan: 0.5 mm/3 years, p=0.003) compared to patients with DN mutations (no losartan versus losartan: 1.2 to 0.8 mm/3 years, p=0.205). The effect of β-blocker therapy on aortic root dilatation rate was comparable between groups.



Examples of HI and DN mutations.

Interpretation: We show that dominant negative FBN1 mutations as well as HI mutations lead to an equally severe clinical phenotype. However, MFS patients with HI FBN1 mutations appear to be more responsive to losartan therapy with respect to inhibition of aortic root dilatation.

P3274 | BEDSIDE
QRS duration is not associated with ventricular arrhythmias in repaired tetralogy of Fallot

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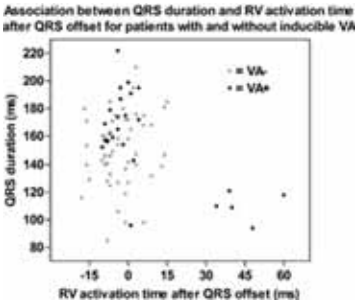
Introduction: QRS duration (QRS-d) has been related to ventricular arrhythmias (VA) in repaired Tetralogy of Fallot (rTOF). More than 80% of VA in rTOF are sustained monomorphic VT (SMVT) due to macroreentry facilitated by slow conduction. RV activation delay may be associated with VA.
Methods: A total of 83 rTOF patients (prior documented SMVT in 13, at risk for VA in 70) underwent programmed stimulation (3 drive cycle length (CL), ≥3 extrastimuli, from ≥2 RV sites, isoproterenol) and electroanatomical activation mapping (EAM). Five patients (pts) were excluded (incomplete EAM, ventricular pacing during EAM). QRS-d, total RV activation time (earliest to latest sharp electrogram on RV EAM) and the intervals between RV activation on/offset and QRS on/offset were measured and compared between pts with and without inducible VA.
Results: Twenty-seven of the included 78 pts (38±16 years, 52 male) were inducible for VA; 24 pts for SMVT (median 1.0 (1.0 – 1.8), VTCL 247 ms (230 – 278)) and 6 pts for sustained polymorphic VT/VF. QRS-d did not differ between pts with vs. without inducible VA (157±33 ms vs. 151±26 ms, p=0.350). Total RV activation time was significantly longer in pts with inducible VA as compared to pts without inducible VA (141±23 ms vs. 125±23 ms, p=0.004). RV activation after QRS offset was longer in pts with VA (5±20 ms vs. -3±8 ms, p=0.048), which was more pronounced in pts with QRS-d <125 ms (figure).



Conclusion: Not QRS duration, but total RV activation time is associated with inducible VA in rTOF.

P3275 | SPOTLIGHT
Mortality in adult congenital heart disease (ACHD): what are the causes, and who is at risk?

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Improvements in management of childhood congenital heart disease have seen a shift in the patient population from being primarily infant-based, to one in which adult survivors predominate. Published mortality data are limited, hindering evaluation and planning of provision of treatment services. This study examined ACHD patient mortality at a specialist ACHD unit to ascertain causes of death, high-risk conditions and identify any other population risk factors, in comparison to published literature.
The unit's ACHD population is ~5800 patients. We examined all deaths in the population for the 12 years to 2013. Examination of clinical records provided information including: date of death: age at death, main diagnoses, comorbidities and presence of cyanosis (O2 saturation <94%). These data were compared to those of published studies.
There were 104 deaths; an overall mortality of 2.0%. Median age of death was 37 years. >50% of deceased patients were cyanosed. Mortality was greatest in the groups: pulmonary arterial hypertension complicating congenital heart disease and complex cyanotic heart disease without pulmonary hypertension (32.5% and 26.5% respectively). In these groups, heart failure was the primary cause of death (68% and 64% respectively). Low mortality (<1%) was associated with ASD & repaired VSD, where 4 of 1373 died. No deaths were seen in some groups e.g. isolated pulmonary valve disease and post arterial switch for transposition of the great arteries.

Overall mortality was found to be lower in this population than in published literature. Groups at highest risk of death correlated with published literature. Heart failure was the commonest cause of death, suggesting that resources be allocated towards palliative care services, and research into ventricular support techniques.

P3276 | BEDSIDE
A different view on predictors of pulmonary hypertension in secundum atrial septal defect

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Purpose: Pulmonary hypertension (PH) is an important complication in hemodynamically relevant atrial septal defects (ASD) and has a known negative impact on outcome. This study aimed at (1) estimating the prevalence and clinical impact of PH in the Belgian secundum ASD population and (2) identifying predictors of development or persistence of PH after ASD closure.
Methods: Consecutive patients with an isolated ASD type secundum from the Belgian Registry on Adult Congenital Heart Disease were studied. Demographic, clinical, echocardiographic and invasive hemodynamic measurements were an-

alyzed. PH was defined based upon the probability of PH, obtained by tricuspid regurgitation velocity on transthoracic echocardiography (>2.8 m/s).
Results: Two hundred ninety-five patients, mean age 46±21 years, 68.8% females, were analyzed. The PH prevalence in the entire ASD population was 15.9%, compared to 13.3% in patients who underwent ASD closure. The median follow-up time was 4.8 (IQR 0.5 – 12.4) years. The presence of PH after ASD closure was significantly related to mortality (p=0.001), the presence of atrial arrhythmia (p<0.001) and right heart failure (p=0.019). Age at repair was the most important predictor for PH (Hazard ratio of 1.11 (95% CI 1.005–1.223)). In the oldest tertile of age at repair (>55 years), the prevalence of PH increased steeply (34%) and mean pulmonary artery pressure (mPAP) at catheterization before closure was related to PH at latest follow-up (Hazard ratio of 1.09 (95% CI 1.004–1.174)). These patients had a significantly increased mortality (p<0.001) and prevalence of atrial arrhythmia (p<0.001) during follow-up, compared to patients with ASD closure ≤55 years. In patients younger than 55 years, the ASD can be closed without impaired outcome, independent of mPAP at initial catheterization. Interestingly, twenty patients in the PH group had mPAP <25 mmHg at catheterization before closure.
Conclusions: PH is present in an important percentage of secundum ASD patients, even after ASD closure. The PH prevalence increased tenfold when the defect was repaired at ages higher than 55 years. The clinical outcome in this patient subgroup was clearly worse. PH still may develop despite normal mPAP before closure. The present findings raise the question whether the cutoff value for mPAP before closure should be age-adjusted.

P3277 | BEDSIDE
Adults with tetralogy of Fallot may have structural brain damage and cognitive impairment

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Background: Patients with congenital heart disease (CHD), especially those with cyanotic defects are at increased risk for structural brain damage through many pathophysiological mechanisms. Even mild but especially more severe defects such as tetralogy of Fallot (TOF) are also associated with unemployment and lower educational levels. Whether this is due to cognitive impairment and if so, if this is caused by structural brain damage, is yet unknown.
Purpose: The primary objective is to evaluate the presence of structural brain damage and assess cognitive functioning among adults with TOF.
Methods: In an ongoing single centre, prospective observational cohort study, brain damage in adult patients with TOF is studied. The target sample size is 100 patients. Magnetic resonance imaging (MRI) of the brain and an abbreviated neuropsychological test battery are added to the standard cardiac MRI. White matter lesions (WML) and (lacunar) cerebral infarcts on MRI are visually rated. Volumetric analysis will take place after the full study sample has been obtained. Neuropsychological testing consist of tests on executive functioning, memory, attention and accuracy. Age and education matched controls are tested to function as a reference group. Exclusion criteria for the study are mental retardation and all contra-indications for MRI.
Results: Thirty two patients were included so far. Median age was 40 years (IQR 31 to 49), 53% were women. From 1 patient, MRI images could not be obtained. WML were seen in 28 of 31 patients (90%): 10 patients (36%) had 1 WML, 5 patients (18%) had 2 WML and 13 patients (46%) had multiple (3 or more) WML. The median age of the patients with multiple WML was 47 years (IQR 39 to 55). Cerebral infarctions were seen in 7 of 31 patients (23%). Neuropsychological analyses have been performed and compared to a reference group for 16 patients. Intelligence quotient (IQ) scores and educational levels were relatively high among these patients (mean IQ 97 for patients, 104 for reference group, p 0.12). Preliminary results show lower scores on 2 tests on executive functioning (TMT-A and WAIS-IV symbol substitution test) and increased scores on the Stroop test, measuring accuracy.
Conclusion: Almost half of the adults with TOF have multiple WML and/or cerebral infarctions at relatively young age. Executive functioning may be somewhat impaired, compensated by increased accuracy. The clinical relevance and consequences of these findings and possible relations with clinical data as surgical history and cardiac morbidity will be further explored once the full sample has been included.

P3278 | BEDSIDE
The unnatural history of tetralogy of fallot: prospective follow-up of 40 years after surgical correction

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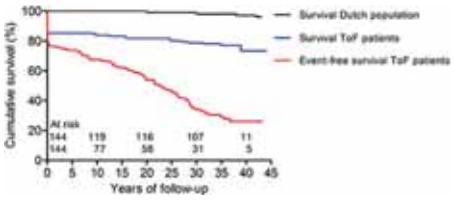
Purpose: To prospectively evaluate outcome up to 43 years after surgical correction of Tetralogy of Fallot (ToF) and to identify predictors for outcome.
Methods: This single-center longitudinal cohort study consists of 144 consecutive ToF patients who underwent surgical repair at age <15 years between 1968-1980 and are investigated every 10 years. The study protocol included medical history, physical examination, electrocardiography, Holter monitoring, bicycle ergometry, echocardiography and cardiac magnetic resonance imaging (CMR).
Results: Cumulative survival was 72% after 40 years. Late mortality (n=12) was due to heart failure (n=3), arrhythmia (n=3), complications of reintervention (n=2), non-cardiac (n=1) or unknown (3). Cumulative survival free from reintervention, arrhythmia, heart failure, stroke and endocarditis was 26% after 40 years. Forty-nine percent of the patients underwent pulmonary valve replacement (PVR), of whom 54% in the last decade. Pacemaker and/or ICD implantation was necessary in 12%. Early postoperative arrhythmias were a predictor for late arrhythmias (HR 3.7 [95%CI 1.3-10.5]), and also for all-cause mortality (HR 2.5 [95%CI 1.2-5.4]). Insertion of a transannular patch was a predictor for late arrhythmias (HR 4.0 [95%CI 1.2-13.4]) and PVR (HR 3.5 [95%CI 1.4-8.9]). Increase in QRS-duration, deterioration of exercise tolerance and ventricular dysfunction did not predict mortality.



Survival and event-free survival.

Conclusions: Forty years after surgical correction of Tetralogy of Fallot in childhood, 72% of the patients are still alive. Morbidity is substantial, with reinterventions in almost half of the patients. Early postoperative arrhythmias are associated with mortality.

P3279 | BEDSIDE
Adults with complex congenital heart disease have impaired skeletal muscle function and lower confidence in performing exercise training compared to healthy age and gender matched controls

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Background: Adults with congenital heart disease usually have reduced aerobic exercise capacity compared to healthy counterparts. However, their skeletal muscle function is less studied.
Material and methods: Unilateral isotonic shoulder flexion, unilateral isotonic heel-lift, maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were tested in 85 adults (35 women, mean age 36.8±14.8) with congenital heart disease, classed as either “complex” (n=43) or “simple”(n=42), and 42 age and gender matched healthy controls (16 women, mean age 36.9±14.9). Maximum counts of shoulder flexions, from 0 to 90 degrees, with the patient sitting position, holding a weight (women 2 kg, men 3 kg) was registered. Maximum counts of heel-lifts performed standing on one leg on a 10-degrees tilted wedge were measured. In both tests, the pace was set by using a metronome. MIP and MEP were tested using a hand-held respiratory pressure meter. The highest value out of three tests was registered. Exercise self-efficacy (ESE), measuring confidence in performing exercise training, was evaluated using the national ESE questionnaire.
Results: Adults with complex lesions performed less shoulder flexions compared to healthy controls and to patients with simple lesions (28.2±11.1 vs. 63.6±40.4, p<0.001 and 28.2±11.1 vs. 54.9±24.9, p<0.001), as well as less heel-lifts compared to controls and patients with simple lesions (17.6±7.7 vs. 26.3±12.8, p<0.001 and 17.6±7.7 vs. 23.2±7.0, p=0.024), lower MIP than controls (80.7±26.7 vs. 111.1±29.9 cmH2O, p<0.001) and lower MEP (110.8±39.9 vs. 141.8±39.5, p<0.001) compared to controls. They rated their confidence in performing exercise training (ESE) lower than controls (28.0±8.3 vs 33.4±6.1, p=0.002). Regression analysis showed that only complexity of the cardiac lesion was associated with impaired muscle function (p<0.001).
Conclusion: Adults with complex congenital heart disease have impaired skeletal muscle function compared to patients with simple lesions and healthy controls. ESE was lower in patients with complex lesions. Thus, this population is well suited for rehabilitation focusing on improving muscle function and confidence in performing exercise training.

P3280 | BENCH
Are the simple congenital heart disease so simple? Results from a longtem follow up

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Aim: To describe long term mortality in patients with "simple" congenital heart disease (CHD), defined as isolated and uncomplicated sec. ASD, VSD, ductus (PDA) or pulmonary stenosis (PS).
Methods: A national cohort of CHD, diagnosed from 1963 to 1974, was collected prospectively. 98.5% of these patients were identifiable in national patient registries (n=4,207). We extracted all patients, that at age 10, fulfilled the criteria of simple CHD and no other congenital or birth related disorders. Using national registries, survival status of all patients was retrieved. Patients were excluded if they later had an additional or corrected CHD diagnosis. A cohort of general population controls with a similar age, gender and geographical distribution was created 1:10 for comparison.
Results: 1,262 patients fulfilled the inclusion criteria, yielding a follow up time of 57,280 patient-years. Mean follow up from diagnosis was 45.3 years (range: 9-72 years). There were 222 patients with ASD sec., 284 with PDA, 147 with PS and 609 with VSD. No statistical differences was found in follow up time between groups (p=0.696). In patients with simple CHD, there were 90 deaths, plus two successful resuscitations not included in analysis. After adjustment for age and gender (Cox proportional hazards), these patients had increased mortality compared to controls (HR: 1.57; CI: 1.234-1.984). The cause of death was sudden/unexplained in 44 (49%), non-sudden cardiac in 13 (14%), and other in 33 (37%). Median age at death was 39 years (12 -56). There were no differences in death rates between the different CHD groups. (p=0.591).
Morbidity data will be presented.

Conclusion: Patients with simple CHD have increased mortality later in life. This suggests that lifelong clinical follow-up, even in simple CHD may be reasonable.

GENERAL AND PAEDIATRIC CONGENITAL CARDIOLOGY

P3282 | BEDSIDE
Cardiac death and myocardial infarction on Kawasaki disease with giant coronary aneurysm: Analysis of recent nationwide survey in Japan

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Background and objective: Long term prognosis of Kawasaki disease (KD) with giant aneurysm is not yet well understood. We conducted a nationwide survey of KD with giant aneurysm for recent 10 years, and analyzed the cases of acute myocardial infarction (AMI) and cardiac death.
Methods: Nationwide epidemiological survey of KD has been conducted every 2 years since 1970 in Japan. We performed questionnaire survey based on 16th – 21th (1999 – 2010) nationwide epidemiological data.
Results: We send questioners to 275 facilities asking about 415 patients who were reported to have giant aneurysm (≥8mm), and collected the data of 334 patients (80.5%). We excluded 84 non-giant aneurysm patients and 36 duplicated cases and difined finally 214 patients. Out of 214 patients, 13 deaths and 32 AMIs were described (6.1% and 15.0%, respectively). The first AMI attack was mostly reported within a few months from KD onset (medium 5 months (0-85 months)). AMI was occurred one time in 26 patients, and two times in 6 cases. Myocardial ischemia was observed in 80% of AMI patients, and 12 patients were received coronary artery bypass graft. Thirteen patients were reported to be dead (medium 1 month (0-23 months) from KD onset). There were 6 cardiac deaths within 1 month from KD onset (5: rupture of aneurysm, 1: AMI). The others were all caused by AMI except for 2 accidental death. Four out of 6 AMI deaths were caused by the first AMI attack. For the remaining 2 AMI deaths, the period from the first AMI to second fatal AMI was 1 month and 6 month, respectively. There were no death reported byond 2 years from KD onset.
Conclusion: AMI and cardiac death of KD with giant aneurysm occurred mostly in early phase of KD onset. When the patients survive the first month of KD onset, and overcome the first AMI, patient survive become promising. And there is no cardiac death beyond 2 years from the onset. These evidences show that treatment strategy in acute phase is extremely important for prognosis for KD with giant aneurysm.

P3283 | BENCH
Suppressing inflammation in Marfan syndrome: be careful

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Purpose: Patients with Marfan syndrome have an increased risk of life-threatening aortic complications, preceded by aortic dilatation. A number of studies have shown increased inflammation in aortic tissue of humans and mice with MFS and we hypothesize that anti-inflammatory medication will reduce the aortic dilatation rate in MFS mice.
Methods: In this study, FBN1C1039G/+ mice (MFS mice) were treated with abatacept (specific T-cell inhibitor), methylprednisolon (general inflammation inhibitor), losartan (angiotensin-II type-1 receptor blocker with anti-inflammatory features) or placebo. Treatment was started at the age of two months and continued for eight weeks.
Results: In the aorta of MFS placebo mice migration of Leukocytes (CD45) and macrophages (MAC) was significantly increased as compared to wild-type mice (CD45: 0.82±0.09 versus 2.53±0.58, $p<0.001$; MAC: 0.93±0.21 versus 2.45±0.65, p=0.004). The anti-inflammatory drugs methylprednisolone and abatacept reduced macrophage and leukocyte infiltration into the aortic wall in MFS mice. However, they did not reduce the aortic root dilatation rate. Beside a reduction in aortic root dilatation rate, losartan was the only treatment which reduced inflammation and pSMAD2 signalling. Furthermore, combining all MFS mice within this experiment, higher pSMAD2 signalling is correlated with faster aortic root dilatation rate (r=0.336, p=0.010).

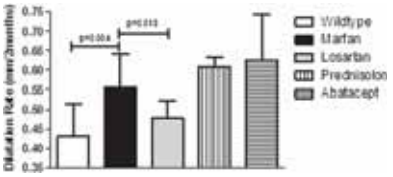

Figure 1. Aortic root dilatation rate.

Conclusion: Inflammation is up-regulated in the MFS C1039G mouse model. Reduction of inflammation by methylprednisolone or abatacept, did not reduce but slightly increased aortic root dilatation rate. Losartan was the only treatment reducing pSMAD2 signalling and aortic root dilatation rate and pSMAD2 thus seems to play the key role in the beneficial effects of losartan treatment.

P3284 | BENCH
Establishment of a german research network for congenital heart defects

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Objectives: The Competence Network for Congenital Heart Defects (CNCHD) was established to facilitate multicentre medical und socio-medical research in the field of congenital heart defects (CHD), which is intended to lead to an improvement of health care and out-come for this relatively new and continuously rising patient group. Due to the characteristics of this disease (high variability of morphological heart defects, chronic illness), the network infrastructure has to overcome specific challenges such as research in underage patients or the implementation of a legal framework for long-term storage of data and biomaterial.

Methods and results: The CNCHD succeeded in implementing a sustainable research infrastructure involving all important stakeholders throughout Germany. The infrastructure is built around the non-profit registered association National Register for Congenital Heart Defects (NRCHD e. V.) that provides a dynamic and flexible IT-platform for different types of database-systems for register studies and a multicentre biorepository that collects blood-derived DNA and cardiac tissue from heart surgery. Thanks to central patient and ID management, data of different formats and recorded at different times can be clearly assigned to respective patients, thus allowing multicentre and longitudinal investigations. Electronic case report forms and remote data entry are used to centrally collect and store the data. Specific role based access rights management can be implemented for decentralised data entry by different users (physicians, researchers, documentation staff, monitors, sample laboratory etc.), e.g. within the scope of multicentre studies. This enables the integration of national and international research units, which is of particular importance with regard to recruiting new cooperation partners.
In January 2014 the National Register comprises 46.333 participants. The majority (64%) is underage, sex is evenly distributed. Simple heart lesions represent 38%, moderate 52%, and severe/complex 10%. The DNA collection currently comprises samples from aproximately 3000 participants covering a wide range of CHD phenotypes. The collection includes also trios (patient + unaffected parents) and families with more than one affected member.
Conclusions: The CNCHD provides a comprehensive basis for high-level research in the field of CHD with high standards of ethics, data privacy, IT management and sample logistics.

P3285 | BENCH
Possible implication of IL-23-IL-17 axis and proline-rich tyrosine kinase 2 in pathogenesis of Kawasaki disease

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Introduction: Although the pathogenesis of Kawasaki disease (KD) is unknown, innate immunity are implicated in the vasculitis. In macrophages and dendritic cells, inflammatory signaling pathways are activated through pattern recognition receptor (PRR). Candida albicans water-soluble fraction (CAWS) which is widely used to make model mice of KD enhances the production of IL-23 by their cells through dectin which is one of PRR, and IL-23 induces to produce IL-17,proinflammatory cytokine, from IL-23 receptor+ cells. Furthermore, among macromolecules regarding in the PRRs-dependent signaling pathways, it has recently emerged that proline-rich tyrosine kinase (PYK2) is involved in the processes through NF-kB activation. We investigated a possible relevance of IL-23-IL-17 axis and Pyk2 in the pathogenesis of KD.
Methods: Pyk2-knock out (Pyk2-KO) and wild-type C57BL/6 mice (WT) were administered CAWS to induce KD-like vasculitis. Extension of the experimental vasculitis and expression of IL-23R and IL-17 were immunohistochemically determined. CAWS-stimulated NF-kB activation was evaluated by quantifying nuclear translocation of NF-kB p65 subunit in peritoneal macrophages isolated from PYK2-KO and wild-type mice in vitro.
Results: Pyk2-KO mice didn't show any apparent defective phenotype. While marked inflammation was observed in the aortic root of CAWS-treated WT mice, such vasculitis was barely detected in CAWS-treated Pyk2-KO mice. IL-23 receptor+ and IL-17+ cells presented in the aortic valves, the proximal region of it and adventitia of the aortic root in both Pyk2-KO and WT mice, and these cells apparently increased in only CAWS-administrated WT mice. Moreover, CAWS-induced NF-kB activation was also less observed in macrophages from Pyk2-KO mice.
Conclusions: These findings suggest that IL-23-IL-17 axis and Pyk2 are involved in the pathogenesis of KD, and can also explain a part of the mechanism to define the site specificity of vasculitis in this model. Pyk2 play indispensable rules in KD, and it may be a potential therapeutic target for KD.

P3286 | BEDSIDE
Fetal cardiovascular programming in pregnancies conceived by assisted reproductive technologies

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Purpose: Children conceived by assisted reproductive technologies (ART) show postnatal hypertension and vascular dysfunction. However it is unknown whether cardiac remodeling is also present and if these changes already manifest in prenatal life. Our aim was to evaluate cardiac and vascular function in fetuses and infants conceived by ART.
Methods: A prospective cohort study including 50 singleton fetuses conceived by ART and 50 controls spontaneously conceived assessed in utero and in the infancy (6 months of age). Fetal echocardiography was performed at 28 weeks of gestation including cardiac morphometry and longitudinal motion by M-mode and tissue Doppler. Infant evaluation included blood pressure and aortic intima-media wall thickness measurements together with echocardiography. Cardiovascular results were calculated by linear regression adjusted by birthweight and preeclampsia.
Results: ART fetuses had with signs of cardiac remodeling including dilated atria (right atrium/heart ratio in controls 1.4% (1.2-1.5) vs. ART 1.6% (1.3-1.8) P=0.011), more globular hearts (right sphericity index in controls 1.6 (1.4-1.7) vs. ART 1.4 (1.2-1.5) P<0.001), thicker myocardial walls (septal wall thickness in controls 2.4 mm (2.2-2.7) vs. ART 2.8 mm (2.4-3) P=0.001), decreased longitudinal systolic function (tricuspid annular excursion in controls 6.5 mm (6.0-7.1) vs. ART 5.5 mm (5.1-6.1) P<0.001) and impaired relaxation (mitral early diastolic annular peak velocity (E') in controls 8.4 cm/s (7.9-9.3) vs. ART 8 cm/s (7-11). Most echocardiographic features persisted postnatally, together with a tendency to higher mean blood pressure (controls 63 mmHg (57-72) vs. ART 67 mmHg (61-75) P=0.188) and aortic wall thickness (controls 0.46 mm (0.35-0.52) vs. ART 0.55 mm (0.52-0.60) P=0.016).
Conclusions: ART is associated with both cardiac and vascular remodeling already present in fetal life that persist postnatally. This opens opportunities for early detection and potential intervention in these children.

P3287 | BENCH
Investigating the cause of transposition of great arteries; exome sequencing analysis

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Introduction: Congenital heart disease (CHD) is the most common congenital abnormality, affecting approximately 7 in 1,000 live births. Transposition of the great arteries (TGA) is the most commonly diagnosed cyanotic heart defect in neonates. TGA is rarely associated with other genetic disorders or extracardiac abnormalities, but is seen in heterotaxy syndrome. We propose that TGA has a genetic cause, likely to be de novo or in genes causing heterotaxy syndrome.
Purpose: Exomes of 9 subjects diagnosed with TGA with no family history of CHD and their unaffected parents (trios) were subject to sequencing. The project aims were to: implement the exome bioinformatic analysis pipeline to identify de novo mutations (DNMs) and validate variants called by the pipeline. This is the first study investigating de novo changes in TGA patients.
Methods: A bioinformatic pipeline was set up to analyse sequencing performed on Illumina GAIIX following exon capture with Agilent Sure Select Exon Capture kit. Programs used included Casava-Gerald after base calling, NovoAlign/BWA for alignment, SAMtools for variant calling. Manual filtering criteria were applied (coverage ≥5, not in db SNP, no rs number, MAF ≤1% in 1000 genomes, Mutation Taster and PolyPhen-2 predicted as deleterious). Additionally the presence of mutations in any of the top 16 heterotaxy/ CHD genes identified from the literature was checked. Integrated Genomics Viewer (IGV) was used to inspect the variants. Variants were validated by Sanger sequencing.
Results: The bioinformatic pipeline identified on average 188 DNMs per trio. 17 variants were chosen for validation. 6 were chosen due to high probability of being true positives based on IGV. 11 variants were chosen on the basis of being in a candidate gene.
Upon validation 1 trio had 2 de novo mutations: a nonsense change in ZNF227 and a missense in PHLPP2. 1 trio had a de novo change in RBP5. 1 trio had an inherited splice site change in RTTN, a candidate gene.
Conclusions: The most interesting change is a nonsense mutation in the ZNF227 gene predicted to cause NMD of the transcript. Little is known about ZNF227 but it belongs to a family of zinc fingers which are known to be involved in transcriptional regulation and are associated with CHD.
The inherited splice site change in RTTN is also interesting as animal models showed that RTTN is essential for left-right (L-R) specification and embryo turning. This makes rotatin a sound candidate that could contribute to developing TGA.
The presence of de novo and inherited mutations suggests a complex polygenic cause of TGA.

P3288 | BEDSIDE
Quality of life of children with congenital heart diseases: a multi-center controlled cross-sectional study

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Purpose: To assess health-related quality of life (QoL) in children with congenital heart diseases (CHD) with a validated questionnaire in comparison with control children.

Methods: This comparative cross-sectional study was carried out between 2009 and 2011 in tertiary care CHD centers (France and Belgium) and in 10 school classes (from 3rd grade to 12th grade) randomly selected from the Education Ministry database. Children's QoL was self-reported with the Kidscreen-52 questionnaire and reported by parents with the Kidscreen-27. QoL scores of each dimension were compared between CHD and controls and between the classes of disease severity defined by Uzark et al. Informed consent was obtained from all parents.
Results: We recruited 282 children with CHD aged 8 to 18 and 180 same-age controls in schools. Centers were comparable for most demographic and clinical data. Self-reported QoL scores did not differ between CHD children and controls except for physical well-being (mean 46.52±10.17 vs. 50.16±8.77, $p<0.001$), financial resources (45.88±11.74 vs. 48.88±10.27, p=0.01) and peers/social support (48.08±12.33 vs. 50.97±10.11, p=0.01). No differences were noted among teenagers. Parent-reported scores were lower in CHD children for physical well-being, peers/social support and school environment (all $p<0.001$), in both age groups (8-12 and 13-18 years). Self-reported scores did not differ between severity classes whereas parent-reported scores were more impacted by severity. QoL of the lowest severity class was similar to that of controls.

CHD severity classification

Severity class 1	Mild CHD requiring no therapy or effectively treated non-operatively (catheter therapy)
Severity class 2	Moderate CHD requiring no therapy or surgically corrected (curative)
Severity class 3	Surgically treated CHD with significant residua or need for additional surgery
Severity class 4	Complex or severe CHD, uncorrectable or palliated (includes single ventricle)

From Uzark et al. Pediatrics 2008.

Conclusion: QoL of children with CHD was close to that of same-age healthy children except for physical well-being, financial resources and peers/social support. QoL for low severity CHD patients was similar to controls. QoL for severe CHD was not always impacted. To our knowledge, this large study is the first in Europe to assess QoL of children with CHD in comparison to controls with a validated questionnaire.

P3289 | BEDSIDE
Leukocyte telomere shortening in grown-up patients with congenital heart disease

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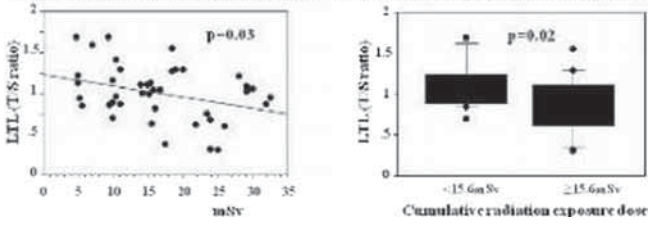
Background: Cardiac imaging procedures frequently expose children with congenital heart disease (CHD) to ionizing radiation, but their contribution to biological and health risks remain unknown. Leukocyte telomere length (LTL), a marker of biological aging, is related to several radiation-associated diseases, including cancer and atherosclerosis. We assessed LTL in grown-up patients with CHD (GUCHs) and a positive history of medical radiation exposure as well as the influence of functional SNPs in DNA repair genes.
Methods: Fifty GUCH patients (26 males; age 25.2±9.0 years) who underwent cardiac ionizing procedures (mostly cardiac catheterization) for CHD in 1965-2000 and 50 healthy matched subjects (20 males; 27.0±3.1, years) who were negative for history of medical radiological exposure were included. In GUCH patients, the cumulative exposure was estimated as effective dose in milliSievert (mSv). LTL was measured by qReal Time-PCR. XRCC1 (Arg194Trp) and XRCC3 (Thr241Met) SNPs were evaluated by RFLP-PCR analysis.
Results: GUCH patients showed significantly shorter LTL than controls (1.0±0.3 vs 1.3±0.4, p=0.001). Estimated cumulative radiation dose was 18±9 mSv (median:15.6mSv; range 4.8–45.0).
GUCH patients with >15.6mSv dose exposure had significantly the shortest LTL (Figure). XRCC1194Trp and XRCC3 Met241 alleles significantly interacted with radiation dose exposure (both $p<0.02$) on LTL. Age-gender adjusted logistic regression analysis showed a 5.0-fold (CI 95%, 1.4-18; p=0.01) increased risk lower LTL value (≤1.02) for risk allele.

Figure. Cumulative radiation exposure dose and leukocyte telomere lenght (LTL) in GUCH patients



Conclusion: GUCH patients have LTL shortening, suggesting evidence of early biologic aging. Common SNPs in DNA repair genes modify the effects of medical exposure on radiation LTL-related degenerative diseases.

P3290 | BEDSIDE
Long term follow-up and prognosis of patients with ALCAPA

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The aim of the study was to assess the long term outcome of patients with ALCAPA
Methods: This study is a retrospective single-center analysis of patients who underwent surgery for ALCAPA from 1980 to 2012. Surgical techniques, demographics, echocardiographic parameters and outcomes were collected. Patients were divided into group I <2 years at diagnosis, group II: >2 years).
Results: 48 patients (28 females) were included, median age 6months (min 4mos, max 65y), median weight 6kg (min 1.9kg): 36 in group I and 12 in II. Symptoms of HF were present in 39 patients (mean age 4y), 9 were asymptomatic (mean age 10y) and Qwave on ECG was present in 87% of cases. Mean LVSF= 24.2% (group I= 26.6% vs II= 37.7%, and 16.6% in patients <6mos of age), LVEDD and LVESD Z-scores were respectively +2 and +5 in groups I and II; 73% had MR:severe in 6%, moderate in 46%, mild in 21%. Left coronary artery ostium located in the left posterior sinus in 31cases, right posterior sinus in 12 and in right pulmonary branch in 4. Direct coronary artery reimplantation was performed in 71%, Takeuchi technique in 6%, Meyer technique in 20% and LCA ligation in 3%. Mean age at surgery was 29mos, mean weight 9kg. Postoperative mechanical circulatory support was required in 3 cases, who had more severe HF, lower LVSF and longer bypass duration. Mean FU was 81mos (6 to 312mos). Freedom from reoperation was 100% at 1y, 91% at 10y and 88% at 20y. LVSF increased by 20% in the early postoperative course and 36% at late FU. MR improved significantly in most of the cases. Overall mortality was 33% (15 in group I died before post-operative Day-30, none in group II), decreasing over time from 55% to 11%, and was lower in patients who underwent direct reimplantation. Q wave disappeared in 82% of the cases; 93% of the survivors were asymptomatic at latest evaluation.
Conclusion: ALCAPA patients have overall good long-term survival and outcome. Age >2y at diagnosis and direct implantation are factors of favourable prognosis.

P3291 | BENCH
Involvement of innate humoral immunity in the pathogenesis of Kawasaki disease-like murine vasculitis

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Objective: Kawasaki disease (KD) is a paediatric sterile vasculitis. Although uncontrolled innate immune responses to some types of pathogens have been implicated in its pathogenesis, its aetiology is still unclear. Based on studies using an established animal model for KD, we aimed to address how humoral innate immune system involved in the pathogenesis of the disease.
Methods: The KD mouse model was prepared by administering a Candida albicans water-soluble extract (CAWS) as reported by Ohno and Miura. Sequential frozen sections of the aortic tissue was subjected to immunohistochemical studies.
Results: The levels of mannose binding lectin-A (MBL-A), immunoglobulin G (IgG) and immunoglobulin M (IgM) gradually increased in the serum of the CAWS-administered mice. Concomitant with an increase in these plasma proteins, deposition of MBL-A, mannose binding lectin-C (MBL-C) and IgM was observed in the aortic root, a predilection site for experimental vasculitis. The deposition patterns of MBLs and IgM were observed to correspond to the marked deposition pattern of the complement component 3 (C3)/C3-derived peptides in the aortic root, suggesting that MBLs and IgM activate complement pathways both independently and synergistically to involve in the pathogenesis of the KD-like murine vasculitis. With regards to the self-reactivity of these molecules, MBL-A and MBL-C were found to interact with histones to activate the lectin pathway in vitro. In addition, a proteomic study revealed that the CAWS-induced IgM antibodies also recognised some specific endogenous proteins.
Conclusions: Taken together, these results suggest that some types of infectious stimuli provoke self-reactive humoral immune molecules (e.g. MBLs and IgM-type autoantibodies) in the mouse model, causing and/or exacerbating KD-like vasculitis through activation of the lectin and/or classical pathway. The complement pathways could be a promising therapeutic target for KD.

P3292 | BEDSIDE
The risk of type 1 diabetes and associated risk factors in patients with congenital heart disease - a case control study

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Purpose: In Sweden patients with a diabetes diagnosis are registered in the National Diabetes Registry (NDR). In this retrospective register study we analysed the risk of mortality and morbidity associated with concurrent congenital heart dis-

ease (CoHD) in patients with type 1 diabetes. Comparison was made to patients with type 1 diabetes and no associated congenital condition.
Methods: This study combined data from the NDR and the national patient registry, looking for patients with CoHD as additional diagnosis. Patients with diabetes but no CoHD served as a control group. The groups were matched regarding year of birth, gender and year of registration. Clinical characteristics analyzed were age, gender, diabetes duration, systolic blood pressure, BMI, waist measurement, retinopathy, HbA1c, smoking, microalbuminuria, antihypertensive treatment, lipid lowering drug use and type of hypoglycaemic treatment. Baseline values were the last registered values in the NDR of every patient.
Results: 157 patients were identified in the NDR with a CoHD and type 1 diabetes and could be matched with 785 patients who served as controls. Patients with CoHD and type 1 diabetes had more registered data, were found to have significantly higher HbA1c (69 vs. 65 mmol/mol, p=0.002) similar use of lipid-lowering drug use (36.3 vs. 32.9%, p=0.46), and smoking (10,8 vs. 14,4%, p=0.31). Patients with CoHD and type 1 diabetes had slightly higher insulin use (96.2 vs. 93.8%, p=0.26) and less use of oral hypoglyceamic agents (3.8 vs. 6.2%, p=0.35). A higher prevalence of cumulative microalbuminuria (20.4 vs. 13.5%, p=0.03) was found in patients with CoHD and diabetes compared to patients without CoHD while there was no significant difference regarding systolic blood pressure (125 vs. 126 mmHq, p=0.48), waist measurement (93 vs. 92 cm, p=0.56) and retinopathy (51.6 vs. 52.9%, p=0.64).
Patients with type 1 diabetes and concurrent CoHD had a higher mortality as compared to controls (p=0.01 Log rank survival estimates), and 5.1% of the CoHD patients died before 50 years old while 2.9% of patients without CoHD died before 50 years old (p=0.07).
Conclusions: In a broad sample of patients from a nationwide registry of patients with type 1 diabetes, we found that coexistence of CoHD and diabetes type 1 was associated with higher degree of microvascular complications and a higher mortality.

P3293 | BEDSIDE
Respiratory modulation of exercise hemodynamics in Fontan patients

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Background: Phasic changes in intrathoracic pressures during respiration influence infradiaphragmatic and pulmonary blood flow in Fontan patients. However, the contribution of respiration to ventricular filling and stroke volumes at rest and during exercise has not been previously evaluated in Fontan patients.
Methods and results: Ten Fontan patients (6 male, 20±4 years) underwent cardiac magnetic resonance (CMR) imaging at rest during normal breathing and the Valsalva manoeuvre. Afterwards, patients underwent real-time CMR during symptom-limited supine exercise. Systemic ventricular volumes were obtained at rest and during low (34±15 Watt), moderate (69±29 Watt), and high (97±36 Watt) intensity. Respiratory dependent end-diastolic volume ((EDVI insp–EDVi exp)/(EDVI insp+EDVI exp)*100) and stroke volume ((SVI insp–SVI exp)/(SVI insp+SVI exp)*100) was calculated.
During normal breathing, inspiration resulted in a higher end-diastolic volume (EDVi) (103.0±10.9 vs 98.4±11.6 mL; P=0.001) and stroke volumes (SVi) (58.6±6.4 vs 55.3±6.3 mL; P=0.001), whereas end-systolic volume (ESVi) was similar (44.4±10.0 vs 43.1±10.0 mL; P=0.096) when compared to expiration. During Valsalva, EDVi (P=0.001), ESVi (P=0.003) and SVi (P=0.005) decreased. The effect of respiration on EDVi (mean change 6±1 mL; P<0.0001 – Interaction P=0.130), ESVi (mean change 1±1 mL; P=0.151 – Interaction P=0.776) and SVi (mean change 4±1 mL; P<0.0001 – Interaction P=0.114) was maintained throughout exercise. Respiratory dependent EDVi (3±2 to 5±3%; P=0.084) and SVi (2±2 to 3±2%; P=0.044) tended to increase slightly during exercise.
Conclusion: Ventricular filling oscillates with respiratory phase such that EDVi and SVi are maximal at end-inspiration. This underscores the importance of respiration for ventricular filling in Fontan patients and provides a rationale for inspiratory muscle training in these patients.

RHYTHM DISTURBANCES IN CONGENITAL HEART DEFECTS

P3295 | BEDSIDE
Low incidence of ventricular arrhythmias and high complication rate of implantable cardiac defibrillators in adult patients with Tetralogy of Fallot

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Purpose: Sudden death due to ventricular arrhythmia is a major cause of fatality in adult congenital heart disease. Repaired Tetralogy of Fallot (TOF) patients are considered to be at high risk. We present long-term follow-up of a large cohort of TOF patients to identify the incidence of ventricular arrhythmias, mortality and the indications and outcomes of implantable cardiac defibrillator (ICD) implantation.
Methods: All TOF patients followed up by a single specialist adult congenital heart disease centre between 2000 and 2013 were included (n=455; mean age 35.6 years). Their medical records were retrospectively reviewed from their first attendance to the end of the year 2013 (mean follow-up 6.9 years).
Results: Thirteen patients (2.86%) had at least one episode of sustained ventricular tachycardia; annual rate 0.41%. Eight patients had an ICD implanted and two patients were treated with VT ablation only. One patient received no treatment as electrophysiological study was negative. The remaining two patients were treated conservatively, as reversible causes were identified. All 13 patients were alive at the time of data collection.
Six patients (1.32%) suffered cardiac arrest. Reversible causes were identified in one case, so ICD was not implanted. The remainder received an ICD.
A number of non-life-threatening cardiac arrhythmia events were noted. Eighteen patients (3.96%) had at least one episode of non-sustained ventricular tachycardia, eight of whom received an ICD for primary prophylaxis.
In total, twenty-one ICD devices were implanted. During a mean post-implant follow-up period of 3.4 years, four patients had appropriate shocks (annual rate 5.59%), whilst five patients experienced inappropriate shocks. The overall complication rate including infection, lead abnormalities and inappropriate shocks was 43% (annual rate 12.6%).
Twenty deaths (4.40%) were registered during the follow up period giving a mean annual mortality rate of 0.64%. Twelve of these were known to be due to causes other than sudden death. The cause of death in the remainder is uncertain.
Conclusions: TOF patients are thought to be at increased risk of ventricular arrhythmias and sudden cardiac death. We show that the overall event rate and all-cause mortality rates are very low, with combined annual incidence of ventricular arrhythmia and cardiac arrest at just 0.60%. There was a high incidence of ICD complications. Physicians should risk assess patients with TOF to avoid over-implanting ICDs and patients should be carefully consented regarding the potential risks and benefits, particularly in primary prevention cases.

P3296 | BEDSIDE
The clinical validity of prior radiofrequency catheter ablation for prevention of recurrent atrial fibrillation after transcatheter closure of atrial septal defect

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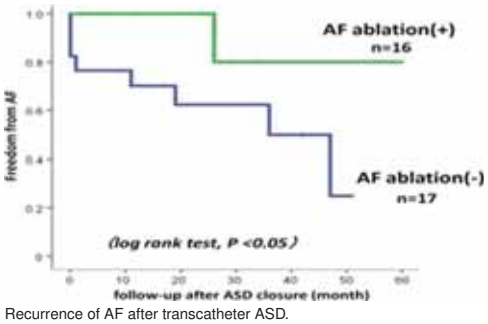
Background: Atrial fibrillation (AF) is highly prevalent in adult patients with atrial septal defect (ASD) and affects cardiac morbidity. Nowadays transcatheter therapies are well-established both in AF and ASD, that is, radiofrequency catheter ablation (RFCA) and transcatheter device closure, respectively. However, the appropriate therapeutic strategy of concomitant AF in patients with an ASD is still unclear. In this study, we assessed the efficacy of prior RFCA to prevent recurrent AF after transcatheter ASD closure.
Methods: We evaluated consecutive 33 patients (age, 62±14 years) who complicated with paroxysmal or persistent AF before transcatheter ASD closure. Recurrence of AF after transcatheter ASD closure was compared between patient groups with and those without prior RFCA for AF.
Results: Sixteen of 33 patients had been undergone RFCA for AF prior to ASD closure. During the follow-up period (mean; 22±14 months) after ASD closure, recurrence of paroxysmal AF was observed in 2 of 16 (17%) with RFCA, contrary in 7 of 17 (41%) without RFCA (P<0.05). Maximal ASD diameter, Qp/Qs and left atrium diameter were similar between patients with and without prior RFCA. Although age at ASD closure was significantly older in patients without prior RFCA (67±12 vs. 56±15 years, P<0.05), there was no significant correlation between age at ASD closure and AF recurrence.



Recurrence of AF after transcatheter ASD.

Conclusion: Prior RFCA for concomitant paroxysmal or persistent AF in patients with an ASD is a valid therapeutic strategy for reducing the recurrence of AF after transcatheter ASD closure.

P3297 | BEDSIDE

Congenital heart disease and atrial fibrillation or flutter: the rate of thromboembolism and bleeding events

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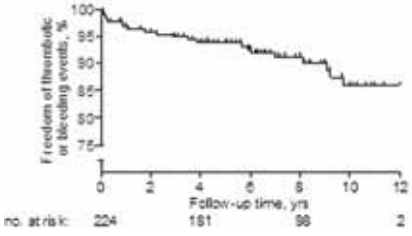
Purpose: Atrial fibrillation or flutter (AF) occurs in 15% of adult patients with congenital heart disease (CHD) and is associated with high morbidity, mainly due to thromboembolic complications. Prior studies in general population with AF have demonstrated a thromboembolic event rate of 1.3% per year. It is not clear whether these numbers apply to CHD patients as well. This study aimed to assess the rate of thromboembolism and bleeding events in CHD patients with AF.

Methods: Adult CHD patients with AF in a single center were selected from a national regstry and study data were collected from the registry and patient's files. Thromboembolism was defined as ischemic cerebrovascular accident (iCVA), transient ischemic attack (TIA), systemic or pulmonary embolism. Major bleeding was defined as intracranial bleeding, fatal bleeding, or symptomatic bleeding leading to intervention or hospitalization.

Results: Between 2002 and 2014, 224 CHD patients were identified with AF (median age 41 years; IQR 32-56). Median follow-up was 8 years (IQR 5-10). In 19 patients, a total of 26 thromboembolic events occurred with an annual event rate of 1.6% (iCVA or TIA n=22, systolic embolism n=3, pulmonary embolism n=1). Furthermore, 10 patients suffered from 12 major bleedings, the annual event rate being 0.7% (intracranial n=3). During the study period 41 deaths occurred, of which 4 (10%) because of bleeding.

Figure 1. Freedom of thromboembolism or bleeding events in CHD patients with AF.



Conclusion: In adult CHD patients with AF the annual event rate of thromboembolism is 1.6% and of major bleeding 0.7%. Even though this study population is relatively young, the rate of thromboembolism is comparable to that of the general population with AF. These preliminary results underline the importance of a well-considered anticoagulative strategy in CHD patients with AF.

P3298 | BEDSIDE

Predictors of supraventricular arrhythmias (SA) and outcome of catheter ablation in patients with ebstein anomaly (EA): a single-center experience

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Introduction: Ebstein anomaly (EA) is a congenital condition which is associated with morphological right heart abnormalities and an increased risk of supraventricular arrhythmias (SA). The aim of the retrospective analysis was to assess the incidence, classification and predictors of SA during a long-term follow-up.

Methods: All adult EA patients registered from January 2000 onwards in the cardiac magnetic resonance (CMR) database of our hospital were selected. Exclusion criteria were the presence of additional complex congenital heart associated abnormality and/or a history of a previous SA or ventricular arrhythmia. The assessment of RA dimensions was performed excluding the atrialized right ventricle and the grading of tricuspid regurgitation was expressed in a scale from none (0) to severe (4). All the patients were followed-up every 6-12 months for an arrhythmic end-point defined as recording of a sustained SA in ECG or Holter recordings or palpitations associated with a positive electrophysiology study (EPS). Clinical and CE-CMR predictors of first arrhythmic event were assessed.

Results: The study population included 97 patients (62 females, mean age 42±14 years). During a mean follow-up of 54±28 months, 39 (40%) patients experienced a SA event. At univariate analysis, a history of palpitation ($p<0.001$), right atrium (RA) size ($p<0.001$) and the degree of tricuspid regurgitation (p=0.03) were significantly associated with arrhythmic event while right ventricular end-diastolic volume was borderline (p=0.08). At multivariate analysis, RA size remained the only independent predictor (HR 1.9/cm^2, 95%CI 1.2-3.1).

Thirty-eight patients underwent EPS and received a final diagnosis of atrial fibrillation in 4, atrial flutter in 7, atrial tachycardia in 7, atrio ventricular re-entry nodal tachycardia in 2 and atrio-ventricular re-entry tachycardia in 16. Twenty-three right-sided APs were mapped and ablated with the most frequent location in the postero-septal location (11), followed by right lateral wall (10) and posterior (2) location. A mean of 1.4 APs per patient were targeted. Four concealed AP were identified (3 postero-septal). The overall success rate for all procedures was 84%. In 11 pts (28.9%) multiple procedures were required. The most frequent substrate needing re-ablation being accessory pathways (AP).

Conclusions: EA is associated with an increased risk of SA. The RA size is significantly associated with arrhythmic events during follow-up. Most SA related to EA are amenable to catheter ablation, however repeat procedures may be necessary.

P3299 | BEDSIDE

The value of reported risk factors to predict the substrate for ventricular tachycardia in repaired tetralogy of Fallot

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Introduction: Several risk factors (RF) have been suggested to predict ventricular arrhythmias (VA) in repaired Tetralogy of Fallot (rTOF). More than 80% of all VA episodes are monomorphic sustained ventricular tachycardia (MSVT) and may be fatal despite a preserved cardiac function if VT is fast. The value of current RF to predict the substrate for MSVT is unclear.

Methods: Seventy-three consecutive rTOF patients with documented MSVT (n=13) and/or at least one RF for VA (age of repair ≥5 years, transannular patch used (TAP), syncope, QRS ≥180 ms, nsVT on holter, depressed LV and/or RV function) underwent programmed stimulation (3 drive cycle length (CL), ≥3 extrastimuli, from ≥2 RV sites, isoproterenol) and electroanatomical substrate mapping to identify anatomical isthmuses related to induced VT. The predictive value of type and total number of risk factors for MSVT substrate was determined.

Results: Patients had 1.9±0.9 RF; 45 patients were repaired ≥5 years with TAP in 31. Five patients had syncope, 11 a QRS≥180 ms, 17 nsVT and 29 (4) moderate or severely depressed RV (LV) function. Twenty-eight patients (all 13 with documented MSVT) were inducible for a median of 1.0 (1.0 – 1.8) mainly fast VT, VTCL 252 ms (231 – 312) with a proven electroanatomical substrate. In univariate analyses only age (OR 1.32 (1.10 – 1.59)/5yrs, p=0.003) and age of repair (OR 1.13 (1.04 – 1.23)/yr, p=0.003) but not syncope, QRS duration, nsVT, cardiac function and the number of RF were associated with a substrate for MSVT.

Patient Characteristics

	Total (n=73)	MSVT inducible– (n=45)	MSVT inducible+ (n=28)	p
Age (years)	40±16	35±15	47±14	0.001
Gender (male)	46 (63%)	27 (60%)	19 (68%)	0.499
Age total repair (years)	8±8	6±5	12±10	0.004
TA-patch	31/65 (48%)	19/39 (49%)	12/26 (46%)	0.839
Syncope	5 (7%)	3 (7%)	2 (7%)	0.938
QRS duration (ms)	155±26	154±25	156±29	0.855
nsVT on holter	17/58 (29%)	11/40 (28%)	6/18 (33%)	0.652
RV function preserved	44 (60%)	28 (62%)	16 (57%)	0.666
LV function preserved	69 (95%)	44 (98%)	25 (89%)	0.121

Conclusion: In rTOF, the present RF for VA cannot predict the substrate for MSVT in rTOF.

P3300 | BEDSIDE

Can we predict onset of ventricular ectopy in patients with congenital heart disease?

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Purpose: Ventricular tachyarrhythmia are common late-operative complications in patients with congenital heart defects (CHD) and may result in sudden cardiac death. The incidence ranges from 7 up to 21%. The purpose of this multicentre study is (1) to examine development of ventricular tachyarrhythmia in a cohort of CHD patients and (2) to retrospectively evaluate clinical and electrophysiological parameters in order to determine their predictive value for the occurrence of ventricular tachyarrhythmia.

Methods: Patients (N=142) were selected from the DaNaRa database. Non-sustained ventricular tachycardia (VT) was defined as ≥10 consecutive beats. Electrocardiograms (ECG) and 24-hour Holters were studied for ventricular ectopy. For patients with VT, QRS duration (QRS) and QTc interval (QTc) were measured on a surface ECG before first VT/VF and compared with earlier ECGs. In addition, echocardiographic examinations were reviewed for cardiac function.

Results: Most patients had ventricular runs (N=84, 59%), VT or ventricular fibrillation (VF) was diagnosed in respectively 43 (30%) and 15 patients (11%). Mean QRS prior to VT/VF was (142±36 ms) and five years before (137±26 ms, p=0.66). Prolonged QRS before VT/VF onset was present in fifteen (71%) of the studied

patients. Mean QTc before VT/VF was 377±40 ms compared to 405±47 ms five years earlier (p=0.04). Prolonged QTc was not observed. Ventricular function was impaired in 11 (26%) patients. Thirty-eight patients received an ICD; shocks were appropriate in eleven and inappropriate, caused by supraventricular tachycardia, in eight patients.
Conclusions: VT/VF onset in CHD patients occurred late after first cardiac surgery. The role of intraventricular conduction delay, dispersion in ventricular refractoriness and cardiac function in order to predict VT/VF development is of limited value. Recurrence of either VT/VF was low.

P3301 | BEDSIDE
Brugada syndrome in childhood: new clinical and prognosis data

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Purpose: Brugada Syndrome (BrS) is an arrhythmogenic disease associated with an increase risk of SCD. This disease is rare in children so only few data are available.
Methods: We collected data from 15 European tertiary hospitals. We recruited patient with diagnosis of BrS performed no later than 18 years old, spontaneously or after a sodium channel blocker challenge. Diagnosis was performed using the last consensus report criteria.
Results: We recruited 85 children with a mean age at diagnosis of 11.2±6.2 years old. Median follow-up was 5.4 [7] years. Circumstances of diagnosis were: family screening (n=48; 56%), syncope (n=13; 15%), fortuitous (n=11; 13%), SVT (n=6; 7%), SCD (n=4; 5%) and others (n=3; 4%). BrS was identified spontaneously in 33 (39%) cases or after provocation tests in 52 cases (61%). During the follow-up: 67 (79%) patients were asymptomatic, 9 (11%) had life threatening arrhythmia (LTA) including VT, VF, and SCD (n=2), 5 (6%) had syncope, 4 (4%) had SVT. SCN5A mutations were founded in 47 out of the 62 (73%) patients tested. ICD was implanted in 19 (22%) patients with complications in 9: lead failures (n=4), inappropriate shocks (n=4), endocarditis (n=2) and 1 hemothorax. Nine of the 11 (13%) children treated by hydroquinidine remained asymptomatic. In 12 cases on 28, fever triggered arrhythmic episodes. Spontaneous Brs type I ECG (p=0.02) and symptoms at diagnosis (p=0.007) were predictors of LTA.

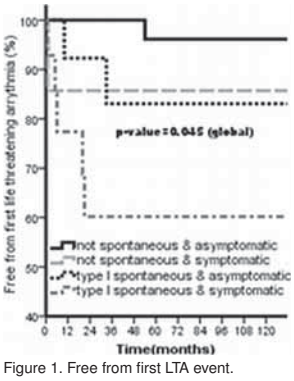

Figure 1. Free from first LTA event.

Conclusion: In BrS children, spontaneous type I ECG and symptoms at diagnosis are significantly predictors of LTA. Fever triggered ventricular arrhythmias. BrS children with spontaneous type I aspect and symptoms are at high risk of LTA whereas asymptomatic one without spontaneous type I ECG have a good prognosis.

P3302 | BEDSIDE
Prognostic significance of QT interval dispersion in the response of intravenous immunogloblin therapy in patients with Kawasaki disease

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Background: QT interval dispersion (QTD) is a sensitive measure on interlead variations of 12-lead electrocardiogram (ECG). Increased QTD reflects cardiac instability in various cardiovascular diseases. We hypothesized that QTD enabled us to assess the disease severity of Kawasaki disease (KD). The purpose of this study was to investigate whether baseline QTD could predict the response to intravenous immunoglobulin therapy (IVIG) in the patients with KD.
Methods: QTD and corrected QTD were measured in 44 patients with KD before IVIG. The patients were divided into two groups; 23 in IVIG responders (group R: age, 3.0±2.0 years), 21 in nonresponders (group N: age, 3.2±1.9 years). The correlation between QTD and response to IVIG were evaluated, and the predictive value for the response was compared with the conventional risk score of Gunma University.
Results: QTD and corrected QTD were significantly increased in group N (group R vs. group N: 21.0±6.1ms vs. 31.2±7.9ms, 31.0±9.1ms vs. 48.0±12.2ms, $p<0.001$, respectively). According to receiver-operating characteristic curve analysis, the area under the curve (AUC) of QTD (AUC=0.85) was larger than that of the conventional score (AUC=0.83). Multiple logistic regression analysis showed QTD was an independent predictor for the response to IVIG after adjustment for the conventional score (Odds ratio: 1.16, 95%CI: 1.025-1.313, $p<0.001$).
Conclusion: QTD was significantly associated with the response to IVIG. Our findings indicated that QTD could be a useful marker for the prediction of IVIG nonresponders who had severe vasculitis and high risk for coronary aneurysm after KD.

P3303 | BEDSIDE
Clinical importance of school cardiac examination with universal ECG screening in the diagnosis of asymptomatic young patients with ASD in Japan

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Background: Japanese government has enforced a law of regular school cardiac examination (SCE) combined with universal electrocardiographic (ECG) screening at 1st, 7th, and 10th grader in 1995. SCE should be effective to identify asymptomatic pediatric patients with specific congenital diseases. The aim of this study was to determine impact of SCE in the management of patients with at atrial septal defect (ASD).
Methods: Subjects were 350 patients who were sent for transcatheter closure of ASD and had documented reasons why patients were sent to cardiologists and received diagnosis of ASD. Patients were divided into 3 groups according to age: A, 14 patients with age less than 6.5 years old who did not undergo SCE; B, 253 patients with age between 6.5 and 35 years old who should have undergone SCE; C, 83 patients with age more than 35 years old who did not undergo SCE. Based on the retrospective chart review, we determined the role of SCE in the diagnosis of ASD.
Results: There was no significant difference in Qp/Qs among 3 groups (2.1±0.6, 2.4±0.9, and 2.5±1.0, respectively). In A, all patients were detected by cardiac murmur. In B, about half of patients (48%) were detected at SCE and the remaining patients were diagnosed at younger age mainly because of cardiac murmur (87%). In C, only 23% of patients were detected by occupational health examination and the remaining patients were mainly detected by symptoms. Among patients detected at SCE in B, three fourths (75%) of patients were identified by ECG screening due to incomplete RBBB with right axis deviation or incomplete RBBB with rR' pattern and the remaining one fourth patients were mainly identified by cardiac murmur. Importantly, 60% of these patients who showed detectably ECG abnormality did not have significant cardiac murmur and there was no significant difference in Qp/Qs between patients with and without significant cardiac murmur.
Conclusions: SCE combined with universal ECG screening has significant role to identify asymptomatic patients with ASD in Japan, though cost effectiveness must be determined.

P3304 | BEDSIDE
Experience with foetal supraventricular arrhythmias

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This study was to review experience and outcomes of supraventricular (SV) arrhythmias in fetus Methods: Cases were divided in groups: SVPB= premature SV beats, NSSVT= non-sustained SV tachycardia, SSVT= sustained SV tachycardia, and AF= atrial flutter. Complication (heart failure) was defined as foetal hydrops or isolated effusion (pericardial or pleural or ascitis). Outcome was favourable if arrhythmia resolved or stabilized until full-term birth, not-favourable if premature birth or foetal death occurred.
Results: 188 fetuses were included:89 in SVPB (47.3%), 31 in NSSVT (16.5%), 60 in SSVT (31.9%), 8 in AF (4.3%), aged at diagnosis 30.8±4.5weeks (no difference between groups). Foetus HR at diagnosis was 241±30bpm in SSVT versus 226±26 in AF. Antiarrhytmic therapy was administered in sustained tachycardia (83% of cases in SSVT and 71% in AF): 28 had 1 medication, 25 had 2 medications, 2 had 3 medications. Complication occurred in 29 cases, all in groups SSVT and AF (29 of 68 = 43%): 18 hydrops, 5 ascitis, 4 pericarditis, 1 pleural effusion and 1 LVdysfunction+MR, and was more frequent in group SSVT (86%: including hydrops in 30%) than in AF (51%: no hydrops), p=0.08. Fetal HF was associated with HR at diagnosis: 251±25bpm in hydrops vs 228±31bpm in no-hydrops (p=0.025). Outcome was favourable in all SVPB and NSSVT, in 45 of SSVT+AF (79%). Tachycardia resolved in 36 cases, more frequently in SSVT (57%) than in AF (25%). HR decreased with persistent tachycardia in 9 cases. Premature birth occurred in 10 cases, foetal death in 2. Outcome was not associated with HR or

weeks of gestation at diagnosis. Not-favourable outcome was more frequent in cases with hydrops or isolated effusion (57%) than in uncomplicated cases (10%, p=0.0002). Resolution was obtained in 45% of hydrops foetus vs 66% of non-hydrops cases. Digoxine utilization decreased from 79% of cases before 2000 to 33% after 2000, while flecaine increased from 14% to 48.5%. There was no relationship between therapy or number of medications and outcomes.
Conclusion: Fetal SSVT more frequently resolves but has worse outcome than AF, especially if HR at diagnosis is high and hydrops occurs. Larger scale prospective studies are needed to evaluate the efficacy of flecaine compared to digoxine therapy.

CONGENITAL CARDIAC SURGERY

P3306

P3307 | BEDSIDE
Outcome after cardiac surgery in adults with congenital- versus acquired heart disease: right-sided anomalies carry the highest mortality risk

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Background: Postoperative care protocols after cardiac surgery are based on complication rates in patients with acquired heart disease (AHD), a group with mainly left-sided heart disease. Applicability of these protocols to patients with congenital heart disease (CHD) is unknown. In this study we compared complications in (1) CHD versus AHD and (2) right-sided CHD versus left-sided CHD and AHD combined.
Methods: In total 1.006 patients were included, of whom 503 consecutive adult CHD patients (56% male, median age 36 years), operated between January 2001 and January 2011 in a tertiary referral centre. A group of 503 gender-matched AHD patients (median age 59 years), operated in the same time period, were also included.
Results: Despite the younger age of CHD patients, the operative mortality rate in patients with CHD and AHD was similar (1,8% versus 1,2%). Right ventricular failure (3,6 versus 0,4%), pulmonary hypertension (2,4 versus 0,8%) and acute kidney injury (4,0 versus 0,8%) occurred more frequently in patients with CHD than in patients with AHD ($p<0.05$, for all). Furthermore, comparison of right- with left-sided CHD and AHD combined, demonstrated a higher operative mortality in right-sided CHD (3,3% versus 1,1%, p=0.02). Cause of death in right-sided CHD was mainly progressive ventricular failure, in AHD more often due to cardiac arrest. Furthermore, right ventricular failure, acute kidney injury, low cardiac output syndrome and atrial fibrillation were most prominent in right-sided CHD ($p<0.05$, for all).
Conclusion: Complication rates after cardiac surgery differ between patients with CHD and AHD, and each group requires specific attention. Particularly adults with right-sided CHD have a high peri-operative mortality and complication rate due to progressive ventricular failure, despite a low median age.

P3308 | BEDSIDE
Increasing severity and complexity in adults with congenital heart disease undergoing heart transplantation: temporal trends – a collaborative study on 97 patients

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Purpose: Despite substantial advances in cardiopediatric surgery, residual abnormalities in cardiac structure and function predispose adults with congenital heart disease (ACHD) to late-onset heart failure and its complications. Therefore, heart transplantation (HT) in ACHD is increasingly used. Meanwhile, post-transplant survival in HT recipients has progressively improved. We investigated the role of temporal trends on profile and outcomes of ACHD recipients.
Methods: Out of a multi-institutional (3 centers) series of 2257 HT from 1988 to 2012, 100 (4.4%) were performed in 97 ACHD (65 men). They represented 45% of ACHD heart transplant recipients in France at that time. We evaluated clinical data, etiology, surgical history, perioperative issues and outcomes. Trends were compared between 2 eras: era 1 (1988-2005, n=48) and era 2 (2006-2012, n=49).
Results: Mean age at HT was 30±10.5 years (range 16-58). Forty-three patients (44%) had univentricular (1V) physiology including 16.5% Fontan-type circulation and 56% had biventricular (2V) physiology including 26% with a systemic right ventricle. Severity of disease was categorized in terms of initial diagnosis (according to classification of 32th ACC Bethesda Conference Task Force 1): 74.2% had a great complexity cardiopathy while 21.7% had a moderate severity disease and 4.1% a simple disease. In-hospital mortality was high (34%). Baseline characteristics did not differ significantly between the 2 eras. Era 2 recipients had less often right heart failure signs before HT (69% vs 39%, p=0.001). Their donors were older. They were more likely to be hospitalized, supported by inotropes and assist devices at the time of HT. The rate of 1V patients did not change over time: 50% in era 1 vs 39% in era 2 (p=0.3). The distribution of severity of disease changed significantly over time (p=0.048). The proportion of recipients with CHD of great complexity was higher in era 2 than era 1 (82% vs 67%) and conversely for those with moderate severity decreased (31% in era 1 vs 12% in era 2). In fact, transposition of the great arteries became a major provider of HT in ACHD in the recent era (31% in era 2 vs 8% in era 1, p=0.006), representing the only primary diagnosis whose proportion increased significantly. Multivariable factors associated with increased in-hospital mortality did not include transplant era.
Conclusion: Despite a worse baseline risk profile, and increasing severity and complexity of ACHD recipients in recent years, mortality after HT has not increased. Further studies are warranted to identify whether earlier HT may improve survival in such patients.

P3309

ABSTRACT WITHDRAWN

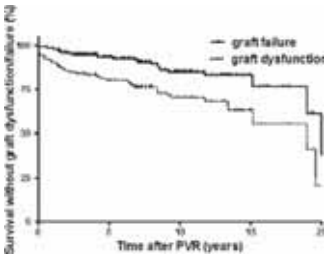

Figure 1. Graft dysfunction and failure after PVR

P3310 | BEDSIDE
Aortic prosthesis-patient mismatch and exercise capacity in adult patients with congenital heart disease

Y.J. Van Slooten[1], J.P. Van Melle[1], H.G. Freling[1], B.J. Bouma[2], A.P.J. Van Dijk[3], M.R.M. Jongbloed[4], M.C. Post[5], T. Ebels[1], A.A. Voors[1], P.G. Pieper[1]. *[1]University Medical Center Groningen, Groningen, Netherlands; [2]Academic Medical Center of Amsterdam, Amsterdam, Netherlands; [3]University Hospital Nijmegen, Nijmegen, Netherlands; [4]Leiden University Medical Center, Leiden, Netherlands; [5]St Antonius Hospital, Nieuwegein, Netherlands*

Purpose: To report the prevalence of aortic valve prosthesis-patient mismatch (PPM) in an adult population with congenital heart disease (CHD) and its impact on exercise capacity. After an aortic valve replacement (AVR) patients require life-long follow-up as they may encounter late prosthesis-related complications such as PPM. In Grown-Ups with CHD (GUCH-patients), the prevalence of aortic PPM is presently unknown, but expected to be high due to somatic growth. PPM has been associated with decreased exercise capacity in elderly patients but the impact on a younger, more active GUCH-population has not been investigated.
Methods: For this multicenter, cross-sectional cohort study we identified GUCH-patients with an aortic valve prosthesis from a national registry. Moderate PPM is defined as an indexed effective orifice area $\leq$0.85 cm^2/m^2, severe PPM as an indexed effective orifice area $\leq$0.65 cm^2/m^2, and exercise capacity is reported as percentage of predicted exercise capacity.
Results: Of the 207 patients, 68% was male, 71% had a mechanical prosthesis, and median age at inclusion was 45 years (interquartile range 35-53). The prevalence of moderate PPM was 19%, the prevalence of severe PPM was 23%, totalling an overall prevalence of 42%. PPM was more prevalent in patients with a mechanical prosthesis ($p<0.001$). The percentage of predicted exercise capacity was lower in patients with PPM (85% vs. 91%; p=0.031). Using a multivariable regression model, PPM remained significantly associated with exercise capacity (β = -11.05, p=0.039), even when corrected for significant univariable parameters (R2 =0.283, F =5.535, $p<0.001$).
Conclusions: In this study we report a high prevalence (42%) of PPM in GUCH-patients with an aortic valve prosthesis. Multivariable regression showed PPM to be independently associated with diminished exercise capacity.

P3311 | BEDSIDE
Graft dysfunction and failure during long-term follow-up after pulmonary valve replacement in tetralogy of Fallot

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Purpose: In patients with Tetralogy of Fallot (TOF), pulmonary regurgitation (PR) can be corrected by surgical pulmonary valve replacement (PVR). However, uncertainty about long-term durability of the graft remains. The aim of this study was to asses long-term graft function and factors associated with graft dysfunction and failure.
Methods: In this retrospective, multicenter study 157 TOF patients (62% male, mean age at PVR 30.8$\pm$11.0 years, follow-up after PVR was 8.8$\pm$4.7 years) who had undergone PVR between 1986 and 2013 were included. Graft function was analyzed on serial echocardiographic examinations. Graft dysfunction was defined as: at least moderate PR or pulmonary stenosis (PS: pressure gradient over pulmonary valve >36mmHg), endocarditis or death. Graft failure was defined as: redo-PVR, balloon dilation of graft or death.
Results: During follow-up 45 (29%) patients developed graft dysfunction (11 PR, 25 PS, 4 endocarditis, 5 death). Graft failure occurred in 22 (14%) patients (15 redo-PVR, 2 balloon dilation, 5 death). Multivariate analysis revealed: immediate post-operative mild PS (>20mmHg) (HR: 4.80, 95% C.I. 2.48-9.26, $p<0.001$), immediate post-operative mild PR (HR: 2.91, 95% C.I. 1.42-5.98, p=0.004) and age under 18 (HR: 2.62, 95% C.I. 1.25-5.47, p=0.011) as independent risk factors for graft dysfunction. In patients without any risk factors, 79% remained free from graft dysfunction after 15 years. Post-operative PS >30mmHg was the only independent predictor for graft failure (HR: 3.74, 95% C.I. 1.50-9.33, p=0.005).
Conclusions: In TOF patients, graft dysfunction and failure occurred in respectively 37% and 17% within 15 years after PVR. Younger age, as well as degree of immediate post-operative PR and PS are prognostic for early graft dysfunction.

P3312 | BEDSIDE
Long-term mitral valve prosthesis-related complications in congenital heart disease

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Purpose: Long-term follow-up data on mitral valve replacement (MVR) in patients with congenital heart defects (CHD) are scarce. As more CHD patients now survive into adulthood there is a need to identify early predictors for long-term valve-related events. We therefore aim to report the long-term mitral valve prosthesis-related complications and its independent predictors.
Methods: For this multicenter, retrospective cohort study we identified 91 GUCH-patients (Grown-Ups with CHD) with a mechanical (n=84) or biological (n=7) systemic atrioventricular prosthesis from a national registry. Outcome measures comprised valve-related complications, early and late mortality, as well as post-operative complications. Cox regression was used to identify predictors for long-term valve-related complications.
Results: At the first MVR median age was 29.4 years (interquartile range 12.9-44.1). During a median follow-up of 12.4 years (interquartile range 5.7- 22.5), 43 patients (47%) encountered valve-related complications that necessitated a redo MVR in 27 patients (30%). Prosthetic sizes ranged from 19mm to 33mm, with smaller prostheses more often in patients with left-sided obstructive heart lesions ((sub)-valvular aortic valve stenosis, mitral valve stenosis or aortic coarctation). After adjustment for age and sex, the presence of left-sided obstructive heart lesions was independently associated with valve-related complications (HR 2.71, 95% CI 1.37 to 5.37, p=0.004) even when corrected for significant univariable predictors (HR 2.30, 95% CI 1.04 to 5.06, p=0.039). Event-free survival is depicted in Fig. 1.

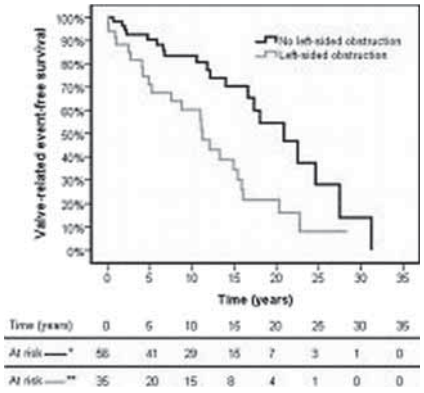

Figure 1

Conclusions: CHD patients with obstructive left-sided heart lesions receive smaller mitral valve prostheses and are at a higher risk of long-term valve-related complications following MVR.

P3313 | BEDSIDE

Additional support to the pulmonary autograft versus the conventional ross procedure: promissing results on neosinus dilatation to mid-term follow-up

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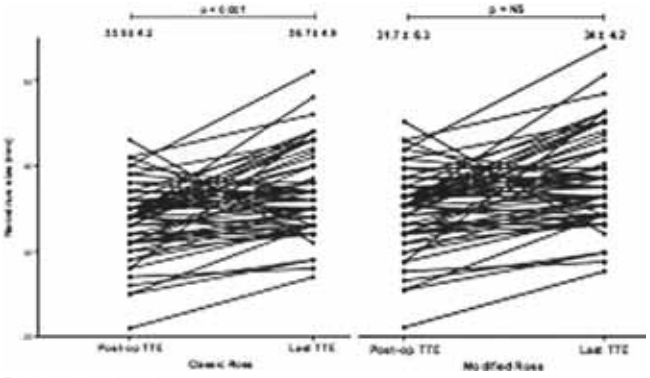
Background: Ross procedure is widely performed for surgical aortic valve repair in growing patients and young adults. However, concerns have raised on this technique because of progressive dilatation of the neosinuses requiring autograft reoperation. Autograft inclusion in a polyester tube prosthesis has been proposed. Yet the short and midterm outcomes of this modified Ross procedure remain largely unknown.

Methods and results: From March 2003 to October 2012, 78 patients underwent a modified Ross procedure with pulmonary autograft reinforcement with a Valsalva Gelweave Dacron® tube.

The midterm follow-up of these patients was compared with a standard Ross population matched for gender, age and aortic valve anatomy. The mean patient age was 30±10 years (range 13 – 51). During the follow-up (2.8±2.4 years) there was no difference between the modified and the standard Ross procedure if we compared deaths (0% vs 2.6%, p=0.17), infectious endocarditis (1.4% vs 1.3%, p=0.95) or reoperations (7% vs 2.6%, p=0.19).

No clinical relevant dilatation of the aortic annulus was observed in both techniques. Conversely, during the mid-term follow-up, a significant and relevant dilatation of the neosinuses was observed in the standard (36.7±4.9mm vs 33.8±4.2mm, p<0,001) but not in the modified procedure (34±4.2mm vs 31.7±6.3, p=NS).



Evolution of neosinus size

Conclusions: Our results show that the modified Ross operation is safe, has good midterm results with no sign of aortic root dilatation as opposed to the standard procedure. Additional long-term data are needed to confirm the efficiency of this strategy to avoid long-term autograft failure.

P3314 | BEDSIDE

Population-based study of long-term outcome of mustard/senning correction for transposition of the great arteries (TGA)

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Background: All transpostion of the great arteries (TGA) operated with the atrial switch operation (Mustard-/Senning operation) was studied. Atrial correction involves extensive surgery in the atria and leaves the right ventricle as the systemic ventricle. Today patients are well into adulthood making evaluation of longterm outcome possible.

Methods: All TGA patients operated with atrial correction were identified (n=468). Using the Scandinavian personal-number systems the outcome was recorded in late 2007 and early 2008.

Results: Perioperative mortality was 20-25%, and increased significantly by the presence of a VSD, LVOTO or if the patients were operated early compared to late in the era. But interestingly, the predictors of perioperative mortality did not predict long term mortality. The survival plots for all the groups that survived the first year shows the same constant fall until the third decade, where ¼ of the patients have died or had HTX (figure1). In the fourth decade mortality increases.

Conclusion: Long term survival of TGA-patients with atrial correction is not predicted by the type of surgery performed. Patients surviving the first year will have 75% chance of reaching the third decade, and then mortality/HTX increases.

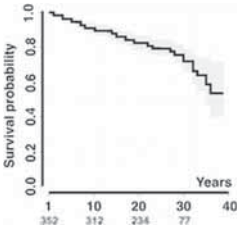

Figure 1. Survival after 1 year.

P3315 | BENCH

Partial pulmonary circulatory assist from inferior vena cava to pulmonary artery improves haemodynamics in the failed Fontan circulation due to high pulmonary vascular resistance

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Purpose: In the Fontan circulation, an increase in pulmonary vascular resistance (PVR) may decrease venous return to the single ventricle and result in the low cardiac output syndrome. Although mechanical pulmonary circulatory assist (PCA) can restore the haemodynamics, total PCA after total cavopulmonary connection (TCPC) may require taking down the cavopulmonary anastomosis between superior vena cava (SVC) and pulmonary artery (PA). Therefore, partial PCA from the inferior vena cava (IVC) to PA may be suitable. To clarify the haemodynamic effects of partial PCA, we performed a theoretical analysis using a computational model.

Methods: A computational model of the Fontan circulation using TCPC was developed with time-varying elastance chamber model and the modified 3-element Windkessel vascular model. PCA device was described as a non-linear function of rotational frequency and pressure gradient between IVC and PA. We varied PVR from 1 to 5 times of normal value while mean systemic arterial pressure was maintained by increasing stressed blood volume without PCA (volume overload model) or by adjusting rotational frequency of PCA (partial and total PCA models).

Results: Despite the increase in PVR, partial PCA as well as total PCA was able to maintain cardiac index at the baseline value. However, volume overload model significantly reduced cardiac index with the increase in PVR. Partial PCA significantly decreased IVC pressure but increased SVC pressure compared to the total PCA.

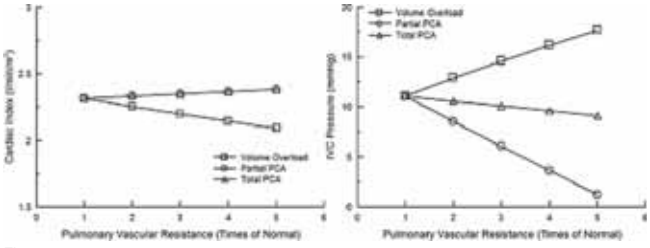

Figure 1

Conclusions: Partial PCA from IVC to PA improved cardiac index in the failed Fontan circulation with high PVR. Partial PCA from IVC to PA may become an alternative to the total PCA.

CATHETER INTERVENTIONS IN CONGENITAL CARDIOLOGY

P3317 | BEDSIDE

Percutaneous closure of muscular and perimembranous ventricular septal defects with the amplatz device: a ten years comparative study

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Purpose: Our objective is to describe our experience with the percutaneous closure of muscular and perimembranous ventricular septal defects (VSD).

Methods: From February 2004 to January 2014, all consecutive patients with VSD attempted for percutaneous closure were included. Baseline characteristics, procedural details, outcomes and follow-up data were analysed.

Results: Sixty-eight patients were included. The mean age was 15±16 years; 45 children and 23 adults. The defect was muscular in 11 patients and perimembranous in 57 (29 associated septal aneurysm and 2 Gerbode-type defect). Six patients in the perimembranous group (2 Fallot, 1 atrial septal defect (ASD), 1 patent ductus arteriosus (PDA), 1 pulmonary valve stenosis (PS), 1 mitral prosthesis) and 1 in the muscular (Fallot) had previous surgery. Four patients in the

Baseline characteristics

Type of defect	Age (years)	p	Male (%)	p	Symptoms (%)	p	Associated procedures (n)	p
Muscular	8±11	0,07	64	0,72	64	0,001	3	0,82
Perimembranous	17±16		58		18		13	

perimembranous group (3 PS, 1 PDA) and 1 in the muscular (PS) had been treated percutaneously. Three patients in the perimembranous group (2 ASD, 1 patent foramen ovale) and 1 in the muscular (ASD) had combined percutaneous treatment in the same procedure. Successful implantation was achieved in 11 muscular and 48 perimembranous defects (p=0,16). In the remaining patients, the device was removed without complications. Immediate complete closure by angiography was observed in 5 muscular and 31 perimembranous defects (p=0,24). No major complications were observed. Pulmonary arterial pressure decreased from 36±19 to 32±13 (p=0,04) and Qp/Qs approached 1. During follow-up, 3 perimembranous and 1 muscular VSD patients needed a pacemaker (atrioventricular block/bradycardia). There were two non-cardiac deaths in the perimembranous group (4 days and 1 year after, due to sepsis and neoplasia). After a mean follow-up period of 5±3 years, all patients remained free of symptoms. One muscular and 3 perimembranous VSD patients presented mild residual shunt by Doppler in follow-up (p=0,74), with complete closure in the remaining patients.
Conclusions: In our experience, although patients with muscular defects were more frequently symptomatic than those with perimembranous defects, percutaneous closure was a safe and effective therapy in both groups.

P3318 | BEDSIDE
Long term outcomes after transcatheter, or surgical closure in 13,522 patients with secundum adult atrial septal defect: national populational based cohort study

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Background: The comparison between long-term outcomes of transcatheter and surgical adult atrial septal defect closure is required.
Methods: From 1997 to 2011, we retrieved medical information of patients more than 18 year-old with secundum septal defect from National Health Insurance Research Database in Taiwan. We monitored the outcomes after transcatheter or surgical correction. We include high grade atrioventricular block, heart failure, atrial fibrillation, atrial flutter, supraventricular tachycardia, ischemic stroke, pulmonary hypertension and mortality as outcomes.
Results: The study enrolled 13,522 patients with adult atrial secundum defect from 1997 to 2010. 31% of patients were male. Mean follow up period is 3.8 years. Surgical closure of adult secundum atrial septal defect resulted in more high grade atrioventricular block, systemic thromboembolism, heart failure, atrial fibrillation, pacemaker implantation and pulmonary hypertension than transcatheter closure and odd ratio were 2.51, 1.9, 2.65, 2.07, 3.50 and 1.76, respectively. Transcatheter closure caused more supraventricular tachycardia. No difference existed between transcather and surgical closure in atrial flutter, and ischemic stroke. However, all-cause mortality was higher in surgical closure group.

Outcomes of treatment status

Outcome	Surgery vs. Amplatzer	
	OR (95% CI)	P
Atrioventricular block	2.51 (1.43–4.41)	0.001
Permanent pacemaker	3.50 (2.03–6.02)	<0.001
Mitral valve disorder	2.25 (1.91–2.66)	<0.001
Systemic thromboembolism	1.90 (1.28–2.83)	0.001
Heart failure	2.65 (2.30–3.05)	<0.001
Arrhythmia	1.42 (1.19–1.68)	<0.001
Ischemic stroke	1.20 (0.86–1.69)	0.288
Pulmonary hypertension	1.76 (1.51–2.05)	<0.001
All-cause mortality	5.62 (4.17–7.57)	<0.001

OR, odds ratio; CI, confidence interval; P, p value.

Conclusions: Patients with transcather closure of adult atrial septal defect had better survival than surgical closure in Taiwan cohort study. However, both of treatments did have their own merits in different outcomes.

P3319 | BEDSIDE
Results of stent repair in patients with coarctation of aorta of complex management. A twenty-year study

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Stent repair of coarctation of aorta is an alternative to surgical correction. However, several anatomic or evolving characteristics of the coarctation through life may create challenging conditions for both, surgical or percutaneous treatment. We retrospectively analyzed our 20-year experience in the percutaneous treatment of complex coarctation of aorta. From November 1993 to July 2013 we have percutaneously treated 59 patients considered to have a complex coarctation of aorta. 23 of them (39%) had one or more previous interventions on the coarctation. Time from first treatment was 9±9 years. 36 patients (61%), mean age 26±17 years, presented with a native coarctation of complex treatment. Adverse conditions for treatment were: 1) Complete interruption of the arch (n=10), 2) Associated aneurysm (n=17), 3) Complex stenosis (n=30) and 4) The need for re-expansion and/or re-stenting (n=21). 17 patients (29%) belonged to more than one group. In patients with interruption of the aortic arch, 9 were type A and 1 was type B, following the classification of Celoria and Patton. The mean length of the interrupted aorta was 9±11 mm. In patients with associated aneurysm, the aneurysm was native in 7 patients, post surgery in 3 and post percutaneous intervention in 7. The aneurysm shape was fusiform in 8 and saccular in 9. Complex stenosis was defined as: a) a long diffuse stenosis (>45 mm) (n=12), b) a very tortuous coarctation, (n=3), c) a stenosis involving a main branch (n=13), or d) a coarctation of unusual location (n=8). Patients previously stented at early age (mean 3±3 years) needed re-expansion and/or re-stenting. Re-expansion was performed at a mean of 13±4 years after first treatment. Stent treatment and successful revascularization was always achieved. One patient died suddenly 3 hours after treatment (1.7%). The remaining 58 patients did well and were followed-up for a mean period of 10±6 years. Associated late surgery of the aortic valve was needed in 4 patients. Late adverse events (death, myocardial infarction or the need for new coarctation treatment) occurred in 3 patients (5%). The remaining 55 patients are symptoms free, with normal baseline blood pressure. The last Doppler gradient across coarctation was 4±5 mmHg. Image techniques showed good patency of the aorta without associated aneurysm or restenosis. The actuarial survival free probability of all patients was 91% at 18 years after treatment.
Conclusions: Stent repair of complex coarctation of aorta is feasible and safe, despite the presence of adverse conditions for treatment. Initial results are maintained at late follow-up.

P3320 | BEDSIDE
The benefit of atrial septal defect closure in the elderly patients

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Objective: Closure of the atrial septal defect in the elderly patients is controversial. The aim of the study was to evaluate the outcomes of transcatheter closure of secundum atrial septal defect (ASD) in elderly patients.
Methods: From a total of 488 pts with ASD who underwent transcatheter closure 75 pts over 60 years (45 F, 30 M) with a mean age of 65.3±15.7 (60-75) were analyzed. All patients had an isolated secundum ASD with a mean Qp:Qs: 2.84±1.9 (1.5-3.9). A symptom-limited treadmill exercise tests with respiratory gas exchange analysis and transthoracic color Doppler echocardiographic study as well as Quality of life (QoL) measured using the SF36 questionnaire (SF36q) were repeated in all pts before procedure and after 12 months of follow-up.
Results: The ASO device was successfully implanted in all pts (procedure time 37.7±4.5 (13-59) minutes, fluoroscopy time 11.2±9.9 (6-40) minutes). There were no major complications. The defect echo diameter was 17.7±15.8 (12 - 30) mm. The mean balloon stretched diameter of ASD was 22.4±7.9 (14 - 34) mm. The diameter of the implanted devices ranged 16 - 34 mm. After 12 months of ASD closure, all the pts showed a significant improvement of exercise capacity parameters. Seven QoL parameters (except mental health) improved at 12 months follow up compared to their baseline data. The mean SF36q scale increased significantly in 66 (88%) pts of mean 46.2±19,1 (5-69). The right ventricular dimension decreased in 67 pts (89.3%) (Table 1).

Table 1

	Before ASD closure	12 months after ASD closure	p value
Time of exercise (min)	9.1±4.1	13.9±5.1	<0.001
VO2peak (ml/kg/min)	8.2±3.3	13.5±5	<0.001
SF36q scale 0–100	20.8±31	61.4±39	< 0.0001
The right atrial area cm^2	24,8±1,3	17.2±1,2	<0.0001
The right ventricular area cm^2	19,5±1,37	12±1,3	<0.0001

Conclusions: Closure of ASD in elderly patients caused a significant clinical and hemodynamic improvement after percutaneous treatment, which is maintained to long-term follow-up what justified this procedure in old age.

P3321 | BEDSIDE
Transcatheter closure of very large atrial septal defects: feasibility and safety in a large adult and pediatric population

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Purpose: Data are needed on safety and efficacy of device closure of large atrial septal defects (ASDs).
Methods: Between 1998 and 2013, 336 patients (161 children <15 years) with very large, isolated, secundum ASDs (balloon-stretched diameter ≥34 mm in adults or echocardiographic diameter >15 mm/m^2 in children) were managed using the Amplatzer device in a Hospital. Transthoracic echocardiographic guidance

was used starting in 2005 (n=219, 65.2%). Balloon-stretched diameter was >40 mm in 36 adults; mean values were 37.6±3.3 mm in other adults and 26.3±6.3 mm/m^2 in children.
Results: Amplatzer closure was successful in 311 (92.6%, 95CI: 0.89-0.95) patients. Superior and posterior rim deficiencies were more common in failed than successful procedures (superior, 24.0% versus 4.8%, P<0.001; posterior, 32.0% versus 4.2%, P<0.001). Device migration occurred in 4 adults; in the 21 remaining failures, the device was unreleased and withdrawn. After a mean follow-up of 6.7±3.2 years, all patients were alive with no history of late complications.
Conclusions: Closure of very large ASDs using the Amplatzer device is safe and effective in both adults and children. Superior and posterior rim deficiencies are associated with procedural failure. Closure can be performed under transthoracic echocardiographic guidance. Long-term follow-up showed no deaths or major complications.

P3322 | BEDSIDE
Comparative study of transcatheter closure, open-heart surgical repair and hybrid procedure for treatments of ventricular septal defect in children

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Objective: To compare retrospectively the indications, success rate and complications of transcatheter closure, open-heart surgical repair and hybrid procedure for treatment of ventricular septal defect in children.
Methods: From January 2010 to December 2012, a total of 267 patients (158 male, 109 female; aged 2 month to 18 years,mean age, 3.9±3.5 years) were divided into interventional group (n=55), the surgical group (n=105) and the hybrid group (n=107).
Results: The success rate was 98% in the interventional group, 99% in the surgical group and 96% in the hybrid group, respectively. Totally there was just one patient died in the surgical group. Patients in the interventional group received intravenous anesthesia, while the patients in the other two groups required general anaesthesia with tracheal intubation and ventilator-assisted breathing. Only the patients in the surgical group required cardiopulmonary bypass support. The length of stay in the intensive care unit or postoperative hospital stay in the surgical group were longer than in the other two groups. Patients in the interventional group underwent the procedure through 0.3 cm incision in their groin. The surgical group and the hybrid group were done through 5 to 10 cm incision on the sternum with remained skin scar. The mean diameters of VSD in the surgical group were larger than the other two groups (p both<0.05). There were no significant difference in the mean diameters of VSD occluder between the interventional group and hybrid group (p>0.05). The transfusion rate and volume of blood transfusion in the surgical group were larger than that in the hybrid group (p<0.05). The complications in the surgical group was much severe than the other two groups (p both <0.05). The operation time of surgical group was longer than the other two groups (p both <0.05).
Conclusions: The transcatheter closure, open-heart surgical repair and hybrid procedure were all effective treatment for VSD in children. The transcatheter closure and hybrid procedure were suitable for the perimembranous and muscular VSD, while Open-heart surgical repair were suitable for all types of VSD. The hybrid procedure has no X-ray radiation but it has scar on the skin and heart.

P3323 | BEDSIDE
Pregnancy in women after transcatheter closure of atrial septal defect

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Purpose: Percutaneous closure of ASD is increasingly performed during the last decade. Many women undergoing this procedure are in childbearing age but the information on the outcome of pregnancy in women with ASD after transcatheter closure is limited. Our aim was to investigate the magnitude and determinants of cardiac and obstetric complications during pregnancy in women with ASD after transcatheter closure.
Methods: Consecutive 85 women with a mean age of 28.2±13.1 (19-44) with ASD after transcatheter closure with the Amplatz Septal Occluder, were analyzed. A total of 85 women gave birth to 85 full-term healthy babies. In total there were 90 pregnancies, including 5 miscarriages (5.9%).
Detailed recordings of each completed pregnancy (n=85, 28.9±15.1 (1-362) months after transcatheter closure) were obtained. Cardiac events were defined as heart failure, stroke, TIA, arrhythmias, endocarditis; obstetric events as PIH, preeclampsia, eclampsia, HELLP syndrome, premature labor, postpartum hemorrhage; neonatal events as premature delivery, small-for-gestational age, fetal mortality, neonatal mortality.
Results: Cardiac events were observed during 10.6% (n=9) of the completed pregnancies and included: supraventricular arrhythmias (n=9.4%) and right heart failure - shin oedema (n=1.2%). None of these complications required hospitalization.
Severe obstetric complications during completed pregnancies were not observed except minor ones: moderate hypertension (n=11.8%), prolonged bleeding (n=5.9%), premature rupture of membranes (n=3.5%). Women >35 years appear to be at greater risk for both cardiac and obstetric complications (Table 1).

Table 1

	Cardiac events (n=9, 10.6%)	Obstetric events (n=18, 21.2%)
Presence of pulmonary hypertension	1.55 (0.31–4.01)	1.34 (0.51–3.31)
History of arrhythmia	3.51 (0.19–5.13)	2.33 (0.52–3.93)
Maternal age >35 years	5.11 (1.41–19.3)*	2.42 (1.2–3.0)*
Presence of RV dilatation	1.33 (0.91–2.13)	1.12 (0.62–3.20)

Data are presented as odds ratios (95%CI). *P<0.05.

Conclusions: Most ASD women tolerate pregnancy well after transcatheter closure with the Amplatz Septal Occluder with the risk of complications comparable to that in general population of healthy women. Maternal complications were seen more often in women >35 years.

P3324 | BENCH
Effect of percutaneous closure of atrial septal defect on mean platelet volume

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Introduction: In this study, we aimed to evaluate the association of mean platelet volume (MPV) levels that a sign of platelet activation with ASD and the effects of treatment of ASD with transcathater closure approach on MPV.
Materials and methods: 76 patients with secundum-type ASD who undergoing transcathater ASD closure and age-sex matched 40 healthy volunteers were prospectively enrolled. Transthoracic and transesophageal echocardiography were performed for each patients. MPV, pulmonary artery pressure (invasive and echo-derived), and right ventricle diameters were measured before and after ASD closure.
Results: MPV levels were significantly higher in ASD population than in healthy volunteers (10.1±1.3 fl to 8.6±0.9 fl, p<0.001). There was a significant correlation between MPV levels and systolic PAP values (r=0.657; p<0.001). Systolic PAP and RV diameter (45.9±11.9 mmHg to 30.2±7.6 mmHg, p<0.001 4.4±1.3 cm vs. 8.6±0.9 cm, p<0.001) were significantly decreased six months after treatment in patients with ASD. MPV levels were also significantly decreased after six months (10.1±1.3 fl vs. 8.6±0.7 fl, p<0.001). When we compared the post treatment MPV levels and systolic PAP values with the healthy volunteers', MPV levels and sPAP were similar between post treatment group and healthy volunteers' (8.6±0.7 vs. 8.6±0.9 fl, p=0.941 and 28.9±3.7 vs. 30.2±7.6, p=0.057).

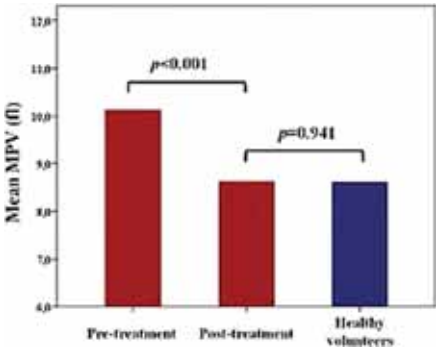

Figure 1

Conclusion: MPV levels that a sign of platelet activation are significantly higher in ASD group than in healthy volunteers. In patients with ASD, MPV levels decreased after treatment of ASD with transcathater closure and it's similarly after six mount treatment and healthy volunteers.

P3325 | BEDSIDE
Single-center long-term clinical follow-up of percutaneous transcatheter closure of atrial septal defects

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Background: Atrial septal defect (ASD) is one of the most common congenital heart diseases detected in adults.Data conducted in registries are very important to reflect real life outcomes and late complications in patients undergoing percutaneous transcatheter closure of ASDs since those results can be missed in clinical trials.
Methods: From June 2002 to May 2012 a total of 200 consecutive patients with type 2 ASD underwent percutaneous closure in our hospital.All patients were included in local ASD closure registry.Follow-up was performed to assess the long-term clinical outcome.
Results: Mean patient age at procedure was 48.3±17.2 years (range 18 to 79), three patients (1.5%) had 3 or more defects and 22 patients (10.0%) had 2 de-

fects. Mean right ventricular systolic pressure was 39.8±12.1 mmHg (range 20 to 90), mean stretched diameter was 17.9±6.0 mm (range 8 to 34), mean diameter in transoesophageal echocardiography was 14.5±5.7 mm (range 4 to 32). Before procedure either right atrial or ventricular dilation was present in 79.6% of patients, 84.3% of patients had clinical symptoms. Device implantation was successful in 99.0% (n=200) of patients with the first attempt and in 100% with second attempt. One unsuccessful case was with significant residual shunt and in other there was device embolization. No other procedural complications were documented. Amplatzer Septal occluder (St.Jude Medical) was used in 87.5% (n=175) and Helex Septal occluder (W.L. Gore & Associates,Inc.) in 12.5% (n=25) of patients. Clinical follow-up was performed in 72,0% (n=144) of patients with mean period of 56.6±27.0 months (range 10 to 117) or 4.2±2.2 years (range 1 to 9). One year mortality was 0.5% (n=2). Five year follow-up reached 59 patients with the mortality rates of 8.4% (n=5). There was statistically significant higher prevalence of atrial fibrillation at the follow-up (22.6% vs 18.2%, $p<0.001$).There was no difference in prevalence of any subjective complaints as dyspnea, chest pain, palpitations or headache. There was one (0.7%) late device embolization with Amplatzer and one (0,7%) device dislocation with Helex occluder. No erosions were documented.

Conclusion: Percutaneous transcatheter closure of secundum type ASDs is effective and safe in long-term with high procedural success rates.

ATRIAL FIBRILLATION ABLATION I

P3327 | BENCH
Pulmonary vein isolation using a circumferential laser ablation in a swine model

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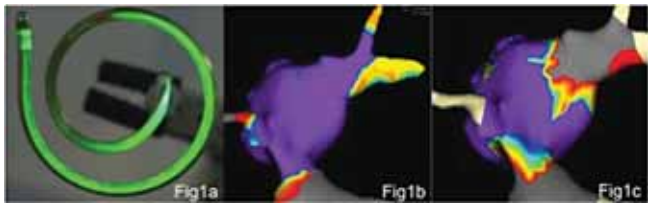
Introduction: Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation (CA) of atrial fibrillation (AF) but remains technically challenging, time-consuming and PV reconnections limit its success. Technologies to achieve rapid and reliable PVI are needed to improve CA outcomes.

Methods: We tested a circular (22-28 mm diameter) catheter equipped with a forward-facing, laser-emitting circumferential fiber-optic (Vimecon, Germany. Fig1a). The left atrium was accessed trans-septally and the catheter was positioned in the right superior (RS) PV ostium in 10 swine (Fig1b). Circumferential laser at 980 nm was delivered at 45 W for 120 s onto the entire PV ostium at once for 2 applications. PVI and lesion location were verified with electro-anatomical mapping (NavX, St Jude). PVI persistence was verified by repeat mapping at 2, 4,6, 8 and 12 weeks (n=2 each). Spleen, Livers, brain (MRI in 1), and kidneys were examined for embolization. Pulmonary veins lesions were examined by pathologist

Results: Electrical isolation of the pulmonary veins was confirmed (Fig1c) in all 10 swine. Histology at ablation sites showed evidence of transmural lesions. There was no evidence of embolic phenomena. All 10 hearts, 10 Kidneys, 8 livers, and 8 spleens were examined macro- and microscopically without evidence of embolization. Brain MRIs were normal.



Conclusions: Circumferential laser ablation can achieve rapid and durable PVI, with lesio transmurality and without evidence of systemic embolization. Further developments are warranted to translate this technology to humans

P3328 | BEDSIDE
Anti-coagulation cessation post atrial fibrillation ablation: impact of implantable loop recorder on decision-making

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Introduction: Atrial fibrillation (AF) significantly increases the risk of thromboembolic complications. Catheter ablation may offer a cure for AF, however, the decision to discontinue anticoagulation can be challenging. Our aim is to assess the impact of the use of an implantable loop recorder (ILR) on rate of anticoagulation discontinuation post AF ablation.

Methods: Between July 2010 and Nov 2012, we randomized 60 patients presenting for AF ablation who were at risk for thromboembolic complications due to one or more of the following: heart failure, hypertension, age>75, DM, prior stroke, TIA, left atrial appendage clot, known severe scar noted on prior EPS study, or poor LA function on echo. All patients received an ILR following AF ablation. Patients were prospectively randomized into two groups: a blinded group whose procedural outcome and long-term anticoagulation were determined according to the standard of care trans-telephonic/holter monitoring, and an un-blinded group that was managed according to the ILR transmissions. The impact of ILR on rate of anticoagulation discontinuation was assessed at 6 month and on long-term follow up.

Results: 60 patients were randomized: 31 un-blinded and 29 blinded. There was no difference in baseline patient characteristics between the two groups. The mean age was 61±8 years vs 67±10 (p=0.474) and EF was 58±8 vs 54±8 (p=0.062) in the un-blinded vs blinded groups respectively. 81% were males in un-blinded vs 90% in the blinded group (p=0.474). 10 patients in the un-blinded group had persistent AF vs 16 patients in the blinded (p=0.117). 11 patients had a prior stroking/TIA in the un-blinded vs 7 in the blinded group (p=0.405). CHADS2 score was 1.8±1.0 in un-blinded vs 1.9±1.0 in blinded. Patients were followed up for a mean of 678±280 days. 22 (71%) patients remained AF free in the un-blinded vs 18 (62%) in the blinded group (p=0.590). At 6 month follow up; anticoagulation was discontinued in 5 patients in the Un-blinded vs 3 in the blinded group (p=0.510). At the last follow up anticoagulation was discontinued in 11 patients in the un-blinded vs 7 in the blinded group (p=0.338). 2 patients in the blinded group had their anticoagulation resumed after brief period of interruption due to AF recurrence.

Conclusion: Our study did not show significant difference in the rate of anticoagulation discontinuation as guided by ILR compared to the standard follow up with trans-telephonic monitoring. Despite documentation of AF free survival, physicians and patients may be reluctant to stop anticoagulants the setting of a high CHADS2 score.

P3329 | BEDSIDE
Addition of posterior inferior linear ablation to pulmonary vein and roof line ablation improves clinical outcome in patients with persistent atrial fibrillation and high recurrence risk

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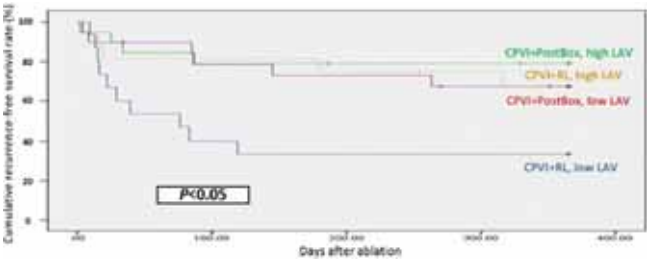
Purpose: Although catheter ablation has become a common practice for persistent atrial fibrillation (AF), technical strategy remains controversial. Circumferential pulmonary vein isolation combined with roof line ablation (CPVI+RL) yielded suboptimal recurrence rates, particularly in persistent AF with low left atrial appendage peak flow velocity (LAV). Addition of posterior inferior linear ablation (CPVI+PostBox) may reduce recurrence in these patients. In this study, we compared 12-month recurrence according to the ablation strategy with reference to LAV.

Methods: We retrospectively analyzed 69 persistent AF patients (age: 63.1±11.1 years; 85.5% men) undergoing an initial catheter ablation. Recurrence-free survival was compared by Kaplan-Meier analysis with log-rank testing regarding strategy and LAV: CPVI+RL with [n=17] and without low LAV [n=14]; CPVI+PostBox with [n=20] and without low LAV [n=20]).

Results: Baseline characteristics were similar among groups. At 12 months, 25 (36%) patients had AF recurrence. Patients in the CPVI+RL group with low LAV had a significantly lower AF recurrence-free survival than the others. The rest of the groups showed similar outcome.



Recurrence-free survival

Conclusion: Addition of posterior inferior linear ablation to CPVI+RL in patients with persistent AF and low LAV improved the recurrence-free survival.

P3330 | BEDSIDE
Short-term ablation outcome and safety profile of nMARQ catheter in atrial fibrillation ablation in comparison to conventional catheters

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Purpose: nMARQ is a circular decapolar catheter designed for mapping and regional multi-electrode ablation to achieve pulmonary vein isolation (PVI). We report short-term ablation outcome and safety data on nMARQ in first-time atrial fibrillation (AF) ablations compared to single-tip irrigated catheters.

Methods: From March to September 2013, we performed 121 first time AF ablations, 48 of which with nMARQ. Another 48 patients undergoing first AF ablations were selected as matched controls. For paroxysmal AF, left atrial circumferential ablation was performed guided by CARTO-3 aimed at PVI. Additional left atrial (LA) ablations were done in persistent AF or atypical atrial flutter as appropriate. For the nMARQ group, no other catheters were required to achieve the additional LA ablations.
Results: Both nMARQ and non-nMARQ cohorts were matched in age, sex and ablation strategies. Procedure duration (164.3±8.1 vs. 229.1±9.0min; $p<0.05$) and ablation time (1851±329.1 vs. 4595±607.0s; $p<0.05$) were shorter in the nMARQ group. Fluoroscopy time was higher in nMARQ (47.0±2.5 vs. 32.6±2.0min; $p<0.05$), reflecting a learning curve in familiarity with a new catheter. Over a 6-month follow-up period, there was no recurrence of atrial arrhythmias in nMARQ vs. 4 in non-nMARQ (p=0.14) (Fig. 1). There were no major complications.

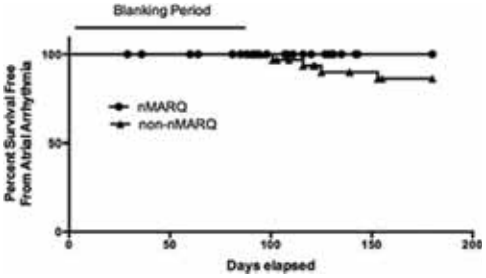

Figure 1

Conclusions: Early experience with nMARQ in AF ablation highlights its safety, timesaving advantage and non-inferiority to conventional catheters in short-term ablation outcome. Long-term safety and efficacy data is needed with longer follow up.

P3331 | BEDSIDE
Novel predictor for successful outcome of atrial fibrillation ablation assessed by speckle tracking echocardiography

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Background: Atrial fibrillation (AF) is associated with left atrial (LA) remodeling and fibrosis caused by LA pressure and/or volume (LAV) overload represented by the elevated left ventricular filling pressure and LA enlargement. Thus pulmonary capillary wedge pressure (PCWP) as well as LAV may be a useful predictor for successful outcome of AF ablation. We previously reported that PCWP could be estimated by the combination of LAV and LA function using the speckle tracking echocardiography (STE). Thus, the aim of this study was to elucidate the most useful predictor for successful outcome in AF ablation including PCWP using the STE.
Methods: We enrolled consecutive 104 patients with paroxysmal AF (59±10 years, 70 men) who underwent pulmonary vein isolation. We measured LAV, LA emptying function (EF), strain and strain rate (SR) using the STE during sinus rhythm before ablation. Echocardiographic parameters were compared between non-recurrence (successful) group (n=81, age 59±9, sinus rhythm was continued for more than 1 year) and recurrence group (n=23, age 60±11). The ePCWP was estimated as 10.7 – 12.4 x log active LAEF/minimum LAV index. LA stiffness was estimated as ePCWP/LA strain. Moreover, we measured PCWP and LA pressure by cardiac catheterization just before AF ablation in 32 patients.
Results: The ePCWP estimated by STE was correlated with PCWP measured by cardiac catheterization ($r=0.72$, $p<0.01$). The ePCWP and minimum LAV before ablation in recurrence group were significantly increased compared with non-recurrence group (14±4 vs. 11±3mmHg and 37±13 vs. 30±12ml/m^2). PCWP measured by cardiac catheterization just before ablation was also elevated in recurrence group compared with non-recurrence group (13±2 vs. 9±3mmHg). LA total EF was decreased and LA stiffness was increased in recurrence group compared with non-recurrence group (37±10 vs. 42±10% and 0.81±0.38 vs. 0.52±0.36, $p<0.05$, respectively). In multivariate analysis, only ePCWP was independently associated with successful ablation. Using 12 mmHg of the ePCWP as an optimal cutoff from the ROC curve, the sensitivity and the specificity for successful ablation were 64 and 83%, and the positive predictive value and the negative predictive value were 93 and 40% (AUC= 0.76).
Conclusion: The elevation of PCWP before ablation but not the LAV was the predictor of AF recurrence (unsuccessful outcome) after AF ablation. This suggested a strong relation between LV filling pressure and the progression of LA remodeling that is responsible for AF. The ePCWP estimated by STE is useful to predict the successful outcome of AF ablation.

P3332 | BEDSIDE
Uninterrupted Rivaroxaban reduces the prevalence of Silent Cerebral Ischemia during radiofrequency ablation of atrial fibrillation

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Introduction: Silent cerebral ischemia (SCI) detected by dMRI, has been reported following radiofrequency catheter ablation of AF. Uninterrupted anticoagulation strategies with warfarin seem to reduce the prevalence of SCI. We compared interrupted and uninterrupted rivaroxaban use before AF ablation and we sought to determine whether this had an impact on the prevalence of SCI.
Methods: Forty nine consecutive patients undergoing ablation of AF while on rivaroxaban 20 mg for at least 3 weeks before the procedure were enrolled in this prospective study. Patients were divided into two groups according to their periprocedural anticoagulation management. 24 patients (group I) discontinued rivaroxaban at least 24 hours before the procedure and were bridged with low molecular weight heparin, while the remaining 25 patients (group II) underwent ablation without rivaroxaban discontinuation. Group I patients underwent heparin bolus after transseptal access was obtained, while group II underwent heparin bolus before transseptal. All patients underwent pre and post ablation dMRI.
Results: All patients had persistent and long standing persistent AF. Baseline characteristics were similar between groups. At post-procedure dMRI, SCI was detected in 7 (29.2%) patients in Group I and in no patient in Group II (p=0.004). In logistic regression analysis, rivaroxaban discontinuation was the strongest predictor of post-procedure SCI [OR= 21.85 (95% CI 1.2 to 408.0) p=0.038]. Periprocedural cardioversion was not associated with SCI [OR = 3.61 (95% CI 0.63 to 20.8) p=0.15]. No major bleeding occurred in this study population.
Conclusions: Uninterrupted rivaroxaban before radiofrequency ablation of AF reduces the prevalence of SCI as detected by dMRI. This might have relevant clinical implications. A controlled randomized study with a larger sample size is warranted to confirm our findings.

P3333 | BEDSIDE
Prospective comparison of the first- and second-generation cryoballoon for atrial fibrillation ablation

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Background: The second-generation cryoballoon is designed to provide a more contiguous lesion and treat a broader range of pulmonary vein anatomies with less effort and improved cooling uniformity. Clinical data remain limited regarding its efficiency and efficacy for atrial fibrillation (AF) ablation.
Methods: This study evaluated the ADV in comparison with first-generation balloon in patients who underwent pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation (PAF). The study consisted of 92 patients undergoing their 1st AF ablation and having given written informed consent, including 58 patients in ADV group and 34 in AFB group (62±12 v. 65±10 years; p=ns. 56% v. 50% male; p=ns). Body mass index was similar in both groups (28±6 v. 28±7 kg/m^2).
Results: Mean procedure time in ADV were significantly shorter compared with AFB (125±24 v.140±29 minutes, p=0.01). The fluoroscopic time was slightly shorter (20±13 v. 22±10 minutes, p=ns). During cryotherapy deliveries, ADV reached specific temperature points significantly faster than AFB (Table 1).
Temporary phrenic nerve palsy (tPNP) occurred in a total of 16 (17%) cases, including weakened diaphragmatic response to pacing; only 1 case had sustained PNP by the end of the procedure. No difference in the rate of tPNP was observed between ADV (17%) and AFB (21%).
During follow-up between 3-6 month after the procedure, 78% of those who completed the follow-up (n=81) were AF free; 86% in ADV and 66% in AFB group (p=0.03).

Table 1

	Time to –20 degree (second)	Time to –30 degree (second)	Time to –40 degree (second)	Time to lowest temperature (second)	Lowest temperature (℃)
AFB	28±5	31±9	57±24	189±33	–50.8±7.9
ADV	18±5	27±6	48±16	193±29	–53.2±4.3
P =	0.005	0.013	0.045	ns	0.082

ADV: Arctic Front Advance; AFB: Arctic Front; ns: not significant; Time: From the onset time of cryotherapy delivery to specific temperature points.

Conclusion: ADV has improved the procedure efficiency by significantly reduced procedure time without increase in the occurrence of PNP. ADV potentially improves the treatment efficacy. Further investigation and long-term follow-up are needed to confirm the findings.

P3334 | BEDSIDE
LA fibrosis predicts LVEF improvement in HF patients undergoing AF ablation

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Background: In patients with heart failure (HF) and atrial fibrillation (AF) improvement of left ventricular ejection fraction (LVEF) has been described following AF catheter ablation. Not all HF patients benefit the same way. Furthermore, presence and amount of left atrial (LA) fibrosis is increasingly recognised as a marker of advanced AF disease status and predictor of ablation success. We thought to investigate the relationship between LA fibrosis and the extent of LVEF improvement in HF patients after successful AF ablation.
Methods: Fourteen patients (14 male, median 64 years, median LVEF 33%) underwent catheter ablation of persistent AF. Pulmonary vein (PV) isolation was performed in all patients. LA voltage mapping was used to identify low voltage zones (LVZ, threshold $<$0.5 mV) outside PVs as surrogate of LA fibrosis. Individualized linear ablation lines were added to dissect/isolate/connect LVZs as substrate modification. Follow-up was performed using implantable devices. LVEF was re-evaluated 3 months later.
Results: Following successful AF ablation LVEF overall significantly improved; 33% (20-40%) vs. 44% (15-55%); p=0.021. LVZ outside PVs were detected in 7/14 (50%) patients. In patients with LVZ there was no improvement of LVEF; 35% (20-35%) vs. 33% (15-50%); p=0.527. In contrary, in patients without LVZ there was a significant improvement of LVEF; 30% (25-40%) vs. 50% (35-55%); p=0.018.
Conclusions: Presence of LA fibrosis predicts the improvement in LVEF after successful AF ablation in HF patients. The data raise the question on AF being the cause or the consequence of HF in patients with and without LA fibrosis.

P3335 | BEDSIDE
Type of recurrent atrial fibrillation is associated with the outcome of redo ablation of persistent atrial fibrillation

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Purpose: Patients with persistent and longstanding persistent atrial fibrillation (AF) have a higher recurrence rate after catheter ablation. This study investigated the impact of the type of recurrent AF on the outcome of redo procedure in patients experiencing recurrence following persistent AF ablation.
Methods: 136 patients who experienced recurrent AF after primary ablation of persistent AF were enrolled while patients presenting atrial flutter and atrial tachycardia were excluded. Patients were grouped according the type of recurrent arrhythmia: R-PAF group–recurrent paroxysmal AF which terminated spontaneously within 7 days; R-PeAF group–recurrent AF persisted for more than 7 days. Kaplan-Meier estimation and Cox proportional hazards model were used to estimate the relationship between recurrent AF type and the outcome of the second ablation. Ablation technique was identical in both procedures including isolation of ipsilateral pulmonary veins and blockage of left atrial roof line, mitral and tricuspid isthmus lines.
Results: During a mean follow-up of 25.9$\pm$8.9 months, 56 (41.2%) patients developed recurrent atrial tachyarrhythmia after the redo procedure. Patients in the group of R-PeAF were more likely to experience arrhythmia recurrence compared to those in the R-PAF group (51.7% vs 33.3%, P=0.03). Multivariate Cox regression analysis revealed that R-PeAF (HR 1.72, 95% CI 1.02-2.21, P=0.04) and duration of AF history (HR 1.08, 95% CI 1.01-1.13, P=0.02) were independent predictors of AF recurrences after the second procedure.
Conclusion: R-PAF was associated with a better prognosis after the second catheter ablation of persistent and longstanding persistent AF. R-PAF might be considered as a step toward sinus rhythm.

P3336 | BEDSIDE
Transcranial detection of cerebral microembolic signals during pulmonary vein isolation and correlation with 3 Tesla MRI detected brain lesions

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Background: Pulmonary vein isolation (PVI) is an established therapeutic option for the treatment of symptomatic atrial fibrillation (AF). But there exist evidence, that subclinical brain lesions caused by microembolization during the ablation procedure could influence the neurological outcome in these patients. Periinterventional transcranial Doppler (TCD) is used for detection of microembolic signals (MES). We used TCD to reveal parts of increased MES occurrence during ablation procedure. Additionally, we correlated the MES occurrence with MRI detected brain lesions after ablation.
Methods and results: In a prospective registry in 20 patients suffering from AF pulmonary vein isolation was performed with irrigated "point by point" ablation (3.5mm tip) and single transseptal puncture with a steerable sheath. The activating clotting time (ACT) was set between 250-300 sec. In all patients permanent periprocedural TCD with discrimination between solid and gaseous MES was performed. These MES were quantified with regard to predefined periprocedural steps. Additionally, 10 patients underwent brain MRI (3-Tesla, T2 high-resolution diffusion-weighted imaging (DWI), fluid attenuated inversion recovery (FLAIR)) within 24 hours prior and after ablation procedure to validate the TCD revealed MES.
The mean total numbers of MES revealed during the complete procedure were 708 gaseous and 83 solid MES. During the predefined procedural steps the following MES were detected: transseptal puncture: 43 gaseous 14 solid; flushing of steerable sheath 25 gaseous, 7 solid; change between diagnostic and ablation catheter (2.5 times per procedure): 21 gaseous, 9 solid; angiography of the PV (mean 4 per procedure): 59 gaseous and solid; anatomical mapping: 12 gaseous, 5 solid, ablation: 539 gaseous, 48 solid; postinterventional protamine administration: 0 gaseous, 0 solid. The higher the ACT, the lower the number of MES during the ablation phase. Astonishingly, in spite of the high number of detected MES no brain lesion could be revealed in the brain MRI after ablation.
Conclusions: During the irrigated PVI the most MES occur during the ablation especially during low ACT values. The post interventional administration of protamine causes no MES. The detected MES do not correlate with MRI revealed brain lesions

P3337 | BEDSIDE
Potential role of the second generation 28mm cryoballoon in persistent atrial fibrillation ablation

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Purpose: A second-generation 28mm cryoballoon (CB-2G) has been recently introduced for pulmonary vein isolation (PVI) in paroxysmal atrial fibrillation (AF) ablation, providing a widened zone of optimal cooling with higher procedural success rate and better outcome compared to the first-generation 28mm CB (CB-1G). However, few data are available in persistent AF. We compared the acute and long-term efficacy of CB-1G and CB-2G PVI in persistent AF.
Methods: PVI using the single big CB technique (28mm) combined with the endoluminal spiral mapping catheter (Achieve, Medtronic) was performed in 36 consecutive patients (pts) with history (4$\pm$3years) of persistent AF (group 1, CB-G1: n=15pts; group 2, CB-G2: n=21pts). Follow-up included regular telephonic interviews, 72-hours-Holter electrocardiographic (ECG), or event recordings. Any symptomatic or documented AF episode $\geq$30 seconds after the procedure without any blanking period was defined as recurrence.
Results: Both groups were comparable for all baseline characteristics except for LA size (group 1: 38$\pm$5mm vs. group 2: 42$\pm$5mm, p=0.046) and EF (group 1: 64$\pm$4 vs. group 2: 59$\pm$6%, respectively, p=0.01). A total of 139 PVs was ablated; acute PVI using only the 28mm CB was achieved in 97% (57/59) and 100% of all the PVs (80/80) in group 1 and group 2, respectively (p=n.s.). The rate of PVs isolation after first attempt ("single shot" PVI) was significantly higher in group 2 (87% vs. 46%, p$<$0.001) whit decreased procedural- (147$\pm$36 vs 87$\pm$21 min p$<$0.001) and fluoroscopy-time (25$\pm$10 vs 12$\pm$4 min; p$<$0.001). After a median of 352 (234-541) days follow-up, 33% of pts in group 1 and 71% in group 2 remained in sinus rhythm (p$<$0.001). Seven pts (group 1) and 3 pts (group 2) suffering from AF recurrence underwent a Re-do procedure. In group 1, PVs reconnection was a typical finding (23/27; 85%) whereas all PVs in group 2 (12/12, 100%) remained chronically isolated.
Conclusions: In persistent AF, the CB-2G appears to significantly improve both, acute and long-term efficacy compared to the CB-1G, with a high rate of "single shot" and chronic PVI.

P3338 | BEDSIDE
Second-generation cryoballoon-based atrial fibrillation ablation without bonus application after proven isolation, a multicentric study

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Introduction: Despite extensive experience with cryoballoon (CB) ablation, it is unknown whether the standard delivery of a "bonus" application (BA) after the achievement of electrical pulmonary vein isolation (PVI) is needed in order to ensure efficacy.
Methods: Consecutive patients from 3 different centers referred for PVI using CB between June 2012 and June 2013 were included. Cryoapplications of 240 sec were used until electrical isolation. Thereafter, no further applications (or BA) were performed. Patients were followed with a clinical evaluation at 4 and 12 months, with 24h-holter performed at 4, 8 and 12 months.
Results: One hundred and sixteen (116) patients [71.5% male; 57.5$\pm$9.4y] were included. Paroxysmal AF was the indication for ablation in 93.1%. CHADSVaSC score was $\leq$1 in 67.2%. A 28-mm balloon was used in 73.3%. Mean procedure, left atrial, and fluoroscopy time were 136.0$\pm$63.3min, 85.8$\pm$30.6min, and

27.3±18.9min respectively. Ablation characteristics are presented in table 1. Thirteen complications occurred in 12 patients: 6 Phrenic Nerve Palsies (all recovered within 6 months), 4 pericardial effusions (2 requiring drainage), 2 groin hematomas, 1 pulmonary embolism. At 4- and 12-months follow-up, 71/94 patients (75.5%) and 21/30 (70.0%) were asymptomatic, 66/95 patients (69.5%) and 25/30 (83.3%) had stopped their anti-arrhythmic drugs, 62/85 (72.9%) and 12/16 (75.0%) patients remained free of recurrence AF.
Conclusion: After a single CB PVI procedure without additional BA lesions, 75.0% of patients remained arrhythmia-free at 12 months of follow-up. These preliminary results suggest that efficacy is not compromised by this approach.

ATRIAL FIBRILLATION ABLATION II

P3340 | BEDSIDE
Clinical success rates of new generation catheter designs for radiofrequency ablation of atrial fibrillation

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Introduction: Pulmonary vein isolation (PVI) is the standard of care in interventional treatment of atrial fibrillation. Conventional ablation catheters (CON) feature a rigid tip with open irrigation for cooling, but no additional features for enhancing tissue contact, which is a critical factor in successful ablation. New ablation catheters add the option of contact force measurement (CF) to continuously monitor tissue contact. Other new catheter types promote a flexible tip (FT) to enable more uniform contact to cardiac tissue in the moving heart. Additionally, it actively directs coolant flow towards the site of tissue contact. We hypothesized that continuous quantitative contact force measurement will offer a significant advantage over the flexible tip design concerning clinical outcome.
Methods: 176 patients with persistent atrial fibrillation who underwent first or repeat PVI using new catheter types (Contact-Force type (n=112), Flexible-Tip type (n=64)) were included consecutively into a database after providing informed consent. All patients had PVI performed by 3D-Mapping guided WACA. Follow-up visits were scheduled at intervals of 3 mo. with clinical interviews, Holter monitoring, QOL assessment. 157 matched controls underwent PVI with conventional catheter tip. Arrhythmia recurrence was defined as a documented episode of atrial fibrillation or any other atrial flutter or tachycardia lasting more than 30 seconds.
Results: Table 1 shows differences in HR for recurrence and procedure time. Acute success (documented PVI) was 100% with new catheter types and 99.5% with conventional design. Mean follow-up was 12 (±6) months. Recurrence was documented in 39 patients (35%) in the CF group, in 14 patients (22%) in the FT group, and in 88 patients (56%) in the CON group. No significant differences were found regarding complication rates.

Table 1. Differences between treatment groups

	Conventional	Contact force	Flexible tip	CON vs. CF	CON vs. FT	CF vs. FT
Cox HR for recurrence	1.0	0.64	0.44	0.019	0.003	0.243
Procedure time [h]	4.5 (±1.3)	3.9 (±1.0)	3.6 (±1.0)	<0.001	<0.001	0.109

Conclusion: Catheters with contact force measurement are superior to conventional tip in terms of clinical success rates. Surprisingly, the flexible tip design was as effective in our cohort of patients.

P3341 | BEDSIDE
The benefits of experience: pulmonary vein isolation with the endoscopic ablation system at a single centre

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Purpose: Novel ablation devices for pulmonary vein isolation (PVI) need a careful evaluation of its efficacy and safety beyond clinical studies in a real world situation. The endoscopic ablation system (EAS) was recently approved for PVI in Europe. We sought to determine the safety, efficacy and learning curve effects in a large volume single center
Methods: Between June 2010 and March 2013 all EAS guided PVI procedures were analyzed. Using a single transseptal access visually guided sequential PVI was performed. Ablation lesions were deployed contiguously encircling each individual PV (5.5W-12W for 20-30 sec). Electrical PVI was assessed with a circular mapping catheter (CMC). In case of residual LA to PV conduction additional ablations using EAS were performed according to the CMC activation sequence. Safety analysis included all peri-procedural complications. To determine efficacy the number of acutely isolated PVs as well as 6 months follow-up results were assessed. Consecutive patients were divided in thirds to assess learning curve for all parameters.

Table 1

Patients	1–50	51–100	101–150	p
Procedure time	148±36	130±24	123±35	<0.001
Fluoroscopy time	15±5	13±6	12±7	0.028
Visually guided PVI	144/196 (73%)	177/194 (91%)	176/193 (91%)	<0.001
PVI after remapping	189/196 (96%)	193/194 (99%)	192/193 (99%)	0.018

Results: All major peri-procedural complications occurred in the first tertial: 1 tamponade, 1 femoral venous laceration requiring surgery and 1 TIA. In 3 patients (2 in 1st and 1 in 2nd third) phrenic nerve palsy was observed (2%). Efficacy and procedural data is displayed in Table 1.
Conclusion: EAS is a safe and efficient novel technology to perform PVI. Increasing experience leads to lower complication rates and higher procedural success with shorter procedure times.

P3342 | BEDSIDE
Close relationship of the left main coronary artery to the left atrium - a potential hazard of left atrial radiofrequency ablation

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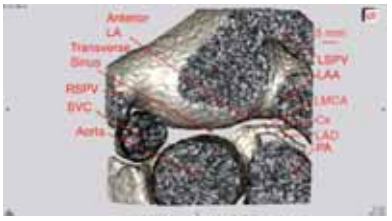
Purpose: The anterior left atrium (LA) and base of left atrial appendage (LAA) are often targeted during radiofrequency ablation (RFA) of atrial fibrillation. Coronary artery damage can occur within 5 mm of RFA. We determined the proximity of the left main coronary artery (LMCA) to LA and LAA.
Methods: CT coronary angiograms obtained with Discovery CT 750 HD with slice thickness of 0.625 mm, performed in 100 consecutive patients with chest pain were reviewed. Distances from the LMCA to endocardium of LA and LAA were measured using OsiriX open-source DICOM viewer.
Results: In 100 patients (55 M, 45 F, age 51±10 years) the LMCA was <5 mm from endocardium of anterior LA or base of LAA in 49% (Group 1) and <5 mm from the tubular part of LAA in 11% (Group 2). In 40% (Group 3) LMCA was >5 mm from LA/LAA. In 31 of the Group 1 patients, the LMCA was <5 mm from both LA and LAA base (Figure) and in the other 18 patients the LMCA was <5 mm from LAA base only. Of the Group 1 patients: mean length of LMCA within 5 mm of LA and base of LAA was 9.4±4.3 mm (range 1 - 20 mm); minimum distance between LMCA and LA was 3±1 mm (range 1 - 5 mm); distance between LMCA ostium and LA/LAA was 4.9±1.8 mm (range 1 - 9 mm); mean myocardial thickness at LA/LAA sites closest to the LMCA was 2.6±0.6 mm (range 1 - 4 mm); the part of LMCA closest to LA/LAA was most commonly the distal third of LMCA (n=22); the LAA was inverted in transverse sinus (TS) in 1. In 5 Group 2 patients LAA was inverted in TS.



Conclusions: LMCA is close to the anterior LA and base of LAA in most patients. Myocardial tissue is thin in these areas. RFA should be limited at these sites to avoid potentially catastrophic LMCA injury.

P3343 | BEDSIDE
The efficacy of a novel hybrid ablation procedure in patients with refractory atrial fibrillation

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Background: Pulmonary vein isolation (PVI) alone is insufficient for many patients (pts) with atrial fibrillation (AF), including pts who have failed >2 prior PVIs for paroxysmal AF (PAF) and those with persistent AF (PeAF). We hypothesized that additional ablation targeted to the posterior left atrium in these pts would result in a high response rate.
Methods: We enrolled consecutive pts who underwent a novel hybrid ablation procedure. First, a CT surgeon entered the pericardial space using transdiaphragmatic access (Fig. 1, left). Second, under direct visualization, a nContact open-irrigated linear RF ablation catheter was used to create contiguous and confluent epicardial linear lesions extending from the antrum of the left to right-sided PVs (Fig. 1, right). Third, an EP confirmed posterior LA electrical silence and completed an endocardial PVI.
Results: We included 22 pts (65±9 yrs, 16 M, mean CHADS2 = 1.3) with PAF (n=3; each failed 3 prior PVIs) or PeAF. The latter had failed (n=9), were intolerant (n=4), or refused a class III antiarrhythmic drug (AAD, n=1) or had failed amio-

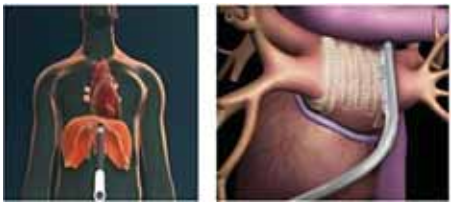

Figure 1

darone (n=5). Epicardial ablation was performed without complications; most pts (n=17) underwent cryoballoon (CB) PVI. At a mean follow-up of 6 mos, 18 pts were in sinus rhythm (no AAD [n=15] or previously unsuccessful AAD [n=3]); 4 pts were within 30 days of procedure.
Conclusions: We describe a novel hybrid technique for ablation in AF pts unlikely to respond to PVI alone. The epicardial ablation was limited exclusively to the posterior left atrium; the endocardial portion was limited to PVI and most commonly used a CB. Short-term follow-up suggests that this technique holds great promise.

P3344 | BEDSIDE
Atrial tachycardias after mini-Maze procedure and concomitant mitral valve surgery in patients with rheumatic heart disease

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Between May 2008 and July 2013, 34 patients with symptomatic incessant post-Maze atria tachycardias (AT) refractory to antiarrhythmic drugs (AADs) were evaluated in our laboratories.All of them underwent valve replacement due to rheumatic disease. Thirty-four patients had 57 kinds of mappable AT and one unmappable AT. The stable mapped ATs included 14 focal ATs (24.6%) and 43 reentry ATs (75.4%). Seventeen patients (50%) had only one single AT, 11 patients (32.4%) had 2 ATs, and 6 patients had ≥3 ATs. Ten of the 14 focal ATs located at PV antrum. One originated from left superior PV. The other 3 ATs located in LA anterior wall, RA septum and crista terminalis. Of the 43 reentry ATs, 16 had macro-reentry AT around mitral annulus (MA), 16 had typical AFL around tricuspid annulus (TA). One patient had a micro-reentry AT around both left atrium and right atrium (Fig. 1).The ATs in 33 patients were successfully eliminated by ablation. One patient with variable unmappable AT could not endurance the procedure and gave up. At a Mean follow-up of 23.6±15.8 months (4.5~66months, median 17.5 months), 26 patients maintained sinus rhythm after single procedure. Three patients occurred paroxysmal AF with amiodarone or persistent AF with metoprolol. Five patients had recurrent AT and two of them underwent successfully redo-procedure. There were 28 patients (82.4%) in sinus rhythm without antiarrhythmia drugs after repeated procedure.
Conclusions: AT after mini-Maze procedure and concomitant mitral valve surgery in patients with rheumatic heart disease mostly related to prior maze lines. Focal AT from PV antrum and reentry AT around MV or TV were very common.

P3345 | BEDSIDE
Catheter ablation of atrial fibrillation: three-dimensional transesophageal echocardiography for pulmonary vein imaging prior to and after pulmonary vein isolation

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Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory AF. However, it is still challenging because of the high degree of variability of the PV anatomy. Therefore, 3-D imaging systems (CT and MRI) are frequently used prior to an ablation procedure. Alternatively, 3-D TEE provides an excellent overview over the individual left atrial morphology without some of the limitations associated with other imaging techniques. Therefore, we have evaluated the usefulness of 3-D TEE for PV imaging before and after catheter ablation of AF.
In 290 patients, 3-D TEE was performed immediately prior to an ablation procedure. The images were available throughout the ablation procedure. In patients with paroxysmal AF, the cryoablation technique was used (Arctic Front Balloon, Medtronic). In the other patients, a circumferential pulmonary vein ablation was performed using the CARTO system (Biosense Webster). At 3-month follow-up, a 3-D TEE was performd in all patients to rule out a PV stenosis.
A 3-D TEE could be performed successfully in all patients prior to the ablation procedure and almost all PV ostia could be evaluated. The image quality was excellent and several variations of the PV anatomy could be visualized precisely. The TEE findings correlated well with the PV angiographies performed during the ablation procedures. All ablation procedures could be performed successfully (mean number of completely isolated PVs: 3.8±0.5 (cryo group), 3.9±0.3 (Carto group)). At 38-month follow-up, 73.1% of all patients were free from an arrhythmia recurrence (cryo group: 77.6%, Carto group: 70.1%). Two cases of a moderate PV stenosis (50%) were detected by 3-D TEE at 3-month follow-up and confirmed by invasive angiography (during a repeat ablation procedure). There were no major complications.
Three-dimensional TEE overcomes most of the limitations of other imaging techniques (CT/MRI) currently used for evaluation of the PV anatomy (such as radiation exposure and inappropriate image quality in the presence of AF). A TEE should be performed prior to an AF ablation procedure to rule out the presence of a left atrial thrombus in all patients anyway. Thus, a 3-D TEE does not result in additional patient discomfort or cost and is less time-consuming than other techniques. Therefore, AF ablation procedures can be performed safely and effectively based on prior 3-D TEE imaging. Furthermore, 3-D transesophageal echocardiography provides reliable information with regard to the detection of PV stenoses after catheter ablation of AF.

P3346 | BEDSIDE
P-wave amplitude smaller than 0.1mV in lead I predicts clinical recurrence after catheter ablation in patients with paroxysmal atrial fibrillation

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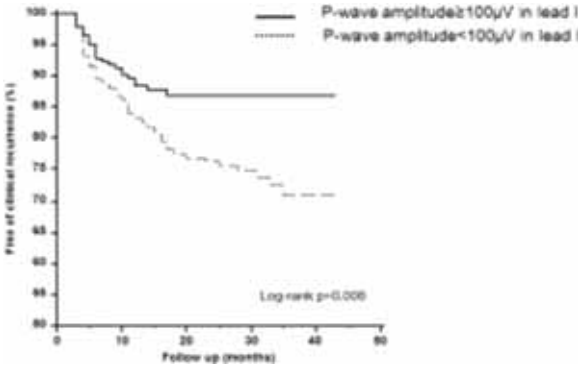
Purpose: P-wave morphology in electrocardiography (ECG) may reflect the atrial remodeling, which is associated with the prognosis of atrial fibrillation (AF). We hypothesized that P-wave amplitude has a predictive value for clinical recurrence of AF after radiofrequency catheter ablation (RFCA) among the patients with paroxysmal AF (PAF).
Methods: We included consecutive 607 PAF patients (76.8% male, 56.6±11.5 years old) who underwent RFCA in the AF Cohort. We analyzed sinus rhythm ECG taken immediately before RFCA without antiarrhythmic drug by customized software, and compared with left atrial (LA) volume (CT), mean voltage (NavX), conduction velocity (CV: NavX), and clinical outcome.
Results: 1. P wave amplitude in lead I has positive correlations with LA voltage (R=0.120, p=0.011) and LA-CV (R=0.198, p<0.001). 2. During 20±11 months follow-up period, clinical recurrence rate was 17.1%, and P wave amplitude in lead I was significantly lower in recurred patients (0.082±0.031 mV vs. 0.097±0.030 mV, p<0.001). 3. P-wave amplitude smaller than 0.1mV in lead I was a significant predictor for clinical recurrence of AF after RFCA for PAF in the multivariate Cox regression analysis (adjusted HR=1.836, 95% CI 1.177-2.864, p=0.007).



Conclusion: Low P-wave amplitude in lead I independently predicts clinical recurrence after RFCA in patients with PAF, and is associated with low voltage and slow CV in LA.

P3347 | BEDSIDE
Posterior left atrial isolation in impaired diastolic function results in better arrhythmia free survival

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Background: Patients with impaired diastolic function (IDF) have higher rates of arrhythmic recurrence following atrial fibrillation (AF) ablation. Past studies have suggested that the posterior left atrium (LA) may be involved in maintaining atrial arrhythmias in conditions that result in atrial stretch. We aimed to investigate the effect of posterior LA isolation in addition to pulmonary vein isolation (PVI) in patients with IDF referred for catheter ablation of AF.
Methods: We conducted a sub-study of a previously published large randomized control study that compared a single ring isolation technique that electrically isolated the pulmonary veins and posterior left atria (PLAI) to a conventional wide antral isolation strategy. Two hundred and twenty consecutive consenting patients referred for catheter ablation of AF (paroxysmal 135, persistent 48, permanent 37) were recruited (female 43, mean age 59±10 years). Transthoracic echocardiography identified 50 (23%) patients with diastolic impairment and preserved LV systolic function (ejection fraction>50%). Cox regression analysis was utilized to identify independent predictors atrial arrhythmia recurrence after ablation.
Results: Patients were followed for median 4.6 (inter quartile range 4.0-5.5) years. Patients with impaired diastolic function having PLAI had better arrhythmia free survival than patients randomized to conventional ablation (Log rank P=0.028). The only independent predictor of recurrence utilizing Cox regression analysis was ablation strategy (2.3 [1.15-4.74], P=0.026). Markers of severity/grade of diastolic dysfunction were not predictive of arrhythmic recurrence.
Conclusion: Posterior isolation of the LA in addition to PVI results in superior arrhythmia free survival in patients with diastolic impairment. This may suggest patients with impaired diastolic function have additional arrhythmia substrate in the posterior LA.

P3348 | BEDSIDE
The occurrence of atrial tachycardia is rare after ganglionated plexus ablation plus antral pulmonary vein isolation in patients with non-paroximal atrial fibrillation

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Iatrogenic atrial tachycardia (AT) after atrial fibrillation (AF) ablation is one of complication that we should avoid, because a patient has often heavy symptom, and rate control is difficult during AT. It has been reported that stepwise approach using termination as procedural endpoint was highly effective approach for persistent AF (PEAF) and long-lasting persistent AF (LLAF). However, AT often occurred after procedure. Ganglionated plexus (GP) ablation is known as alternative procedure for treatment of AF. The occurrence rate of AT after GP ablation plus antral pulmonary vein isolation (GPPVI) is not known. The aim of this study is to investigate the efficacy and AT occurrence rate of high frequency stimulation (HFS) guided GPPVI in patients with PEAF and LLAF.
Methods: GPPVI were performed in 92 patients (60.2±9.0 years, 76 male, PEAF: 57 patients, LLAF: 35 patients). The five major left atrial GP were localized by delivering HFS (20Hz, 20V, 10 ms pulse width) to the atrial tissue where the GP was presumed to be located. Sites showing a parasympathetic response, which is defined as ≥50% increase in mean R-R interval during AF, was assigned as a GP site. Radiofrequency current was applied to that site to eliminate the parasympathetic response. After GP ablation, PVI was performed. Follow-up included regular outpatient clinic, ECG, and Holter ECG. A symptomatic or documented AF episodes ≥30 seconds after a blanking periods of 3 months was defined as recurrence.
Result: We could detect 22.6±7.9 GP sites in PEAF patient and 21.6±5.5 in LLAF and were able to achieve electrical PVI in all patients. Radiofrequency energy delivery durations for GPPVI were 41.9±11.9 minutes. AF was terminated during GPPVI in 13 PEAF patients (22.8%) and 5 LLAF patients (14%). The rate of freedom from AF was 82.5% in PEAF patients after 1.16 procedure, and 68.6% in LLAF patients after 1.26 (follow-up periods: 16.9±8.8 month). After single procedure, the rate of freedom from AF was 66.7% in PEAF patients, and 60.0% in LLAF. AT occurred in 4 PEAF patients (7%) and 4 LLAF patients (11.4%) during follow-up periods. One AT occurred only in blanking periods. Five patients underwent repeat procedures. Two ATs were perimitral AT, two ATs were common AFL, and one AT was PV gap related. All 5 ATs were ablated successfully. There was no major complication in this study.
Conclusion: AF termination rate was low during GPPVI. However, GPPVI is powerful treatment option even in persistent and long-lasting persistent. AT occurrence rate after GPPVI might be lower than stepwise approach.

P3349 | BEDSIDE
The frontward P wave duration in magnetocardiography is a novel parameter to estimate pulmonary vein reconnections after radiofrequency catheter ablation of atrial fibrillation

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Introduction: Radiofrequency catheter ablation (RFCA) is widely performed as a first-line therapy for atrial fibrillation (AF). Reconnections between the left atrium (LA) and pulmonary veins (PVs) are a main reason for recurrences after RFCA including PV isolation (PVI). However, LA-PV reconnections are difficult to detect non-invasively. This study aimed to evaluate the diagnostic value of magnetocardiograms (MCGs) for estimating LA-PV reconnections.
Methods: Forty-five patients with AF recurrences after their first RFCA session were included in this study. They also received second sessions in our hospital. In all patients, MCGs during sinus rhythm were recorded one day before and one day after RFCA during both the first and second sessions. The MCG parameters were analyzed retrospectively.
Results: In 43 of 45 patients (96%), LA-PV reconnections were found in the second session. The patients were divided into 3 groups depending on the reconnection sites: group 1 = left PV (n=5), group 2 = right PV (n=11), and group 3 = both left and right PVs (n=27). In group 1 and group 2, the MCG parameters did not significantly change between after the first session and before the second session. However, in group 3, the frontward P wave duration (fPWD) before the second session was significantly longer than after the first session (after first sessions: 122.9±17.2 [ms], before second sessions: 128.3±15.0 [ms], p=0.01) (Table 1). Furthermore, the fPWD became shorter after the re-isolation in the second session only in group 3 (before: 128.3±15.0 [ms], and after the second session: 124.0±17.0 [ms], p=0.006).
Conclusion: The fPWD in the MCG was useful for estimating LA-PV reconnections especially for the right and left PVs.

Table 1. Characteristics of patients

Group	Reconnection PVs	Frontward P wave duration				p-value (*1,*2) (ANOVA)
		Before 1st 1st RFCA	After 1st RFCA (*1)	Before 2nd RFCA (*2)	After 2nd RFCA	
Group 1	Left	136.2±18.2	129.0±18.9	135.5±20.9	136.4±22.3	0.51
Group 2	Right	115.0±8.9	113.5±9.5	114.9±11.4	115.4±9.4	0.57
Group 3	Left & Right	124.9±12.9	122.9±17.2	128.3±15.0	124.0±17.0	0.01

P3350 | BEDSIDE
MRI characterization of cryoballoon ablation lesions: Predicting recurrences after pulmonary vein isolation

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Introduction: Cryoablation is a safe and effective technique for pulmonary vein isolation (PVI). Delayed-enhanced cardiac magnetic resonance (DE-CMR) can detect scar and gaps after ablation. The aim was to characterize the scar and gaps of prior ablation lesions on DE-CMR after cryoablation, as well as evaluate the differences between patients with and without AF recurrence.
Methods: Sixteen patients (54±10 years, 13 paroxysmal AF, 9 with AF recurrence) referred for PVI with cryoballoon were included. A post-procedural DE-CMR was performed after 7.2±4.1 months. The endocardium and epicardium of the left atrium (LA) were manually segmented on axial plane slices. A 3D volume-rendered LA reconstruction was created using the segmented DE-CMR data. A pixel signal intensity map was projected on the 3D reconstruction and color-coded to display healthy areas and scar. The gap size was defined as the proportion (%) between the gap length and the total perimeter of the PV antrum. A ROC curve analysis was performed to determine the optimal cut-off value of gap size to predict recurrences.
Results: A total of 64 PV were analyzed. There were no differences in the number of cryoballoon applications or occlusion grade between patients with and without recurrences. All patients had gaps ≥1 PV and 12 patients had gaps in all PVs. Compared to patients without recurrences, the patients with recurrences had gaps in all PVs more often (43% vs. 100%, p=0.019) and of bigger size (29% vs. 51%, p=0.03). The cut-off of gap size to predict recurrences was 45% (Se 67%, Sp 86%; AUC 0.93).
Conclusion: Anatomic gaps around PVs detected by DE-CMR were common after AF cryoablation. Patients with AF recurrence had more gaps and of bigger size than patients without recurrence.

P3351 | BEDSIDE
A new intellatip MiFi XP ablation catheter can facilitate a pacing study for cardiac tachyarrhythmias

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Purpose: A pacing study for cardiac tachyarrhythmias may sometimes be challenging because of a high pacing threshold (PT) and long saturation artifact duration (SAD) after entrainment pacing. A new IntellaTip MiFi XP ablation catheter (MiFi) with three diagnostic mini electrodes (MEs) embedded to the distal tip electrode has recently been approved by the FDA. The purpose of this study was to investigate usefulness of the MiFi during a pacing study for cardiac tachyarrhythmias.
Methods: The MiFi was tested in 14 consecutive patients who underwent catheter ablation of cavo-tricuspid isthmus (CTI) dependent atrial flutter (AFL). Entrainment pacing was performed from the MiFi positioned at the CTI with a cycle length of AFL cycle length – 20ms and an output of 10mA/2ms and 5mA/2ms in bipolar pair configurations as follows: ABL 1-2 (tip to first ring electrode/conventional bipole) and ME 1-2 (ME 1 to ME 2). The SAD after entrainment pacing and PT at the CTI were measured.
Results: The SAD after entrainment pacing was significantly shorter in the ME 1-2 than the ABL 1-2 (10mA/2ms; 211±22ms vs. 521±99ms, p<0.05, 5mA/2ms; 178±18ms vs. 344±20ms, p<0.05). As the result, the local atrial electrograms recorded immediately after the cessation of the entrainment pacing with an output of 10mA/2ms was constantly appreciated for measurement of a post pacing interval with the ME 1-2 whereas it was never appreciated with the ABL 1-2. The pacing threshold of the ME 1-2, ME 2-3, and ME 3-1 was significantly smaller than that of the ABL 1-2 (p<0.05, respectively) (Fig. 1).

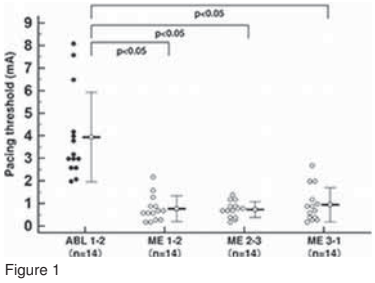

Figure 1

Conclusion: The MEs could reduce the SAD after entrainment pacing and PT at the CTI. These findings suggested that the MiFi could facilitate a pacing study for cardiac tachyarrhythmias.

ELECTROPHYSIOLOGY – DIAGNOSING

P3353 | BEDSIDE
Prolonged PR interval reflects advanced electroanatomical remodeling of left atrium and predicts the clinical outcome after catheter ablation of atrial fibrillation

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Background: Prolonged PR interval (PRI) has been known to be a poor prognostic factor in cardiovascular disease. We hypothesized that PRI is associated with electroanatomical remodeling of left atrium (LA) and predicts the clinical outcome of radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF).
Methods: We prospectively included 930 patients with AF (75.2% male, 57.6±11.2years old, 68.2% paroxysmal AF) who underwent RFCA. All enrolled patients were categorized into 4 groups based on the quartile values of pre-procedural PRI (166, 182, 202ms) in sinus rhythm, and were analyzed according to LA volume (CT), LA voltage (NavX), and clinical outcome of AF ablation.
Results: 1. Based on quartile value, group 4 (PRI≥202ms) was oldest ($p<0.001$), and most likely to have persistent AF ($p<0.001$), hypertension ($p=0.002$), and the highest body mass index ($p=0.034$) compared with other groups. 2. Group 4 had the greatest LA dimension ($p<0.001$) and volume index ($p<0.001$), and the lowest LA appendage emptying velocity ($p<0.005$) and LA voltage ($p<0.001$) compared with the others. 3. For mean 13.1±8.1 months, the classification based on PR interval was an independent predictor for AF recurrence after RFCA for AF, though adjusting other contributing factors (HR=1.699, 95% CI 1.279-2.257, $p<0.001$).

Baseline characteristics

	Q1 (~166)	Q2 (166–182)	Q3 (182–202)	Q4 (202–)	p
n=930	224	216	256	234	
Age (years)	55.5±11.7	57.3±11.0	57.6±11.3	60.3±10.4	<0.001
Paroxysmal AF (%)	78.1	77.8	68.8	51.7	<0.001
BMI (kg/m^2)	24.6±2.7	24.5±3.7	25.1±3.0	25.2±2.9	0.034
$CHADS_2$ score	0.8±1.0	0.9±1.1	1.1±1.1	1.0±1.1	0.051
Hypertension (%)	36.0	49.1	50.4	52.3	0.002
LA dimension (mm)	40.0±5.7	40.5±6.0	42.1±6.3	43.4±6.2	<0.001
LA volume index (ml/m^2)	32.7±11.8	33.2±12.2	35.8±12.7	38.9±11.6	<0.001
LAA emptying velocity (cm/s)	54.4±23.1	51.0±22.5	49.0±22.1	44.4±20.1	0.005
LA volume/BSA (ml/m^2; CT)	74.7±22.7	77.5±24.7	82.6±24.2	91.2±24.4	<0.001
Mean LA voltage (mV)	1.4±0.7	1.2±0.6	1.2±0.7	1.0±0.6	<0.001

Clinical characteristics and LA remodeling.

Conclusions: Prolonged PRI was closely associated with advanced LA remodeling by AF, and had a non-invasive independent predictive value on clinical recurrence of AF after RFCA.

P3354 | BEDSIDE
Prediction of the macroreentrant circuit of atrial flutter using the synthesized 18-lead ecg

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Purpose: The synthesized 18-lead ECG is well known and accepted as a detector of left ventricular posterior wall ischemia. However, it is unknown whether it is useful for determining local electrical activity. Therefore, we attempted to verify whether the synthesized 18-lead ECG was a useful diagnostic tool for atrial flutter (AFL).
Method: We retrospectively reviewed 150 consecutive patients with AFL recorded by the synthesized 18-lead ECG. We evaluated their ECGs for the presence of an F-wave morphology. The type of the macroreentrant circuit was revealed by an electrophysiologic study (EPS). During the EPS, multipolar catheters were used to record the activation. In some recurrence cases after pulmonary vein isolation for paroxysmal atrial fibrillation, a CARTO electroanatomical system was used to define the macroreentrant circuit.
Results: A total of 119 (79.3%) patients were diagnosed with typical AFL and 27 (18%) with reverse typical AFL by their EPSs. The CARTO activation revealed that 3 (2%) AFL circuits passed through the mitral isthmus and 1 (0.6%) involved the left atrial roof.
Figure 1 shows an AFL macroreentrant circuit algorithm for predicting the type of AFL circuit according to the F-wave morphology. A left atrial roof dependent circuit could showed isoelectric or negative F-waves in leadI. 27 reverse typical AFL had positive F-waves in lead I, and negative F-waves in leads V3R-V5R. 3 AFL circuits passing through the mitral isthmus exhibited positive F-waves in lead I, negative F-waves in leads V3R-V5R and isoelectric or negative F-waves in leads V7-9. A total of 119 typical AFL had positive F-waves in lead I, negative F-waves in leads V3R-V5R and positive F-wave in leads V7-9.
Conclusions: The synthesized 18-lead ECG could predict the macroreentrant circuit of AFL.

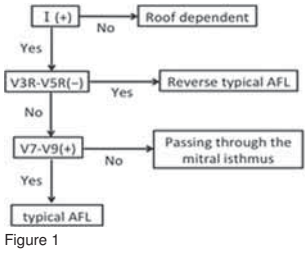

Figure 1

P3355 | BEDSIDE
The difference in the waveforms during pacemapping at subdivided portions within the outflow tract: The usefulness of synthesized 18-lead electrocardiograms

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Introduction: There have been many reports about the electrocardiography (ECG) characteristics of idiopathic outflow tract ventricular arrhythmias (OT-VAs). However, the OT-VAs origins were decided depending on the successful radiofrequency catheter ablation (RFCA) sites in those studies. Therefore, the overlap of the parameter values among the different origins was not so small because of inaccurate locating of the origins. This study aimed to evaluate the synthesized 18-lead ECG derived from the 12-lead ECG that provided the right-sided chest lead [V5R, V4R, V3R] and back lead [V7, V8, V9] virtual waveforms for differentiating the OT-VAs origins using pacemapping.
Methods and results: Twenty-eight patients with OT-VAs who underwent RFCA were included in this study. In each patient, several sites out of the 5 different sites were paced at threshold: anterior and posterior right ventricular OT (RVOT-ant, RVOT-post), right and left coronary cusps (RCC, LCC), and the junction of these cusps (RLJ). The pacing sites were confirmed by CARTOSOUND and fluoroscopy. The 18-lead ECGs during pacemapping were compared among 5 sites. The dominant QRS morphology pattern in the V5R significantly differed among these sites (see table).

QRS in V5R and OT-VAs origins

QRS in V5R	RVOT-ant n=19	RVOT-post n=19	RCC n=18	RLJ n=17	LCC n=14
Rs	12 (63%)	2 (11%)	0 (0%)	0 (0%)	0 (0%)
rS	2 (18%)	11 (58%)	0 (0%)	0 (0%)	0 (0%)
QS	0 (0%)	5 (26%)	15 (83%)	0 (0%)	0 (0%)
qR	0 (0%)	0 (0%)	2 (11%)	15 (88%)	0 (0%)
R	5 (26%)	1 (5%)	1 (6%)	2 (12%)	14 (100%)

	Sensitivity	Specificity	PPV	NPV	p
"Rs" for predicting RVOT-ant	63%	97%	86%	90%	<0.001
"rS" for predicting RVOT-post	58%	97%	85%	89%	<0.001
"QS" for predicting RCC	83%	93%	75%	96%	<0.001
"qR" for predicting RLJ	88%	97%	88%	97%	<0.001
"R" for predicting LCC	100%	88%	61%	100%	<0.001

Conclusion: The QRS morphology pattern in V5R was simple parameter and useful for differentiating the detailed OT-VA origin sites.

P3356 | BEDSIDE
Impact of prophylactic catheter ablation for total cavo-pulmonary connection candidates upon arrhythmias and hemodynamics: consideration for the roles of twin atrioventricular nodal physiology

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Background: Twin atriovetricular nodes (tAVNs) are sometimes associated with complex congenital heart disease such as heterotaxy syndrome and can be a cause of AV reentrant tachycardia (AVRT). Therefore, electrophysiological evaluation is important for total-cavo pulmonary connection (TCPC) candidates because catheter access to the atrium and AV valve is restricted after TCPC, and prophylactic catheter ablation (CA) is occasionally performed to inducible AVRT. On the other hand, few investigators have reported that ablating one of tAVNs might cause interventricular dyssynchrony and systemic ventricular dysfunction. The aim of this retrospective study is to investigate clinical results of prophylactic CA of unilateral AVN in TCPC candidates.
Methods: Electrophysiologic study was performed in 10 TCPC candidates (median age; 3 years) who had undergone Glenn operation and associated with common AV valve. Nine patients were heterotaxy syndrome (asplenia in 6 and polysplenia in 3). Spontaneous narrow QRS tachycardia had been demonstrated at the palliative operation and/or diagnostic catheterization in all patients.
Results: Two different QRS complexes without preexcitation were observed and two distinct His bundle electgrams were recorded at the anterior aspect and the posterior aspect of the common AV valve in all 10 patients. AVRT involiving tAVNs was also induced in all patients and then we decided to perform CA of unilateral AVN. Successful RFCA of one AVN which showed recessive anterograde conduction was achieved and no further AVRT was inducible in all cases. The QRS duration was 80ms (63-90ms) before CA and 85ms (68-95ms) after CA.The ventricular ejection fraction was 62% (55-68%) before CA and 60% (53-69%) after CA.

Conclusion: Prophylactic CA of unilateral AVN for TCPC candidates with inducible AVRT involving tAVNs may be one therapeutic option. Iatrogenic ventricular dyssynchrony after CA was never observed in our experience.

P3357 | BEDSIDE
Evaluation of an automatic delineation algorithm for activation mapping of focal ventricular tachycardias

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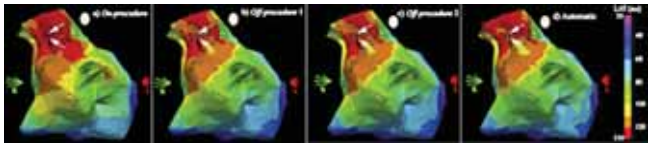
Purpose: Activation mapping (AM) based on electrogram (EGM) analysis is used to guide ablation treatments of focal tachycardias. However, AM based on EGM activation onset is a manual, observer-dependent and time-consuming task within the EP lab. We propose and evaluate an automatic EGM onset detection algorithm for AM.
Methods: Clinical data correspond to 8 patients (9 electroanatomical maps, a total of 1673 mapping points) admitted for ablation procedure due to non-tolerated premature ventricular contraction (PVC) beats. During the intervention, for each mapping point, a 2.5 s EGM segment was recorded including a PVC beat and the bipolar EGM activation onset was manually marked (on-procedure annotation). After the intervention, an automatic EGM activation onset algorithm was applied and electroanatomical maps were reconstructed using the automatically measured local activation times (LATs). Additionally, two different experts manually blind-annotated those maps after the intervention (off-procedure annotations).
Results: Consdering the average value of the two off-procedure annotation sets as the reference for evaluation, we measured the error (mean ± standard deviation) of LATs computation committed by the automatic algorithm. For comparison purposes, the error is also computed for the on-procedure annotations. The errors were, for automatic method: 2.1±10.9 ms, and for on-procedure annotations: -2.6±6.8 ms. The off-procedure inter-expert difference is -0.8±4.5 ms. The figure shows a representative example in RAO view obtained with the 4 sets of annotations.



Example of reconstructed activation maps

Conclusions: Automatic EGM activation onset detection during clinical routine allows an observer-independent, accurate estimate of LATs which could be extended to AM in high-density catheter configurations.

P3358 | BENCH
Substrate electroanatomical mapping to navigate surgical reconstruction of the left ventricle aneurysms in patients after myocardial infarction

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Introduction: Ischemic heart disease is one of the most common cause of ventricular tachyarrhythmias (VTA). Arrhythmogenic substrate is typically myocardial infarction (MI) scar. In patients with post MI aneurysm left ventricle remodeling surgery might be indicated. There is the evidence that aneurysmectomy itself usually cannot eliminate VTA. The purpose of this study was to evaluate the efficacy of the electroanatomical mapping (EAM) prior aneurysmectomy to identify the arhythmogenic areas and of the myocardium in order to help the surgeons to navigate resection and cryodestruction of the most critical areas of the myocardium.
Patients and method: 39 pts were included, Ø age 64 (38–79), 28 m/11 w, all with documented post MI aneurysms (Echo, MRi, LV angiography). In all pts we confirmed inducibility of VTA prior to surgery. Electroanatomical mapping (EAM) was performed with identification of border zones, specific late and fractionated potentials which we assigned by RF application. Surgeon used the predefined EAM to navigate the surgery to eliminated most of the arrhythogenic zones by resection of the aneurysm plus cryoablation. EAM with programmed ventricular stimulation was repeated 2-3 months after aneurysmectomy to evaluate the effect of the surgical procedure.
Results: In all 39 pts we created EAM as a guide for surgical LV remodeling plus cryo-destruction of the most important areas indicated by aplication of RF energy during previous catheter mapping procedure. Prior surgery VT was inducible in 26 pts (67%), after surgery we could induce VT in only 3 pts (7,6%). 1-2 months after surgery EAM was performed in 37 pts and in all we demonstrated significant change of the substrate including reduction of late and fractionated potentials.
Mean fluoro time per mapping procedure was 12,4 min and mean total time per one procedure was 109 min. Average of follow-up is 18.8 monts (4-34) with only 2 deaths due to noncardiac reasons.

Table 1

Pt	Before LVAR	After LVAR (1-3m)
n	39	39
Ø LV EF	27.8% (20-55)	45.6% (35-60)
Ø ESV	131.6 ml	95.5 ml
Ø NYHA	2.7	1.8

Conclusion: EAM reconstruction prior the aneurysmectomy could play important role: 1. navigate arrhythmic surgery; 2. performed adequate LV reconstruction; 3. specific substrate cryoablation; 4. reduction of VTA induction.

P3359 | BEDSIDE
Impact of the earliest activation site location in the septal right ventricular outflow tract in the differentiation of left vs right outflow tract origin of idiopathic ventricular tachycardia

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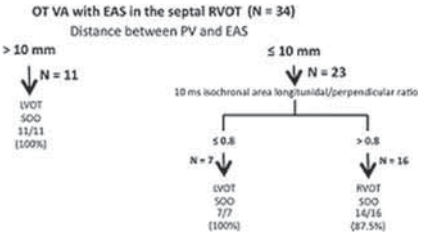
Introduction: We hypothesized that the earliest activation site (EAS) in the septal right ventricle (RV) outflow tract (OT) could be an additional mapping data predictor of the left vs right origin of idiopathic ventricular arrhythmias (VAs).
Methods: Electroanatomic maps obtained in 34 patients with OT VA (20 LVOT, 14 RVOT) with the location of the earliest activation site (EAS) during activation mapping in the septal RVOT were analysed. Pulmonary valve (PV) was defined by voltage scanning after validation of voltage tresholds by image integration against preprocedure CT scan or MRI. The distance between PV and the earliest activation site in the septal RVOT, 10 ms isochronal map area and longitudinal/perpendicular ratio were obtained in order to differentiate LVOT vs RVOT site of origin (SOO).
Results: A cut-off value of 1,9 V was able to accurately define PV level with a 90% sensitivity and 96% specificity. EAS≥1 cm below PV excluded RVOT SOO. Distance between PV and EAS was significantly shorter in VAs arising from left coronary cusp than in the rest of locations in LVOT (5.7±6.4 vs 9.2±7 mm; p 0.034). The 10 ms isochronal area longitudinal/perpendicular diameter ratio was higher in the RVOT than in LVOT SOO group (1.97±1.2 vs 0,79±0.49, respectively; p 0.001). A cut-off value of ≤0,8 predicted an LVOT SOO with 68% sensitivity and 100% specificity. An algorithm based on the EAS-PV distance and the 10 ms isochronal area longitudinal/perpendicular diameter ratio predicted a LVOT SOO with 90% sensitivity and 100% specificity.



Conclusion: RVOT SOO can be excluded in OT VAs with an EAS>10 mm below PV. An algorithm based on the EAS-PV distance and the 10-ms-isochronal-area longitudinal/perpendicular diameter ratio accurately predicts LVOT vs RVOT SOO in OT VAs.

P3360 | BEDSIDE
Prolongation of coupling interval is a predictor of delayed success of radiofrequency ablation for idiopathic ventricular arrhythmias

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Background: We have experienced delayed elimination of arrhythmias in the acute failure cases of radiofrequency catheter ablation (RFCA) for idiopathic ventricular arrhythmias (IVAs). However, a reliable RFCA endpoint has not been established in such cases.
Methods: We retrospectively investigated consecutive 195 patients who underwent RFCA for IVAs in our hospital from January 2009 to August 2012. Twenty-seven patients (14%) were the acute failure cases whose IVAs were not eliminated during RFCA procedure. However, it was observed that IVAs were disappeared completely late after RFCA in 9 of the acute failure cases. We divided the acute failure cases into two groups (late-success group and failure group) and evaluated the electrocardiographic parameters (QRS morphology of IVAs, sinus cycle length, coupling interval) before and after RFCA and electrophysiological characteristics during RFCA procedure (local activation time preceding QRS, pace mapping, occurrence of repetitive ventricular acceleration, the origin sites of IVAs, application energy and duration of RFCA) between two groups.
Results: In the late-success group, coupling interval (CI) of IVAs was significantly prolonged after RFCA (623±145 ms) compared with that in the baseline (451±90

ms, $p<0.05$), while it did not change in the failure group (491±139 vs. 489±110 [ms], NS). Prematurity Index (PI), which was defined as the ratio of CI of IVAs to the preceding R-R interval of the sinus cycle just before VAs in the electrocardiogram, was significantly greater in the late-success group than in the failure group after RFCA (0.83±0.09 vs. 0.66±0.14, $p<0.05$). The presence of IVA's QRS morphology change following RFCA also was significantly greater in the late success group than in the failure group (33% vs. 67%, $p<0.05$). No significant difference was observed in echocardiographic parameters, morphology at baseline (the origin sites of IVAs), local activation time, pace mapping score, occurrence of ventricular acceleration and total application energy.
Conclusion: Even in the cases that IVAs were not disappeared by RFCA procedure, delayed elimination of IVAs might be expected when the CI was prolonged.

P3361 | BEDSIDE
Electroanatomical substrate characteristics are associated with the cycle length of spontaneous ventricular tachycardia after myocardial infarction

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Introduction: Electroanatomical (EA) scar after myocardial infarction (MI) has been associated with the occurrence of spontaneous sustained monomorphic VT (SMVT). Specific EA scar characteristics may determine cycle length (CL) of clinical and induced VT in post-MI patients.
Methods: Consecutive post-MI pts referred for symptomatic ventricular arrhythmia ablation underwent programmed electrical stimulation and left ventricular EA mapping during sinus rhythm (n=82) or ventricular pacing (n=11). Bipolar electrograms (EG) were displayed (0.13mV, 200mm/sec) and evaluated for voltage (BV), duration (EGD, first to last sharp peak deflection) and morphological characteristics (presence/duration of fragmented signals [FS: BV<1.5 mV, EGD ≥50ms], presence/timing of late potentials [LP: onset after QRS, separation >20 ms]. The scar area (SA, BV<1.5mV), dense scar (DS, BV<0.5mV) and border zone (BZ, BV >0.5mV,<1.5mV) were measured.
Results: Ninety-three pts (68±10 yrs, 83 male, LVEF 34±12%) referred for ablation of VA (clinically documented SMVT in 83 [max CL 386±84ms, min CL 369±85ms]) were included. In 85 (91%) pts, 3.5±2.5 VT/pt (max CL 402±116 ms, min CL 292±79ms) were induced. LPs were present in 75% of pts (max duration from offset QRS: 98±55 ms (LPmax)) and FS in all (max duration 126±36 ms (FSmax)). Mean SA was 68±39 cm^2, DS 31±29 cm^2 and BZ 37±21 cm^2. For clinical VTs, the total scar area, percentage of DS of the total SA, LPmax and FSmax were related to the max VTCL (all $p<0.002$) and min VTCL (all $p<0.001$). Compared to pts with slow clinical VTs (VTCL≥300ms), pts with only fast clinical VTs had smaller SA ($p=0.003$), lower percentage of DS ($p<0.0001$), shorter FSmax ($p=0.021$) and LPmax ($p=0.006$). For induced VTs, substrate characteristics also correlated with max VTCL (all $p<0.001$) but not with the CL of the fastest induced VT (all $p\geq0.071$).
Conclusions: Specific EA scar characteristics are associated with the CL of spontaneous VTs. No specific substrate could be identified for fast non-clinical induced VTs. These findings may have implications for substrate-based VT ablation in post-MI patients.

P3362 | BEDSIDE
Para-hisian pacing enables assessment of left bundle branch conduction and left ventricular myocardial conduction even in cases with complete right bundle branch block

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Background: We recently found that bundle branch conduction and ventricular myocardial conduction can be separately assessed by para-Hisian pacing in cases without bundle branch blocks (ESC2013).
Purposes: We examined if para-Hisian pacing (PHP) test is usable for assessments of left bundle branch conduction and left ventricular (LV) myocardial conduction regardless presence or absence of complete right bundle branch block (CRBBB).
Methods: We analyzed 164 consecutive patients (52.8±7.1 years old, 59.8% male) who underwent PHP test in electrophysiological examinations for arrhythmias. PHP test was conducted according to the original method reported by Hirao, et al. To record ventricular potentials in right ventricular (RV) apex and basal lateral LV region, electrode catheters were located at RV apex and in the coronary sinus. We placed a pacing catheter at a locus where high output stimulation induced narrow QRS and then gradually reduced pacing output until QRS widened. Under high output stimulation leading to narrow QRS, a time interval from stimulation to RV apex potential (Sn-RVA) and an interval from stimulation to basal lateral LV region (Sn-BLLV) potential were determined as an index of right bundle branch conduction and that of left bundle branch conduction, respectively. Under low output stimulation leading to wide QRS, a time interval from stimulation to RV apex potential (Sw-RVA) and an interval from stimulation to basal lateral LV potential (Sw-BLLV) were determined as an index of septal ventricular myocardial conduction and that of LV myocardial conduction, respectively.
Results: In 158 of 164 patients (96.3%), all of four parameters could be measured: Sn-RVA (57.1±14.1 ms), Sn-BLLV (88.5±21.0 ms), Sw-RVA (68.5±18.3 ms), and Sw-BLLV (111.9±23.9 ms). Sn-RVA was significantly longer In CRBBB group (n=19) than in non-CRBBB group (n=139) (65.8±14.3 ms vs. 55.9±13.8 ms, $p=0.004$), confirming that Sn-RVA reflect right bundle branch conduction, though Sw-RVA was similar in the two groups (72.4±14.2 ms vs. 68.0±18.8 ms, $p=0.323$). In contrast to the indices of RV conduction, both Sn-BLLV (97.0±23.5 ms vs. 87.3±20.4 ms, $p=0.059$) and Sw-BLLV (117.3±20.8 ms vs. 111.2±24.2 ms, $p=0.296$) were comparable in the CRBBB and non-CRBBB groups. In CRBBB group, Sn-RVA was not significantly correalted with Sn-BLLV or Sw-BLLV, indicating lack of significant influence of CRBBB on the indices of LV conduction.
Conclusion: PHP test enables separate assessment of left bundle branch conduction and LV myocardial conduction even in the presence of CRBBB.

NON-INVASIVE DIAGNOSIS I

P3364 | BEDSIDE
Arrhythmic storm in patients with Heart Mate II. Incidence, risk factors and management

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Background: – Rhythmic complications seem common after left ventricular (LV) assist device (LVAD), especially in the early phase of implantation (<30 days), which can worsen the prognosis. We sought to identify the incidence and risk factors of arrhythmic storm occuring after Heart Mate® 2 (HM2) implantation.
Methods: – All patients with HM2 implanted in our institution have been studied. Clinical data, occurrence of arrythmia, implantable cardioverter-defibrillator (ICD), ultrasound parameters as well as follow-up have been analyzed.
Results: – From January 2008 to April 2013, 33 patients (30 men, 58±10 years, LV Ejection Fraction 20±5%, ischaemic cardiomyopathy 82%, 70% bridge to transplant), were included. Before implantation, 15 had ICD (12 for primary prévention) and 11 had a history of sustained ventricular tachycardia (VT). The overall mortality rate was 48% with a mean follow-up of 11±11 months. Post-LVAD arrhythmic storm (10 patients, including 9 in the first 30 days) were more frequent in patients with prior VT (70% vs 17%, $p<0.01$), prior ICD (80% vs 30%, $p=0.01$), larger LV end diastolic diameter (77±9 vs 67±6 mm, $p=0.02$) and non ischaemic cardiomyopathy (40 vs 8.4%, $p=0.053$). Arrhythmic storm occuring just prior LVAD implantation (8 patients) was not associated with arrhythmic storm recurrence after. Betablocker initiation post-LVAD was carried out within the first month for only 4 patients. Endocardial VT ablation was performed in 6. The substrate was not related to HM2 cannula.
Conclusion: – Arrhythmic storm were frequent (33.3%) after Heart Mate® 2 implantation, often occurring within one month in patients with prior VT episode.

P3365 | BENCH
Determining the origin of the ectopic beat in idiopathic ventricular arrhythmias with a computational model

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Purpose: Idiopathic arrhythmias require long procedures to acquire invasive electro-anatomical maps and ascertain the right ventricular (RV) or left ventricular (LV) origin of the ectopic beat. A recent study suggests a correlation between the shape of the activation-map isochrones in the RV outflow tract (RVOT) and the origin of the ectopic beat. We propose to study and validate this relationship with a computational model.
Material and methods: A detailed anatomical model of the LV and RV including the outflow tracts was built from a magnetic resonance image of a patient. A finite element mesh was then generated where myofibre architecture was synthetically introduced. Electrophysiological simulations were performed for 150ms after the ectopic beat. Four different origins of ectopic beats were analysed: the left (LV-LAC), non-coronary (LV-NCAC) and right (LV-RAC) aortic cusps; and the middle of the RVOT. A post-processing step was implemented to derive 20ms-isochrones around the earliest activated area in the RVOT and their shape was characterized (area, axis ratio computed as the maximum over minimum diameters of the isochrones).
Results: The axis ratio and area indices characterizing the 20ms-isochrones for

Figure 1. Simulations with different origins.

the four different configurations were: 2.43 and 2.25 cm^2 for LV-LAC; 1.74 and 2.55 cm^2 for LV-NCAC; 1.16 and 2.95 cm^2 for LV-RAC; 2.59 and 1.18 cm^2 for RVOT origin. The earliest activated area in the RVOT appeared 100 ms, 150 ms, 70 ms and 3 ms after the ectopic beat for LV-LAC, LV-NCAC, LV-RAC and RVOT, respectively.
Conclusions: The developed computational model reproduces the electrical activation patterns observed in clinical data, clearly identifying larger isochronal areas and smaller axis ratios with LVOT rather than RVOT origin of the ectopic beat.

P3366 | BEDSIDE
Predictors and implications of mechanical trauma of the left bundle branch during ventricular tachycardia mapping in patients with structural heart disease

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Aims: Ablation of ventricular tachycardia (VT) in patients with structural heart disease (SHD) may be limited by the risk of significant complications. Tamponade, systemic embolism, and damage to the His-Purkinje system by radiofrequency application are among the most relevant. However, the incidence, predictors and consequences of mechanical trauma of the left bundle branch (MT-LBBB) at SHD-VT ablation have never been reported.
Methods: The incidence of MT-LBBB was studied in a series of 142 consecutive patients with SHD and sustained monomorphic VT, who underwent 184 ablation procedures. 31 patients were excluded because showed left bundle branch block/ left intraventricular conduction defect (LBBB) with a QRS>150 ms at baseline. Another 6 patients were excluded because they had right ventricular dysplasia and no catheter was introduced in the left ventricle (LV). MT-LBBB was defined as new onset of LBBB during catheter manipulation within the left ventricle, which was not related to radiofrequency application and which persisted at the end of the procedure. The clinical predictors for MT-LBBB were compared between patients developing it and the last 31 patients enrolled in the whole series.
Results: MT-LBBB developed in 7 patients (6.7%). The age, sex, type of SHD, scar location, QRS duration, and HV interval were not significantly different between patients with and without MT-LBBB. A combine variable of presence of LV ejection fraction <35% and QRS duration 110> ms was significantly more frequent in patients with MT-LBBB than is those without it (40% vs 8.7%, P=0.03). At follow-up, MT-LBBB was transient and solved in <24 hours after the procedure in 1 patient. One patient had persistent complete AV block (preexisting RBBB before ablation) and had a cardiac resynchronization therapy (CRT) defibrillator implanted. 5 patients developed heart failure refractory to pharmacological therapy and required implantation of a CRT device.
Conclusions: MT-LBBB during LV ablation catheter manipulation in patients with SHD is infrequent but often results in significant clinical implications. The combination of a wider QRS complex and severe LV dysfunction appears a risk factor for it.

P3367 | BEDSIDE
Qt interval characteristics in patients with early repolarization and brugada syndromes: insight into an overlapping mechanism of lethal arrhythmias

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Purpose: We have reported impaired QT-rate dependent in early repolarization syndrome (ERS). Recent epidemiological data reported peak incidence of sudden cardiac death (SCD) in ERS and Brugada syndrome (BrS) from 0-6 AM. Taken together we tested the QT-interval characteristics in both syndromes.
Methods: Ambulatory ECG-derived parameters (QT, QTc, and QT/RR slope) were measured in a total of 122 subjects including: 11 ERS, 11 BrS patients, the majority of whom are survivors of an aborted SCD, and 100 controls.
Results: There was no significant difference in the average QT or QTc; however, the 24-hour QT/RR slope was significantly smaller in ERS and BrS patients than in the controls (Table).

QT indices in the study population

	ERS (n=11)	BrS (n=11)	Control (n=100)	P
Age	51.2±12	49.6±13	48.6±18	0.365
HR (beat/min)	57.4±7.9	67.7±6.5	67.5±10.2	0.111
24-hour QT (ms)	413±29	388.9±21	399.8±29	0.209
24-hour QTc (ms)	405.5±26.5	411.6±18	420.5±23	0.609
24-hour QT/RR	0.103±0.01¶¶	0.106±0.01‡	0.156±0.03	<0.001
Day-time QT	392±22	375±27	381±29	0.306
Night QT	415±28	399±21	418±26	0.154
QT day-night difference	19±18.7¶	24±14**	40±22	0.007
Early night QT/RR	0.1±0.03	0.125±0.04	0.153±0.04	0.068
Mid night QT/RR	0.076±0.02¶	0.092±0.04*	0.117±0.04	0.004
Early morning QT/RR	0.074±0.03¶¶	0.079±0.02‡	0.118±0.04	<0.001

Values are expressed as mean ± SD. P values refer to the total significance of differences (ANOVA) among the 3 groups. ¶¶P<0.001, ¶P<0.01: ERS vs Control ‡P<0.001, **P<0.01, *P<0.05: BrS vs Control.

Detailed QT analysis showed lower day-night QT difference in ERS and BrS patients than in the controls, with the lowest QT/RR slopes seen in the ERS and BrS groups from 0-3:00AM and from 3-6AM.
Conclusions: (1) In contrast to age and gender-matched control subjects, ERS and BrS patients had atatenuated QT-rate adaptation and blunted QT day-night modulation which may provide a baseline reentrant substrate and facilitate phase 2 reentry. (2) Importantly, QT/RR maladaptation was most evident at midnight, which may explain their propensity toward SCD during such critical period.

P3368 | BEDSIDE
Differentiating the origin of outflow tract ventricular arrhythmia using a simple novel approach

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Aim: To assess a simple criterion for localization of outflow tract ventricular arrhythmias during electrophysiology study.
Background: Numerous ECG criteria have been proposed for identifying the localization of outflow tract ventricular arrhythmias. However, in some cases it is difficult to accurately localize the origin of outflow tract arrhythmia using the surface ECG.
Method: We measured the interval from the onset of the earliest QRS complex of premature ventricular contractions (PVCs) to the distal right ventricular apical signal (QRS-RVA interval) in 66 patients (31 male, age 53.3±14.4, RVOT origin 37) referred for ablation of symptomatic outflow tract PVCs.
Results: There was no difference in QRS duration of PVCs, arising from the right (RVOT) and the left (LVOT) outflow tracts (141.7±15.9 vs. 137.0±15.3, p=0.25). Compared to patients with RVOT-PVCs, the QRS-RVA interval was significantly longer in patients with LVOT-PVCs (69.8±13.9 vs. 33.4±10.4, p<0.001). Receiver operating characteristic analysis showed that a QRS-RVA interval ≥49 ms has a sensitivity, specificity, positive and negative predictive values of 100%, 95%, 94%, 100% respectively, for prediction of an LVOT origin.
Conclusion: A QRS-RVA interval ≥49 ms suggests an LVOT origin. The QRS-RVA interval is a simple and accurate criterion for differentiating the origin of outflow tract arrhythmia during EPS.

P3369

P3370 | BEDSIDE

Value of cardiac magnetic resonance imaging to predict the occurrence of ventricular tachycardia in post-infarct patients

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Introduction: The use of implantable cardioverter-defibrillators (ICD) is recommended to prevent sudden cardiac death (SCD) in patients with a reduced (≤30-35%) left ventricular ejection fraction (LVEF) due to previous myocardial infarction (MI). Many of these patients, however, never receive adequate ICD intervention during the lifespan of their index ICD. We studied whether the characteristics of MI scar, as assessed by magnetic resonance imaging (MRI), could predict the occurrence of ventricular tachycardia (VT) after ICD implantation.
Methods: Fifty-one patients (41 men, mean age=59±11 years) with a remote (>6 months) MI and a class I primary prevention indication for ICD implantation underwent a cardiac MRI study 3 to 6 days before ICD implantation. Delayed contrast enhancement (DCE) was used to delineate post-MI scars.
Results: Mean follow-up duration was 43±24 months (range: 12-91 months) after ICD implantation. VT episodes occurred in 15 patients (29%). There were no statistical differences between patients who experienced VT and those who did not with regard to the following parameters: age at implant, gender, infarct location, history of coronary artery revascularization, LVEF, left ventricular (LV) end-diastolic volume, LV mass, MI volume and MI surface. At infarct borders, MRI showed areas with intramural and/or epicardial scar (adjacent to areas showing endocardial or transmural scar) in all but one patient. Epicardial scar volume (2±1.2 vs. 0.9±1.0 cm^3; p=0.001), epicardial scar surface (3.6±0.5 vs. 1.4±0.3 cm^2; p=0.0005) as well as intramural scar volume (1.7±1.7 vs. 0.8±1.2 cm^3; p=0.03) and intramural scar surface (4.0±0.6 vs. 1.8±0.4 cm^2; p=0.002) were greater in patients with VT. A cut-off value >1.6cm^2 for intramural scar had a 100% sensitivity to predict the occurrence of VT.
Conclusion: Our study suggests that the presence of a critical volume (and surface) of both intramural and epicardial scars at an infarct border are key factors for the occurrence of VT in post-MI patients.

P3371 | BEDSIDE

A clinical score to evaluate the survival and recurrence risk in patients undergoing ventricular tachycardia ablation

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Aim: To assess the value of a decision rule based on several prognostic factors for overall survival and ventricular tachycardia (VT) recurrence-free survival, in a sample of patients with structural heart disease. The final goal is to identify high risk patients who might require specific pre-procedure care to reduce the risk of subsequent procedure-related morbidity.
Methods: Prognostic factors data, including demographic, clinical and treatment related data were collected for 282 patients. The Survival Tree (ST) method is a tree-structured survival analysis based on a recursive partitioning algorithm. Kaplan-Meier survival curves were obtained for sensible groupings of patients derived from ST. Cox regression was applied to evaluate differences among groups.
Results: LVEF, aetiology (ISCHEMIC vs NON-ISCHEMIC), amiodarone use (AMD) and hypertension (HTN) were identified by the ST method as best predictors of a VT recurrence. Thyroid disfunction (THYROID), age >60 years, chronic kidney disease (RENAL), respiratory disease (RD), number of coronary artery vessels disease (CVN), were identified by the ST method as the best predictor of DEATH events. Three groups were identified based on Hazard Ratio; these groups showed significantly different survival rates. In HIGH risk groups 58.8% patients survived and 24.4% were free from VT recurrence at 24 months; in MEDIUM and LOW risk groups 86.0% and 94.9% patients respectively survived, 66.3% and 83.6% were free from VT recurrence at 24 months.

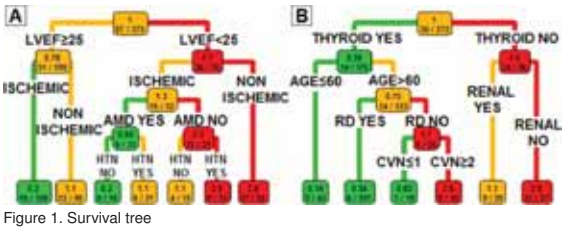

Figure 1. Survival tree

Conclusion: Survival tree analysis provided a preoperative assessment of the arrhythmia recurrence and survival in patients undergoing VT ablation. We found that LVEF and THYROID DISFUNCTION were the most important determining factors for prediction of VT recurrence and survival respectively.

P3372 | BEDSIDE

Multimodal method of estimating distinctions of the immune response among patients with ventricular premature beats with structurally normal heart and healthy volunteers

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Introduction: 30% of patients with cardiac arrhythmias show no signs of any organic heart disease. One of the possible causes of idiopathic arrhythmias is considered to be inflammatory heart disease, including those of autoimmune nature.
Materials and methods: The research studied 91 patients (27 men, mean age 36,53±11,49 years) with VPB more than II grading Lown without signs of organic heart disease. The control group comprised 31 healthy volunteers. In addition to standard clinical examination, a study of NT-pro-BNP, cellular and humoral immune parameters, markers of infections, levels of autoantibodies to synthesized peptide sequences simulating different parts of β1-adrenoceptors (β25, β8) and M2-cholinoreceptor (MRIMRIV, MRI) were completed.
Results: In patients with VPB levels of NT-pro-BNP were 2 times higher than in the control group (p<0,001). Individuals with VPB had significantly higher levels of CD3+CD95+, CD3+HLA-DR+ than in control group. CD19+ indexes were higher among healthy individuals (p=0.007). In the study of autoimmune response IgM titers to β25, MRIMRIV, MRI were significantly higher in patients with VPB than in the control group. Based on these results, a model of a combination of parameters associated with the development VPB (NT-pro-BNP, CD3+CD95+, phagocytic activity of neutrophils, CD19+, β25 IgM) was rated. To estimate the total contribution of the theese parameters in the development of VPB XBDS parameter was introduced and designed which formed its range of values (Fig. 1).

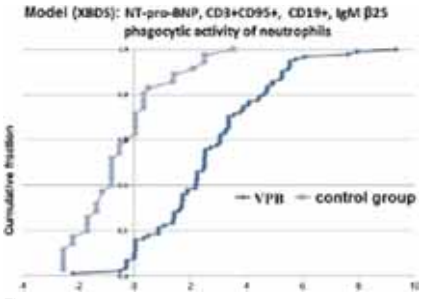

Figure 1

Conclusion: The study demonstrated that patients with VPB were significantly different from the control group not only in individual indicators of immune response, but also in their combination, which in turn may also indicate the presence of immunopathological process in the myocardium.

P3373 | BEDSIDE

Differential diagnosis between early/minor arrhythmogenic right ventricular cardiomyopathy and idiopathic right ventricular outflow tract tachycardia based on ectopic beats QRS morphology

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Background: In patients with ventricular arrhythmias showing a left bundle branch block/inferior axis morphology, the differential diagnosis between idiopathic right ventricular outflow track tachycardia (RVOT-VT) and arrhythmogenic right ventricular cardiomyopathy (ARVC) may be challenging. In particular, patients with early/minor ARVC phenotypic expression may show a normal electrocardiogram (ECG) and minimal echocardiographic abnormalities. We aimed to assess whether specific features of the ventricular ectopic beats QRS morphology may differentiate between the two conditions.
Methods: The study population included 20 patients (13 females, mean age 36 years) with early/minor ARVC defined as the absence of major ECG or echocardiographic abnormalities according to the 2010 International Task Force Criteria and 33 age- and sex- matched RVOT patients. The diagnostic accuracy of several morphologic features of the ectopic beats, suggesting different origin within the RVOT (septum versus free wall and epicardium versus endocardium), was evaluated.
Results: We identified 5 features of the QRS morphology of the ventricular ectopic beats that were significantly more common in ARVC than in RVOT-VT patients: QRS duration >160ms (60% vs 27%, p=0.02), intrinsecoid deviation >80ms (65% vs 24%, p=0.01), initial QRS slurring (40% vs 12%, p=0.04), QS pattern in lead V1 (90% vs 36%, p90° in limb leads (60% vs 24%, p=0.01). At multivariate analysis, intrinsecoid deviation >80ms (OR=9.9), QS lead in lead V1 (OR=28) and QRS axis >90% (OR=5.7) remained independent predictors of ARVC diagnosis. The presence of 1, 2 and 3 parameters yielded a sensitivity of 95%, 90% and 55% and a specificity of 60%, 70% and 94% for ARVC diagnosis.

Conclusions: In patients with arrhythmias of RVOT origin and no major electrocardiographic or echocardiographic abnormalities, a simple evaluation of the ectopic QRS morphology helps in the differential diagnosis between idiopathic RVOT-VT and early/minor ARVC.

SUPRAVENTRICULAR ARRHYTHMIAS

P3375 | BEDSIDE
The importance of waiting time after achieving bidirectional block of the cavotricuspid isthmus in patients with typical atrial flutter

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Introduction: Cavotricuspid isthmus (CTI) ablation is the most effective treatment strategy for patients (pts) with typical atrial flutter, and an acute success rate of up to 100% is reached when an irrigated catheter and a pre-shaped angled sheath are used. However, arrhythmia recurrence is sometimes seen. Therefore, longer waiting times might increase long term success rate.
Methods: Consecutive pts undergoing radiofrequency (RF) catheter ablation for ongoing or documented typical flutter were included. In order to optimize contact force, a 180° angulated sheath (Fast-Cath RAMP, Saint Jude Medical) was used together with an irrigated ablation catheter (Celsius ThermoCool, F-Type, Biosense Webster, 50W, 48°C, 17ml/min) in all pts. Multipolar catheters along the right atrial wall, in the proximal coronary sinus, and at the His, as well as a 3D navigation system (LocaLisa, Medtronic) were routinely employed. Success was defined by termination and/or change in the activation sequence of the lateral wall as well as demonstration of bidirectional conduction block (defined as widely split double potentials across the length of the line and using differential pacing). A waiting time of at least 20 minutes was observed in each procedure.
Results: After 27 (19, 36) and 6 (4, 9) min of procedure (since catheter insertion) and RF time, acute success was achieved in all 91 pts [70 (62, 75) years, 62 (68%) male]. During the waiting time, recurrence of CTI-conduction was observed in 22 (24%) pts 53 (16, 610) sec after achievement of bidirectional block. In addition, recovery of conduction was observed once, twice and 3 times, in 18, 3, and 1 pts, respectively. Furthermore, recurrence was observed within 5 min after success in 15 (68%) pts, 6 - 10 min in 2 (9%) pts, and 11 - 20 min in 5 (23%) pts. After recovery of conduction, a slightly longer waiting time was observed, and this accounts for a total procedural and waiting time of 70 (61, 85) and 29 (26, 33) min, respectively. No acute complications occurred.
Conclusions: In pts undergoing CTI ablation, despite the use of an angulated sheath, an irrigated ablation catheter and 3D mapping, recovery of conduction can occur. Almost 25% of the recurrences are seen $>$10 min after achievement of bidirectional block. Therefore, adopting a relatively long waiting time of $\geq$20min may increase long-term success rate.

P3376 | BEDSIDE
PSVT in patients with short PR syndrome - lateral and/or decremental rather than atria-fascicular pathways

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Background: Atrio-fascicular accessory pathways (AP) are presumed to be the cause of short PR syndrome without pre-excitation (Lown-Ganong-Levine), which supposedly is a rare cause of paroxysmal supraventricular tachycardia (PSVT).
Aims: To identify ECG, EP and anatomical characteristics of APs in patients with short PR and without overt pre-excitation presenting with PSVT.
Methods: We retrospectively analyzed 200 patients with orthodromic atrioventricular reentrant tachycardia (ortoAVRT) without documented pre-excitation. In only 14 of them baseline PR interval was short i.e. 120 ms (mean age 27 5 years, 9 men).
Results: During sinus rhythm (SR) there were taller than expected r waves in leads V1-3 in 10 out of 14 patients. In all 14 patients QRS during during ortoAVRT was narrower than in sinus rhythm (8010 ms vs 9510 ms, $p<0.05$). In 10 out of 14 patients there was also a significant shift QRS axis in the frontal plane during ortoAVRT by comparison with SR, concomitantly with diminished r wave potential in leads V1-3. In all patients AP were left-sided and mapping of the mitral annulus during ortoAVRT revealed V-A fusion on the lateral aspect (n=8) or postero-lateral (n=6). Mapping the same anatomical location during SR revealed A-V fusion despite the absence of overt pre-excitation. In 7 out of 14 patients atrial rapid stimulation revealed overt pre-excitation. QRS width, morphology and axis changed after successful ablation in 10 out of 14 patients (matching the QRS during ortoAVRT).
Conclusions: A short PR interval without overt pre-excitation in patients with documented PSVT should rise the suspicion of left lateral APs rather than atriofascicular APs, especially in the settings of a taller than expected r waves in leads V1-3.

P3377 | BEDSIDE
Feasibility of atrial pacemapping using multiple intracardiac signals as reference: comparison with surface P wave with visual and correlation coefficient analysis

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Localization of focal atrial rhythms can be challenging particularly if they appear transiently. Atrial pacemapping, based on visual comparison of P wave morphology contour has been found useful but a precise identification of P wave is frequently limited during tachycardias. Mathematical waveform analysis has recently been implemented in recording systems to improve waveform comparisons.
Purpose: To explore by pacing at different sites if waveform analysis of a group of intracardiac recordings at fixed but distant sites could be used as a reference template to compare atrial activation resulting from beats originated at different sites.
Methods: Bipolar left atrial pacing trains (400-500 ms) at threshold was performed from several bipoles of a multipolar circular catheter located at each pulmonary vein ostium and at several left atrial sites in 15 patients during a procedure of circunferencial pulmonary vein ablation. During left atrial pacing, unipolar and bipolar recordings were obtained from a reference doudecapolar catheter (two sets of 10 poles separated by 6 cm) located at the coronary sinus and lateral right atrium, as well as the 12-lead surface ECG. Both visual analysis and waveform analysis based in a correlation coefficient ("template matching tool", Lab system) were applied to each pair of pacing sites, as well as to two beats of the same paced site to identify the ability to correctly recognize if a paced beat originated at the same or a different site.
Results: Stimulation was performed from 376 different sites, and 1128 pairs of atrial paced beats were compared, with a mean distance between pairs of 15 ± 10 mm. For the template matching tool the cut-off value of correlation above which 2 paced beats were considered to be originated at the same site was established as the value met by 95% of pairs of beats from the same pacing site. This cut-off value was 71%, 85% and 21% for the P wave, the unipolar and bipolar intracardiacs (I) respectively. Sensitivity and specificity were as follows, respectively: Visual analysis: P wave: 85 and 75%, unipolar I: 87 and 77%, bipolar I: 78 and 72%. Correlation coeficient analysis: P wave: 19 and 95%, unipolar I: 89 and 95%, bipolar I: 15 and 95%.
Conclusions: Intracardiac recordings from multiple, distant and fixed sites can be suitable for atrial pacemapping, having the advantage over the P wave that they are less obscured by ventricular signals during tachycardias. Correlation coefficient analysis offers best results with intracardiac unipolar signals and, with these signals, it could be more accurate than visual analysis.

P3378 | BEDSIDE
Functional and structural reverse cardiac remodelling after ablation of typical persistent atrial flutter: echocardiographic insights

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Purpose: To analyze morphologic and functional cardiac parameters after cavotricuspid isthmus ablation (CTA) of typical persistent atrial flutter (AFL).
Methods: We enrolled 31 consecutive patients (26 males, aged 67.8 ± 18.4 years) with typical persistent AFL (duration 5.4 ± 3.2 months) and normal baseline left ventricular ejection fraction (LVEF). All patients underwent successful CTA. Clinical evaluation, 12-lead-ECG and echocardiography were performed for all patients at baseline and at 1 week, 2 weeks, 1 month, 6 months and 12 months follow-up (FU) after ablation.
Result: Since 2 weeks after CTA, we observed a diastolic and systolic significant reduction of right atrium (RA), right ventricle (RV) and left atrium (LA) areas. The decrease of those parameters was progressive at each successive FU (maximum decrease at 12 months FU: RA end-diastolic area: -5.8%, p=0.002; LA end-diastolic area: -6.4%, $p<0.02$; RV end-diastolic area: -5.2%, p=0.048). A significant increase in RA contraction fraction was found at 6 months (+20.0%, p=0.047); on the contrary, LA contraction fraction improved later, at 12 months FU (+15.2%, p=0.047). No significant variations of left ventricular end-diastolic volumes (LVEDV) and LVEF were observed during the whole FU, perhaps due to the normal LVEDV and LVEF values at baseline. At 1 year, echocardiographic transmitral diastolic pattern showed a significant improvement, expressed by a progressive 4-levels dysfunction scale (Table 1).

Table 1. Overall analysis of diastolic pattern variations after CTA for AFL

Transmitral diastolic pattern	Baseline no. of pts (%)	1 year FU no. of pts (%)
Normal	9 (29%)	19 (62%)
Impaired relaxation	14 (45%)	10 (32%)
Pseudonormal	1 (3%)	1 (3%)
Restrictive	7 (23%)	1 (3%)

p=0.029.

Conclusion: AFL ablation with restoration of sinus rhythm provides a morphologic reverse remodelling of RA, LA and RV, that begins soon after discharge. This phenomenon is progressive and leads to an increase of both RA and LA

contraction fraction. Along with these morpho-functional changes, CTA of AFL - by means of manteinance of sinus rhythm- promotes the restoration of impaired transmitral filling pattern detected at baseline, with improvement of left ventricular diastolic function.

P3379 | BEDSIDE
Clinical significance of negative programmed atrial stimulation in patients suspected but no documented paroxysmal supraventricular tachycardia

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Purpose of the study: To determine the factors of negativity of electrophysiological study (EPS) in patients suspected of paroxysmal supraventricular tachycardia (SVT) and the significance. When noninvasive studies remain negative, the diagnosis is a dilemma. EPS is the only means to evaluate the nature of symptoms when event recorders are not interpretable.
Methods: 568 patients, aged from 6 to 89 years, mean 34±17, 211 males, 357 females complained of tachycardia and were suspected of SVT; they had a normal or near normal ECG in sinus rhythm; 67 patients had a relatively short PR interval (0.12 sec), 8 a first d AV block (AVB). Transesophageal or intracardiac EPS consisted of programmed atrial stimulation with 1 and 2 extrastimuli in control state and after isoproterenol. Patients were followed from 3 months up to 20 years (mean 5±4 years).
Results: No sustained tachycardia (>30 sec) was inducible after complete EPS. Double nodal pathway was noted in 25 patients; non sustained (NS) AV node reentrant tachycardia (AVNRT) was induced in 20 patients; 28 patients presented an excessive sinus tachycardia and 8 patients had NS atrial tachycardia. During follow-up, organic arrhythmia occurred in 27 patients (5%) (group I): a) 23 patients developed a SVT (3%): AVNRT 11, atrial flutter or fibrillation 12); b) one 26 year old patient presented a complete AVB (patient with initially a 1st dAVB); c) 3 patients had ventricular tachycardia. Remaining patients had no organic tachycardia (group II). Long-term Holter monitoring only indicated sinus tachycardia. Tilt test was positive in 71 of 156 patients with dizziness/syncope. The sensitivity of negative EPS was 95%. The analysis of factors that differentiated group I and II indicated that age was higher in group I (48±16) than in group I (38±17) ($p<0.05$) and dizziness/syncope associated with tachycardia was less frequent in group I (22%) than in group II (41%) (p 0.03), while female gender (59 vs 63%), associated chest pain (15 vs 23%), familial history of SVT (4 vs 5%), moderate associated heart disease (18 vs 14%), familial stress (0 vs 4%), or relatively short PR interval (4 vs 12%) were not significantly different in group I and II.
Conclusions: The sensitivity of a negative EPS to predict the absence of organic tachycardia was high (95%). The rare false negatives (5%) were noted in older patients without syncope.

P3380 | BEDSIDE
Pediatric catheter ablation made simple: single-catheter technique

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Radiofrequency ablation is a standard technique used for definitive cure in most cases of tachycardias in old children. Number of catheters used for these procedure might be a handicap when patients are small in weight or age. Description of single catheter technique for ablation of tachycardia substrate in these small patients is presented and discussed. Results are compared to older pediatric population in a single pediatric center.
Patients, methods and results: From 1995 to 2013, 1280 cardiac ablations were performed in children under 18 years of age in a pediatric electrophysiology service. Of those, 111 procedures were performed to 101 patients weighting less than 15 kg due to drug-refractory tachycardias. All of them were done under sedation or general anesthesia. Radiofrequency energy was used in all cases. Single catheter technique was used in 85 procedures (75.2%). In the other 26 cases, only two catheters were used. Primary success rate in a single procedure was 98% of cases. Nine patients needed a second procedure for reccurency. In only one patient, affected of severe Ebstein disease, a third procedure was needed. The mean procedural time was 44.5±24.2 minutes, with a mean radiation time of 10.8±8.7 minutes. Complications were the following: one complete AV bock that completely recovered 24 hour after the procedure, 1 pericardial effusion that resolved with pericardial aspiration within the same procedure, 1 ventricular fibrillation that needed electric cardioversion with no further complications, 1 moderate mitral regurgitation freee of medication after 7 years of follow-up.These results are similar to those seen in older children in our series exept for the rate of single catheter technique that is less used in older patients (11%).
Conclusion: Ablation in small pediatric population is feasable and safe when performed in large pediatric units. Single catheter technique is an excellent option for those small patients requiring ablation.

P3381 | BEDSIDE
Atrial flutter in elderly patients. Clinical data and follow-up after ablation

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Purpose of the study: To look for the influence of advanced age on atrial flutter (AFL)-related clinical data and the long-term results of AFL radiofrequency ablation. Age-related differences were reported for arrhythmias.
Methods: 1171 patients, 896 males, 275 females, mean age 64±12 years were consecutively referred for radiofrequency ablation of recurrent or poorly-tolerated AFL. 903 patients had an underlying heart disease. Clinical history and data of echocardiography were collected. Patients were followed from 1 month to 10 years (mean 2.1±2 years).
Results: 433 patients were aged from 70 to 93 years (group I), 338 from 70 to 79 years (group IA) and 95 from 80 to 93 years (group IB). They were compared to 728 patients <70 years (group II). Heart disease (HD) was more frequent in group I (82%) (group IA: 82%, group IB: 82%) than in group I (74%) ($p<0.002$). Previous atrial fibrillation (AF) was as frequent in group I (31%) and II (32%) (group IA: 30%, group IB: 37%) (NS;0.2). AFL-related rhythmic cardiomyopathy and presentation with 1/1 AFL were less frequent in group I (5%, 3%) ($p<0.01$) than in group II (9%, 12%) ($p<0.001$). The differences were similar for groups IA (5%, 3%) and IB (6%, 2%). At the time of ablation AFL ablation-related major complications were as frequent in group I (1.7%) and II (1.2%) (IA: 1.8%, IB: 1.2%). Restoration of sinus rhythm with bidirectional isthmus block was as frequently obtained in group I (88%) and II (90%) (IA: 88%, IB: 86%). After ablation, AFL recurrences were less frequent in group I (9%) than in group II (15%) ($p<0.001$) (group IA: 10%, $p<0.02$, group IB: 4%, $p<0.0001$). AF occurrence was as frequent in group I (22%) and II (23%) (group IA: 23.5%, group IB: 16%). Among patients without AF before ablation, AF risk remained similar in group I (13%) and II (13%) (group IA: 15%, group IB: 11%). Cardiac mortality was higher in group I (8.5%) than in group II (4.5%) ($p<0.007$) (group IA: 9%, group IB: 6%).
Conclusions: Among patients aged ≥70 years, there were no difference between patients <80 years and those ≥80 years. Compared to younger patients, elderly patients had less rhythmic cardiomyopathy and presentation with 1:1 AFL. Despite a more common associated HD in elderly patients, the success of ablation, the rate of complications and the risk of AF occurrence were similar in young and old patients. However cardiac mortality remained higher in old than in younger patients.

P3382 | BEDSIDE
Is the risk of atrial fibrillation in patients with history of paroxysmal supraventricular tachycardia dependent on the mechanism of tachycardia?

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Purpose of the study: To evaluate the role of the mechanism of paroxysmal of paroxysmal supraventricular tachycardia (SVT) on the incidence of spontaneous atrial fibrillation (AF). The relation between SVT and AF is well-known but its frequency could depend on the mechanism of SVT.
Methods: 1559 patients with SVT and a normal ECG in sinus rhythm were referred for electrophysiological study (EPS); mean age was 49±19 years. Patients with anterograde conduction over an accessory pathway (AP) were excluded. EPS was performed in control state and after isoproterenol. Patients were followed from 3 months up to 20 years (mean 3±2 years).
Results: SVT was related to atrioventricular nodal re-entrant tachycardia (AVNRT) in 1363 patients (group I) that was typical in 1180 patients (group IA) and atypical in 183 patients (group IB). In remaining 296 patients SVT was related to a concealed AP with atrioventricular re-entrant tachycardia (AVRT) (group II). At the initial evaluation 47 patients of group I (3%) (44 of group IA, 3.7%, 3 of group IB, 2%) and 6 of group II (2%) had presented at least one episode of sustained AF (NS). During follow-up, 97 patients developed AF, 86 of group I (6%) (71 of group IA, 6%, 15 of group IB, 8%) and 11 of group II (4%). The risk of AF only was higher in group IB than in group II ($p<0.03$). When patients with AF at first study were excluded, the risk of AF during follow-up was similar in all groups: AF occurred in 63 patients of group I (4.6%) (51 of group IA 4%, 12 of group IB 6.5%) (0.06) and 9 of group II (3%). Ablation of slow pathway or AP was performed in 1099 patients, 909 of group I (66.6%) (816 of group IA, 69%, 93 of group IB, 51%) and 189 of group II (64%) (NS). The risk of AF was paradoxically higher in patients in whom ablation was performed in group I (6.7% in group I, 7% in group IA, 13% in group IB), compared to patients without ablation (4% in group I, 4% in group IA, 3% in group IB) ($p<0.022$) and was unchanged in group II (4% after ablation and 3% in patients without ablation.)
Conclusions: In patients with a normal ECG AF-related SVT was rare (3%), independent on the mechanism of SVT. The risk of subsequent AF after a follow-up of 3 years increased to 6% and was near 5% in patients without AF at initial evaluation; it was only higher in patients with atypical AVNRT than in patients with concealed AP. The risk was not affected by the ablation of the slow pathway or the accessory pathway.

P3383 | BEDSIDE

Variation of maximum P-wave duration and P-wave dispersion: markers of atrial reverse remodeling and predictors of sinus rhythm maintenance after cavotricuspidal ablation for typical atrial flutter

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Purpose: To find a correlation between simple ECG parameters and sinus rhythm maintenance or arrhythmic relapses after cavotricuspidalic ablation for typical persistent atrial flutter.
Methods: 31 consecutive patients (26 males, mean age 67.8±18.4 ys) with typical persistent atrial flutter (duration 5.4±3.2 months) underwent cavotricuspidalic ablation with restoration of sinus rhythm. In all patients, 12 lead-ECGs were recorded at a speed of 50 mm/s 36 hours, 1 month and 6 months after cavotricuspidalic ablation. In all ECGs, we measured maximum P wave duration, minimum P wave duration and P wave dispersion; then we compared 6 months ECG evaluations with 36 hour and 1 month ECG evaluations. No antiarrhythmic drugs were administered after cavotricuspidalic ablation.
Results: Cavotricuspidalic ablation was effective for sinus rhythm restoration in all patients, without arrhythmic relapses within 6 months. P wave maximum duration and P wave dispersion measured at 6 months significantly decreased compared to P wave maximum duration and P wave dispersion recorded at 36 hours (respectively 128.2±17.1 ms Vs 132.3±14.3 ms: p=0.008 and 33.6±12.9 ms Vs 39.3±13.1 ms: p=0.03) and 1 month (respectively 128.2±17.1 ms Vs 131.6±16.9 ms: p=0.01 and 33.6±12.9 ms Vs 36.8±11.6 ms: p=0.02).
Conclusions: P wave dispersion is considered a marker of inhomogeneous atrial conduction, and in literature it has been proposed as a predictor for paroxysmal atrial fibrillation. At our knowledge, this is the first time that P wave dispersion has been evaluated after cavotricuspidalic typical atrial flutter ablation. In our patients, the efficacy of cavotricuspidalic ablation in restoring sinus rhythm (that persisted without antiarrhythmic drugs) was associated with a progressive reduction of P wave dispersion and maximum P wave duration since 1 month after ablation, even more reduced after 6 months. This could be related with a progressive electrical atrial reverse remodelling with a restoration of atrial electrical homogeneity that started 1 month after ablation. Since the P wave is the expression of the atrial activity of both atria, it might be hypothesized that the restoration of electrical homogeneity of both atria could contribute to the prevention of right and left sided atrial arrhythmias.

P3384 | BEDSIDE

A novel porous tip open-irrigated catheter for cavo-tricuspid isthmus ablation

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Background: Atrial flutter is common sustained arrhythmia in clinical practice, and associated with atrial fibrillation. However, sometimes creation of complete isthmus block by using irrigated tip RF catheter was difficult. Irrigated tip radiofrequency (RF) ablation catheter is the most frequently used technology for pulmonary vein isolation. The purpose of this study was to compare the efficiency and the safety of 2 different open irrigated tip RF ablation catheters for creation of complete cavo-tricuspid isthmus block.
Methods: RF ablation for creation of cavo-tricuspid isthmus block in 100 patients with AF (34.5% persistent AF, 76.7% male, 64±9 years) undergoing RF ablation for pulmonary vein isolation was performed by using 2 different irrigated tip catheters: the novel Thermocool surround flow (SF) catheter with a porous tip (56 holes) in 50 patients or the Thermocool catheter with 6 irrigation holes at the distal tip in 50 patients in both power- and temperature-controlled modes. The endpoint criteria was determined to identify complete block consisted of an atrial activation sequence around the tricuspid annulus consistent with complete block, negative initial polarity of the electrograms recorded just lateral to the ablation line during coronary sinus pacing and the presence of double potentials along the entire ablation line.
Results: Ninety-three% of patients by using Thermocool SF, could achieved complete isthmus block while only 54% of patients by using Thermocool could achieved complete isthmus block. RF delivery points and RF delivery energies were significantly smaller with Thermocool SF versus Thermocool catheter: 10.1 points versus 18.6 points ($p<0.01$) and17.5kJ versus 31.0kJ ($p<0.01$), respectively. Similarly, RF duration time was shorter with Thermocool SF versus Thermocool catheter: 8.9 minutes versus 16.5 minutes ($p<0.01$).
Conclusions: Creation of complete cavo-tricuspid isthmus block by using the novel irrigated tip Thermocool SF catheter is more effective than Thermocool catheter.

ATRIAL FIBRILLATION ABLATION III

P3386 | BEDSIDE

Is the prognosis of idiopathic atrial flutter better than the prognosis of atrial flutter associated with heart disease?

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Purpose of the study: To look for the characteristics of apparently idiopathic typical atrial flutter (AFL). Associated heart disease (HD) should modify the incidence of previous history of atrial fibrillation (AF) and later occurrence of AF after AFL radiofrequency ablation that is a treatment of choice of typical AFL.
Methods: 1170 patients, mean age 64±12 years, were consecutively referred for ablation of recurrent or poorly-tolerated AFL. Clinical history, previous AF, medical treatment and data of echocardiography were collected. Patients were followed from 3 months up to 10 years (mean 2.1±2 years). Antiarrhythmic drugs were stopped after ablation except in patients with history of AF before ablation.
Results: AFL was apparently idiopathic in 269 patients. HD was present in 901 patients (77%): hypertensive disease (HTD) (n=256), ischemic HD (IHD) (n=196), valvular HD (VHD) (n=129), dilated cardiomyopathy (DCM) (n=109), respiratory failure (resp) (n=102), congenital HD (cong) (n=43), miscellaneous HD (n=66). Prior AF was more frequent in patients without HD (44%) than in patients with HD (28%) ($p<0.00001$). Differences were significant for all subgroups of HD. However antiarrhythmic drugs or beta-blockers were prescribed more frequently in patients with HD (68.5%) than in those without HD (55%) ($p<0.001$). During the follow-up, 52 patients without HD (21%), 194 with HD (23%) developed AF (NS). AF ablation was performed in 3% of patients with and without AF. There were no differences among all subgroups of HD. The risk of AF among patients without prior AF was lower in patients without HD (8%) than in patients with HD (14%) (0.006). Among subgroups with HD, patients with cong HD had a higher risk of AF (26.5%) than patients without HD ($p<0.001$) or patients with HD (11%) ($p<0.014$). Differences were not significant for other HD's. As expected cardiac mortality was higher in patients with HD (8%) than in patients without HD (4%) ($p<0.001$).
Conclusions: After a follow-up of 2 years, the presence of HD does not increase the risk of AF in patients with atrial flutter. Among patients with HD, patients with congenital HD seem to have a higher risk of developing AF than patients with HD of other origin. Therefore the indication of AFL ablation should not differ in patients with and without HD.

P3387 | BEDSIDE

Evaluation of the transeptal puncture site guided by fluoroscopy or electroanatomic mapping

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Purpose: Transeptal puncture (TSP) guided only by fluoroscopy is common practice in Europe. More recently the use of electroanatomical mapping (EM) has been proposed to guide and optimized TSP. The aim of this study was to validate EM for TSP and to compare the selected TSP sites by this imaging technique and fluoroscopy.
Methods: Patients (P) referred for atrial fibrillation ablation were prospectively enrolled in this study. Previous TSP was considered exclusion criteria. The right atrium (RA) and fossa ovals (FO) geometries were reconstructed with a 3D electroanatomical mapping system. The transeptal sheath and needle were taken into the superior vena cava with fluoroscopy and the needle connected with a cocodrile clamp to the EM system. Then the sheath with the needle tip assembled at the very dilator end were moved to the fosa ovals without fluoroscopy with the only guide of the EM system and the final site for TSP tagged on the EM. The suitability of this site for TSP and the distance of this site to the best one for TSP was assessed by intracardiac echocardiography (ICE) which was considered the gold standard. Following this the array was pulled-back, the EM disconnected and the sheath-needle array relocated on the the FO guided by fluoroscopy for TSP. The EM was reconnected and the TSP site tagged on it. Again, the suitability of this site for TSP and the distance of this site to the best one for TSP was assessed by ICE.
Results: 15 P were enrolled in the study. A suitable TSP site on FO was obtained by EM and fluoroscopy in 82% and 73% patients respectively. The distances from the selected TSP site to the the best TSP site selected by ICE were 14.2±11.3 mm for EM and 18.2±11.9 mm for fluoroscopy with no significant differences between them.
Conclusion: EM appears to be at least as accurate as fluoroscopy to localize the best TSP site. EM may be used in combination with fluoroscopy in order to facilitate or improve the selection of the TSP site by less experienced operators or in patients with distorted anatomies.

P3388 | BEDSIDE
Issues associated with catheter ablation via the transconduit approach after an extracardiac total cavo-pulmonary connection

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Background: We aimed to clarify the issues of the transconduit approach and the results of catheter ablation of supraventricular tachycardia with an extracardiac total cavopulmonary connection (eTCPC)
Method: Five cases with tachyarrhythmias after the eTCPC undergoing catheter ablation via transconduit approach were included in this study. We analyzed the patient characteristics, the issue associated with the transconduit puncture and catheter ablation, and results.
Results: The age at the time of the catheter ablation was from 4 to 19. The median height was 151 cm (102-155cm).Three had a right isomerism heart and single ventricle and others had a double outlet of the right ventricle and single ventricle. The targeted arrhythmias were atrioventricuar reciprocating tachycardia via accessory pathway (AVRT via AP) in one, a tachycardia involving twin atrioventricular nodes (TAVN) in one, AVRT via AP and TAVN in one, intraatrial reentrant tachycardia in one, and paroxysmal junctional tachycardia in one. All patients were successfully ablated via transconduit approach. The interval from the eTCPC to the catheter ablation was three months to twelve years. It was difficult to puncture the straight shaped conduit and ringed artificial conduit. We need to devise a way to advance the long sheath into atrium and had a hard time treating complicated arrhythmias such as intraatrial reentrant tachycardia and junctional tachycardia.
Conclusion: We experienced five cases that underwent catheter ablation of tachyarrhythmias using transconduit approach. This technique will be a useful technique for treating increasing tachycardias after an eTCPC. It is important to clarify the further issues and establish the safety of this technique in the future.

P3389 | BEDSIDE
Focal radiofrequency ablation for macroreentrant left atrial tachycardias

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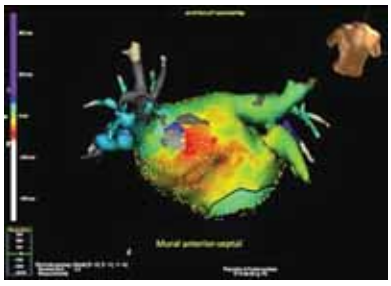
Aims: Linear ablation is used for left atrial flutters (LAFl), requiring extensive lesions but bidirectional block is not always attainable. We hypothesized that a detailed characterization of the circuit reveals critical isthmi susceptible of focal ablation (FAb).
Methods: Macrorreentry was demonstrated by entrainment with fusion. Detailed return cycles (RC) and activation maps were developed. The critical isthmus was identified by RC <+10 ms and concealed entrainment or non-propagated termination at sites with diastolic egms. We used the term "mural rentry" for those located on the atrial wall unrelated to anatomic barriers. The endpoint was termination and no reinducibility.
Results: 32 (68±11 years, 57% males) underwent 38 EP studies during which ≥1 LAFl circuit was ablated. 43 LAFl were studied (median CL 320 ms, range 210-580 ms): 11 mural anterior, 11 around PVs, 7 mural posterior, 6 perimitral circuits, 4 left atrial appendage AFl, 2 left septal AFl, 1 mural lateral and 1 CS circuit. Acute success was obtained in 41 circuits (95%), 2 cases could not be ablated focally. Median RF time to termination was 14 s (range 2–94 s). Median duration and amplitude of the local electrogram were 98 ms (range 51 – 240 ms) and 0,08 mV (range 0,03 – 1,1 mV).
During follow-up (median 44 months, range 3 – 95) the ablated circuit recurred in 3 P (9%) and 2 P (6%) presented a new circuit (all successfully ablated), 3 P (9%) had a single recurrence of atypical AFl, 2 P (6%) developed permanent AF, 2 P (6%) require AVN ablation. Globally, 63% of P were totally arrhythmia-free and 3/43 circuits recurred (7%).



Conclusion: Ablation of LAFl is feasible with focal RF applications: this strategy seems successful on the long term and should be considered a valid alternative to linear ablation.

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Catheter maze (dallas lesion set) in addition to circumferential pulmonary vein isolation does not improve clinical outcome in paroxysmal atrial fibrillation patients: prospective randomized study

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Purpose: Although the concept for radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) was derived from maze surgery, whether linear ablation in addition to circumferential pulmonary vein isolation (CPVI) reduces recurrence rate is unclear in patients with paroxysmal AF (PAF). Therefore, we compared clinical outcomes of catheter maze (Dallas lesion set) and CPVI as prospective randomized controlled study among the patients with PAF.
Methods: This study enrolled 100 PAF patients (male 75.0%, 56.4±11.6 years old) who underwent RFCA, and randomly assigned to CPVI group (n=50) and catheter maze group (CPVI, Posterior box lesion, and anterior linear ablation, n=50).
Results: 1. Catheter maze group required longer procedure time (190.3±46.3 min vs. 161.1±30.3 min, p<0.001) and ablation time (5345.4±1676.4 sec vs. 4027.2±878.0 sec, p<0.001) than CPVI group. 2. Complete bidirectional conduction block rate was 68.0% in catheter maze group and 100% in CPVI group, respectively. 3. Procedure related complication rates were not significantly different between catheter maze group (0%) and CPVI group (4%, p=0.157). 4. During 16.3±4.0 months follow-up, the clinical recurrence rates were not significantly different between two groups (16.0% in catheter maze group vs. 12.0% in CPVI group, p=0.564), regardless of the achievement of complete bidirectional conduction blocks of linear ablation.
Conclusion: Linear ablation in addition to CPVI (catheter maze) did not improve clinical outcome of RFCA for PAF patients, requiring longer procedure time.

P3391 | BEDSIDE
Level of ablation scar after pulmonary veins isolation: comparison of different ablation strategies

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Purpose: Electrical isolation of pulmonary veins (PVI) is an established endpoint of ablation of atrial fibrillation (AF) and can be achieved through either a wide ablation line encircling the entire PV antrum or a separate isolation of individual PVs. We sought to determine the level of ablation scar after PVI and the size of left atrial isolated surface area (ISA) for radiofrequency catheter guided ablations (RFC) in comparison to balloon guided ablation (Laser, LB; Cryo, CB).
Methods: In 45 patients undergoing PVI a bipolar voltage re-mapping using Navx Velocity was performed before and after PVI in sinus rhythm. The ablation procedure was performed using irrigated RFC (30-40W, 17-25ml/h flow, 43°C; n=15), the 28mm CB Advance (n=15) or the HeartLight LB (n=15).
The level of ablation scar after PVI was identified by the presence of low voltage (<0.5mV). We determined:
1. the left and right isolated antral surface area (IASA-L and IASA-R), defined as the low voltage areas around the ipsilateral PV ostia (cm^2);
2. the total isolated antral surface area (IASA-T= IASA-L+IASA-R; cm^2);
3. the LA posterior wall area between the scars (LA PW, cm^2);
4. the relative size of the scar, the ISA (%)=IASA-T/(IASA-T +LA PW)×100.
Results: Acute PVI was achieved in 100%. The 3 groups did not differ with regards to baseline characteristics including LA size (40±6mm) and type of AF (80% paroxysmal). IASA-T was significantly higher in CB: 58±15 cm^2 vs. 41±11 cm^2 (RFC) vs. 40±15 cm^2 (LB), p=0.002, due to significantly wider IASA-R: 32±9 cm^2 (CB) vs. 23±6 cm^2 (RFC) vs. 21±11 cm^2 (LB), p=0.004. No significant differences were observed for both IASA-L and LA PW. The largest ISA was: 65±8% (CB) vs. 62±11% (RFC) and 54±11% (LB), (p=0.023) (Fig.1). Total procedure time was significantly higher in LB: 143±33 min vs RFC: 109±33min vs CB: 102±16 min, p=0.001) while fluoroscopy time was lower in LB: 11±3 vs RFC: 15±6 vs CB: 13±2 min; p=0.012. Mean re-mapping time was not different among the three groups (18±3 min). No complications were observed.
Conclusions: The level of ablation scar after PVI varies with different ablation technologies. CB provides the widest and most extensive antral isolation area in particular at the septal PVs. The impact on long-term outcome remains to be determined.

P3392 | BEDSIDE
Mitral isthmus linear ablation does not affect mitral valve function

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Background: Mitral isthmus linear ablation (MIL) is utilized to prevent mitral annulus dependent flutter in patients with atrial fibrillation (AF) undergoing pulmonary vein isolation. However, the effect MIL on mitral valve (MV) function is not known. We aimed to characterize the effect of MIL ablation on MV function.
Methods: Two hundred and twelve consecutive highly symptomatic patients (females 37, age 59±10) referred for AF ablation (paroxysmal 132, persistent 45, permanent 35) were randomly assigned to have MIL (n=113) versus no MIL

(n=99) ablation during pulmonary vein isolation of AF. Transthoracic echocardiography was performed before ablation, 1 day after ablation, 3 months and 6 months after ablation. All studies were carefully evaluated for mitral regurgitation (MR) and graded for severity (mild, moderate or severe) utilizing standard American Society of Echocardiography criteria. Serial echocardiogram results were compared (among patients with (16 patients) and without (196 patients) significant MR) to determine the impact of MIL ablation on MV function.
Results: Among patients with initially normal MV function, 3 (3%) patients with MIL and 4 (4%) patients without MIL developed significant MR following the procedure (P=0.72). Sixteen patients had significant MR pre-procedurally (13 MIL vs 3 no MIL). Following the procedure, MR improved significantly in 9 (69%) patients with MIL and in 2 (66%) without MIL (P=1.0). MV function did not deteriorate significantly following MIL in patients with pre-existing MV regurgitation (0 (0%) MIL vs 1 (33%) no MIL; P=0.19).
Conclusion: MV function is not affected by MIL ablation regardless of pre-existing MR. This has important implications for selection of ablative strategies in patients with AF, especially in patients with pre-existing MR.

P3393 | BEDSIDE
Management of stand-alone atrial fibrillation: advantages of the hybrid approach

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Background: The hybrid approach combines an epicardial ablation with a percutaneous endocardial ablation in a single-step or sequential procedure.We present our results with this technique in patients with lone atrial fibrillation (LAF).
Methods: The study group consisted of 78 consecutive patients referred for ablation of AF (77% male, aged 60±5 years) between 2009 and 2012. LAF was defined following the ACC/AHA/ESC Guidelines. Indication for epicardial surgical ablation was based on the HRS/EHRA/ECAS Guidelines. Fifteen patients (19.2%) had long-standing persistent AF, while thirty-four (43.6%) had persistent and twenty-nine (37.2%) paroxysmal AF. A continuous 7-day Holter Monitoring (HM) after hospital discharge, at 3 mounths, 6 mounths and 1 year was performed. Monitoring was carried out with an external loop recorder and analyzed with Lifescreen Software. Success was defined as no episode of AF, atrial flutter (AFL) or any atrial tachycardia (AT) lasting more than 30 seconds off antiarrhythmic drugs (AAD) after the three months blanking period. We conduced a 1 year follow-up study of all patients. The mean follow-up duration was 24 months [interquartile range (IQR) 12-36].
Results: There were neither early nor late deaths. It was possible to complete all the procedures as planned without any conversion to cardiopulmonary bypass. No patient had evidence of phrenic nerve paralysis. No procedure-related events or thromboembolic/bleeding complications were observed during the follow-up. Perioperative complications were observed in six patients (8%). The percentage of patients in sinus rhythm with no episode of AF, AFL or AT lasting longer than 30 seconds and off antiarrhythmic drugs (ADD) was of 87% (n=68) at one year. Success rates were 100% (15) in long standing persistent AF, 82% (n=28) in persistent and 76% (n=22) in paroxysmal AF (P=0.08), off AAD, respectively, at the last follow-up. Among these patients, 13% (n=10) required percutaneous ablation for recurrent AF or left AFL after the hybrid procedure. Therefore we showed a success rate of 74% (n=58) after a single procedure.
Conclusions: Thoracoscopic hybrid epicardial endocardial approach was, in our experience, a safe technique with satisfactory 1-year results. Despite good preliminary results, large, multicentre trials of hybrid AF ablation are necessary to establish whether this approach may represent, in the future, a gold-standard treatment for AF.

P3394 | SPOTLIGHT
Long term results of stand-alone, totally endoscopic surgical ablation of atrial fibrillation

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Purpose: Minimally invasive surgical treatment of atrial fibrillation (AF) has gained popularity during the past decade, albeit there is paucity of data about the long-term outcomes of this novel approach.
Methods: Study population included 111 consecutive patients undergoing stand-alone surgical treatment of atrial fibrillation via a closed-chest, monolateral thoracoscopic approach and epicardial isolation of all pulmonary veins and posterior left atrium ("box" lesion set) by means of uni/bipolar radiofrequency energy. Mean age was 63.3±10.3 yrs, and the prevalence of paroxysmal, persistent and long-standing (LS-persistent) AF was 39.6%, 11.7% and 48.6% respectively with a median AF duration of 48 months. Mean left atrial diameter was 47.5±8.2 mm.
Results: The procedure could be successfully accomplished via an endoscopic approach in all patients but one requiring conversion to mini-sternotomy. Hospital mortality was 0% and no major complications occurred during the post-operative stay except for a thrombo-embolic event occurring only in 1 patient (0.9%). Multivariate Cox regression analysis identified long-standing persistent AF (OR: 9.5; CI=2.5-35.4; p=0.001) and female gender (OR: 3.03; CI=1.06-8.7; p=0.039) as independent risk factors for AF recurrence; instead, paroxysmal AF was associated with improved rhythm outcomes (OR: 0.12; CI=0.04-0.36; p<0.001). At a median follow-up of 57 months, overall stable sinus rhythm was achieved in 80.2% (89/22 pts.) (paroxysmal:90.9%, 40/44 pts.; persistent:84.6%, 11/13 pts.; LS-persistent: 70.3%, 38/54 pts.); Finally, there was a trend towards the stabilization of rhythm over the follow-up time, as depicted by Spearman analysis showing a positive correlation among sinus rhythm restoration and follow-up duration (rho=0.82).
Conclusions: Totally endoscopic AF surgical ablation is a safe and effective procedure with excellent results at long-term especially for paroxysmal and persistent AF, while patients with LS-persistent AF may benefit from additional hybrid procedures.

P3395 | BEDSIDE
A tailored approach to catheter ablation of paroxysmal atrial fibrillation: pulmonary vein or stepwise catheter ablation approach

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Background: Previous studies have demonstrated that the ablation of the pulmonary vein (PV) potentials recorded from a circular multipolar electrode catheter is the primary endpoint for catheter ablation in patients with paroxysmal atrial fibrillation (AF). However, the efficacy of this catheter ablation procedure may not be equally effective or efficient in all patients with AF. The recurrence rate of atrial arrhythmias is higher in patients with structural heart disease than in patients with paroxysmal AF without heart disease after isolation of PV. We investigated whether the presence and clinical outcome in patients with paroxysmal AF after circumferential pulmonary vein isolation or stepwise catheter ablation approach.
Methods and results: Catheter ablation was performed in 100 consecutive patients (mean age, 61.9±8.2 years) with symptomatic paroxysmal AF. Forty patients underwent pulmonary veins isolation. The remaining 60 patients underwent a stepwise catheter ablation approach. The end point of ablation of pulmonary vein was confirmed by entrance block, whereas in patients who underwent a stepwise ablation was restoration of sinus rhytm and the noninducibility of AF. Patients were followed-up for 12 months. After 1 year of follow-up with repeated Holter monitoring, the percentages of SR maintenance were 67 (67%) patients. At the end of follow-up, patients treated with a stepwise ablation had a lower recurrence rate of atrial arrhythmia than patients in whom paroxysmal AF was did not terminate (55% vs 75%, P=0.009). Atrial fibrillation occurred in 55% (18 patients) in patients in whom AF were treated with PV isolation and in 13% (8 patients) in patients treated with a stepwise ablation procedure (p>0.001).The remaining 7 patients (12%) had a recurrence of atrial tachycardia. As compared with the subjects who were treated with ablation of PV, the adjusted hazard ratios (HRs) of SR maintenance were significantly higher for those treated with a stepwise ablation (HR=2.1; p=0.001).
Conclusions: A stepwise ablation in patients with paroxysmal AF may be associated with a better long-term clinical outcome than when AF was merely treated with PV isolation.

NON-INVASIVE DIAGNOSIS II

P3397 | BEDSIDE
Diastolic dysfunction associated with Long QT syndrome in children

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Purpose: Long QT syndrome (LQTS) is characterized by prolonged ventricular repolarization due to persistent sodium or potassium inward currents and disrupting calcium (Ca2+) homeostasis. Abnormal Ca2+ exchange may manifests of disruption relaxation. The aim of the study is to evaluate the diastolic function of the heart in young patients with LQTS.
Methods: Echocardiography (ECHO, VIVID 7, GE) was performed in 100 LQTS patients aged from 3 to 19 years (12.3±4.4 y.). In addition to conventional echo measurements tissue doppler (TD) was performed. Electromechanical disparity time (EMD - interval from the aortic valve closure or the end of systolic wall motion to the end of QT interval) and isovolumic relaxation time (IVRT) were assessed by spectral (SpD) and tissue doppler (TD) in 12 segments of LV. The velocity Em and Am were assessed in 12 segments of LV and free wall of RV.

Echo characteristics of LQTS patients

Parameters	Patients with DD	Patients without DD	p-value
HR, beats/min	62.8±11	62.8±13	0.99
QTc, ms	497.3±46	480.4±43	0.13
EF, %	72.4±4	72.1±9	0.9
EMD (SpD), ms	112.8±34	97.4±44	0.15
EMD (TD), ms	116.5±47	90.5±46	0.03
IVRT (SpD), ms	68.3±11	62.2±11	0.03
IVRT (TD), ms	81.7±10	76.6±11	0.0005
IVRT dispersion, ms	35.8±12	27.7±10	0.002

Results: Diastolic dysfunction (DD) of RV (Em/Am<1) was found in 19 pts (1 pt had biventricular dysfunction). Patients with DD compared with patients without DD characterized by more prolonged EMD, IVRT and dispersion of IVRT. There were no differences on genetic forms, age, heart rate (HR), QTc duration and systolic function between groups. Pts with syncope was predominated in group with DD (84% vs. 46%, p=0,002).
Conclusion: Young LQTS patients showed diastolic disorders manifested by prolonged isovolumic relaxation time and abnormal ratio Em/Am. Diastolic dysfunction is more common in pts with syncope and more pronounced electromechanical disparity.

P3398 | BEDSIDE
Dynamicity and characteristics of early repolarization pattern in healthy population of our country

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Background: Early repolarization pattern (ERP) has been considered a normal variant of electrocardiography (ECG) for a long time. Nevertheless, increasing evidence is demonstrating its association with adverse outcomes.
Purposes: The present study aimed to evaluate the prevalence of ERP in general population and demonstrate its clinical and ECG correlates.
Materials and methods: A prospective cohort was conducted among population recruiting 1424 consecutive healthy adult individuals. ERP prevalence and ECG morphology was investigated and after a period of follow-up visits, clinical and ECG variables were compared between significant and non-significant ERP cases.
Results: ERP was present in 136 out of 1424 subjects (9.6%). Slurring constituted the most frequent morphology followed by notching. ERP was predominantly positive in inferior leads followed by anterolateral leads. Subjects over the age of 40 years old had a higher prevalence of ERP (p=0.06). There was also a significant male preponderance in ERP positive group. Mean diastolic pressure was significantly lower in ERP positive group than in ERP negative group (p=0.03). However, despite a lower systolic blood pressure in ERP positive subjects, the difference was not statistically significant (p=0.06). Alternance rate was 32.6% in ERP significant group and 13.3% in non-significant group (p=0.03).
Conclusion: ERP is present in 9.6% of healthy individuals with more frequency in inferior leads and slurring as the most prevalent morphology. Additionally, there was a male preponderance and middle-aged trend for ERP. There was also a 32.6% alternance rate among ERP patients which inversely correlated with age.

P3399 | BEDSIDE
Relationship between J wave and ventricular fibrillation caused by coronary spastic angina

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Background: Coronary spastic angina (CSA) is known to be complicated with ventricular fibrillation (VF), but its risk factors are not fully elucidated. J wave has been reported to be associated with idiopathic VF and has been gaining attention as a possible marker for VF. The aim of this study is to investigate the relationship between J wave and VF in CSA.
Method: One hundred consecutive patients diagnosed with CSA by provocation test for coronary spasm in two hospitals from April 2009 to March 2012. The diagnosis of CSA was made on the coronary narrowing more than 90 percent or occlusion by the provocation of acetylcholine. J wave was defined as notches or slurs at the terminal portion the QRS complexes and amplitude more than 0.1mV above the isoelectric line in at least two contiguous leads in inferior site (II, III, aVF) or lateral site (I, aVL, V4-6) on the base line electrocardiograms (ECG).
We evaluated the correspondence of J wave location to the site of coronary spasm, which was defined as J wave of inferior lead correlated with right coronary spasm or J wave of lateral lead correlated with left circumflex coronary spasm.
Results: Seventy six in 100 patients who diagnosed with CSA were men.
Twenty eight in 100 patients had J wave on the baseline ECG. Twenty patients had J wave located in the inferior site, four patients in lateral site and four patients in both inferior and lateral sites.
Twelve of 28 patients with J wave corresponded with the J wave location and the site of coronary spasm (correspondent group). Sixteen patients did not correspond (non- correspondent group).
VF episodes complicated in 6 patients (50%) of correspondent group significantly more than one (6%) of non-correspondent group. (P=0.022, Odds ratio 15)
On the other hand, ten (11%) in 72 patients without J wave had VF history.
Conclusions: It was suggested that J wave location corresponded with the site of coronary spasm might relate to VF in CSA.

P3400 | BEDSIDE
Significance of interlead difference of tpeak-end intervals and t-wave current density alternans in long QT syndrome with icd implantation

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Background: The existence of M cells may relate QT elongation. The noninvasive evaluation of repolarization phase in patients with lethal ventricular arrhythmias is an important issue. In this study, we verified a novel algorithm of two-dimensional interlead difference of Tpeak-end intervals (Tp-e dispersion) and T-wave current density alternans (TWCA) using synthesized 187-channel body surface mapping.
Method and results: In this present study, we used originally developed 187-channel signal-averaged vector-projected high resolution ECG (DREAM-ECG) that can evaluate 12-leads and XYZ ECGs, and abnormalities of ventricular depolarization and repolarization. This DREAM-ECG consisted of an input box with high resolving power amplification, vector-projected matrix lead synthesizer, A/D converter and data handling section. We obtained synthesized 187-channel ECG based on vector-projection theory. We recorded 10 minutes of body surface ECG by using Mason-Likar lead system at resting supine position. The existence of LPs was defined by the LAS40 $\geq$44 msec and fQRS $\geq$127 msec on signal averaged XYZ leads ECG. The values for the mean activation recovery time (RT) dispersion were automatically calculated by the mean difference between the greatest RT interval (RTmax) and the smallest RT interval (RTmin). The value of Tp-e dispersion was automatically calculated as the mean difference between the greatest and smallest Tp-e intervals. Corrected RT intervals and Tpeak-end intervals were calculated by Bazzet's formula. The TWCA value was also determined from the relative changes in the averaged current density at the T-wave zone (Tpeak$\pm$50 ms) between two types of T-wave. We registered 20 normal controls and 16 LQTS with ICD implantation. The value of LPs was negative in all patients with LQTS. The QTc interval values in the LQTS were higher than those in the control (483$\pm$55 ms vs. 415$\pm$19 ms, P<0.001). The two dimensional Tp-e dispersion values among the LQTS were higher than those in the control subjects (53$\pm$13 ms in LQT vs. 24$\pm$10 ms in control, P<0.01). The mean TWCA value was also higher in the LQTS (1.3$\pm$0.5% in LQTS vs. 0.5$\pm$0.2% in control). Interestingly, the two dimensional distribution of Tp-e dispersion and TWCA in LQTS was inhomogeneous. Representative cases were indicated in figure 1.
Conclusion: We conclude that a novel algorithm of two dimensional Tp-e dispersion and TWCA using DREAM-ECG may provide a new insight for evaluating LQTS with ICD implantation.

P3401 | BEDSIDE
Magnetic field imaging for the prediction of sustained ventricular arrhythmias and sudden cardiac death in ICD carriers: two-year outcomes of a prospective registry

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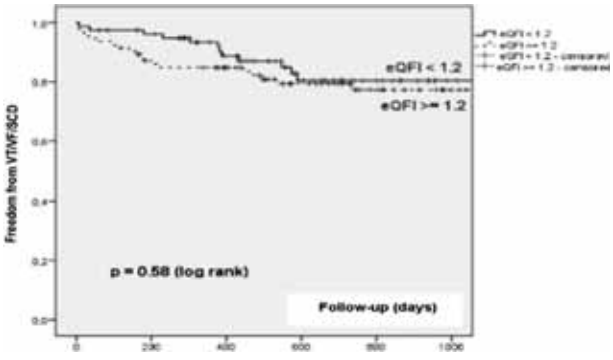
Purpose: Magnetic field imaging (MFI) is a non-invasive method used to evaluate cardiac electromagnetic activity. Early reports have demonstrated a positive predictive value of the electromagnetic QRS fragmentation index (eQFI) for the occurrence of ventricular arrhythmias and death. The aim of this study was to investigate whether an elevated eQFI could predict the occurrence of sudden cardiac death or ventricular arrhythmias in ICD carriers.
Methods: Between 12/2009 and 12/2012, 173 consecutive patients underwent a MFI investigation prior to receiving an ICD. The Apollo CXS MFI system was used for data acquisition. An eQFI $\geq$1.2 was considered to be pathologic. Median follow-up time was 749 days (IQR 551-1037). Study endpoints were sudden cardiac death and sustained ventricular arrhythmias.
Results: Ninety-four patients (54%) had an elevated eQFI. Independent predictors of elevated eQFI were atrial fibrillation and QRS width over 110 msec. The overall occurrence of ventricular arrhythmias and/or sudden cardiac death was 19.7%: 21.3% among patients with elevated vs 15.2% among patients with low eQFI (p=0.3). In a multivariate analysis with adjustment for 6 clinical parameters,



elevated eQFI was not associated with an increased total mortality or occurrence of ventricular arrhythmias (HR 1.03, 95% CI 0.45-2.38).
Conclusion: One half of the patients scheduled to undergo ICD implantation had an elevated eQFI. After a median follow up time of more than two years, the occurrence of sudden cardiac death and/or sustained ventricular arrhythmias was 20% and did not significantly differ between patients with low versus elevated eQFI.

P3402 | BENCH
Multiple sclerosis patients have longer QRS and QT interval duration and different QRS axis than healthy controls

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Background: Patients with multiple sclerosis (MS) have dysfunction of autonomic nervous system which may influence the electrocardiography (ECG) pattern.
Aim: To compare basic ECG parameters in rest in relapsing-remitting MS patients and healthy controls. Also, to examine correlation between MS features and ECG parameters.
Methods: Standard 12-leads ECG after 5 minutes of rest and computer analysis of QRS duration, PR interval, QT interval, QTc interval, QRS axis and the frequency of right bundle branch block (RBBB) was compared between 101 patients with relapsing-remitting MS in remission and 101 age and sex matched healthy controls. All measured ECG parameters were correlate with age, duration of MS, disease activity relapse rate at 3 years and the invalidity score (EDSS score).
Results: All patients were in sinus rhythm. MS patients had longer QRS duration [92 (86-98 ms) vs 87 ms (81-92 ms), $p<0.001$],longer QT interval [381 (363-403 ms) vs 259 ms (342-377 ms), $p<0.001$], longer QTc interval [416 (399-431 ms) vs 399 ms (389-416 ms), $p<0.001$] and different QRS axis ([7o (0-66o) vs 55o (29-71o), $p<0.001$] than healthy controls. PR interval was similar. Some degree of RBBB was more common in MS patients (40.6% vs 19.8%, p=0.002). Neither age or MS duration, nor disease activity (relapse rate), nor EDSS score were associated with the ECG parameters in MS patients.
Conclusion: Patients with MS have prolonged QRS duration and QT interval, more vertical QRS axis and more frequent presence of RBBB than healthy controls.

P3403 | SPOTLIGHT
The revealing timely ECG changes decreases the likelihood of undesirable cardiac events-trial

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Introduction: ECG technology is extremely useful in the diagnosis of a wide variety of cardiac diseases. Plenty of arrhythmic and ischemic conditions however are hard to diagnose and therefore treat because they don't appear during the physician's consultation. For cases with persistent or recurrent problems single-lead event recorders, holters or implantable devices have been developed to diagnose the underlying disease or symptoms. However due to their susceptibility to artefacts and the fact that they don't provide 12-lead ECG information data the information provided is of limited value. We investigated whether a self-imposed and personalized twelve-lead mobile ECG system was offering additional value in the management of patients with cardiac preconditions.
Methods: Patients meeting the following inclusion criteria were enrolled in this monocentric trial: 18 - 80 years of age, with at least one of the following: CABG, PCI, AMI in the last 12 months, AP treated pharmacologically, significant rhythm disturbance for which they received either a pharmacological or electrophysiological intervention, or recurrent palpitations of unknown origin. Further they had to be able to deal with the device, had to have regular access to the internet and signed the informed consent form. For a period of 3 months patients were asked to undertake measures once weekly and every time they were experiencing symptoms.
Results: In total 51 patients were recruited (45% female, average age 50,4 years). Main conditions were palpitations (41,2%), atypical chest pain (17,6%) and angina pectoris (13,7%). The patients recorded in total 1.237 ECG-readings with 2,2% of the measurements recordings being symptom-induced and the rest being undertaken during weekly measurements. In five patients (9,8%) the CardioSecur device was crucial in diagnosing a new or so far undiagnosed condition: 1 patient was suffering from severe ischemia, 4 patients were diagnosed with arrhythmias. Out of those patients 2 were suffering from atrial fibrillation, 1 from monofocal ventricular premature beats, with bi- and trigeminia and 1 from AV nodal re-entry tachycardia. During the study period no events were reported that the device should have been able to detect. Further patients reported a high ease of use.
Conclusion: We showed that CardioSecur is an important tool for diagnosing cardiovascular disease and adds value in the management of patients with rhythm disturbances and ischemic episodes. Further research is needed to validate this first results in larger patient cohorts over a longer period of time.

P3404 | BEDSIDE
Heterogeneous repolarization on magnetocardiography predicts adverse outcomes in patients with dilated cardiomyopathy

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Background: Prognostic significance of abnormal ventricular repolarization in heart failure (HF) patients has not been fully determined. Multi-channel magnetocardiography (MCG) is potentially useful for accurately evaluating heterogeneity of repolarization process, because it has a theoretical advantage to offer instantaneous mapping of "primary" current distribution with better spatial resolution compared to ECG modalities.
Methods: Patients (n=76) with HF due to dilated cardiomyopathy (LVEF 27±9%) underwent 64-channel MCG recordings (1kHz), yielding 2-D current mapping during ventricular repolarization. We excluded patients with complete right and left bundle branch block. Heterogeneous repolarization was defined to be present, when (1) two or more main currents without any continuity appeared during the ST-T phase (temporal heterogeneity) or (2) multiple currents (diverged >45 degree) was observed at some time point (spatial heterogeneity). Major cardiac events (cardiac death, sustained ventricular tachycardia, ventricular fibrillation, inappropriate ICD discharge, and admission due to acute heart failure) were investigated. Normal 24 subjects served as Control.
Results: All but one patient had abnormal Rep, differing from monotonic Rep in Control. Heterogeneous repolarization (HR) was found in 28 (Group-A), but not in 48 (Group-B). During the mean follow-up period of 24±17 months, MACE occurred more frequently in Group-A (17/28, 61%) than in Group-B (13/48, 27%; $p<0.0038$). Multivariate analysis (including LVEF, QRS duration, QTc and others) revealed HR as the only independent predictor (p=0.0162).

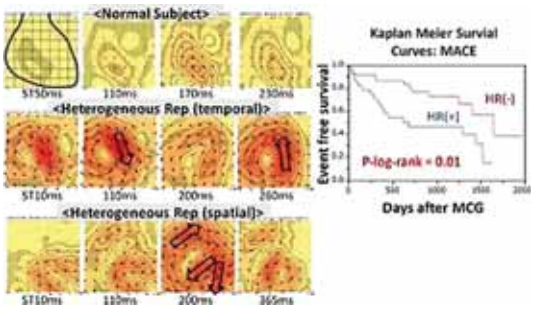

Figure 1. Representative ST-T maps and prognosis.

Conclusion: Heterogeneous repolarization revealed by high-resolution MCG analysis may serve to identify heart failure patients at high risk of adverse outcome.

P3405 | BEDSIDE
Microvolt T-Wave alternans in leads V1 V2 as a diagnostic criteria for Brugada syndrome

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Introduction: Presence of type 1 morphology in precordial leads positioned in a higher ICS, and augmentation of ST changes during recovery from exercise has diagnostic and prognostic implications in BrS. We hypothesize that TWA,

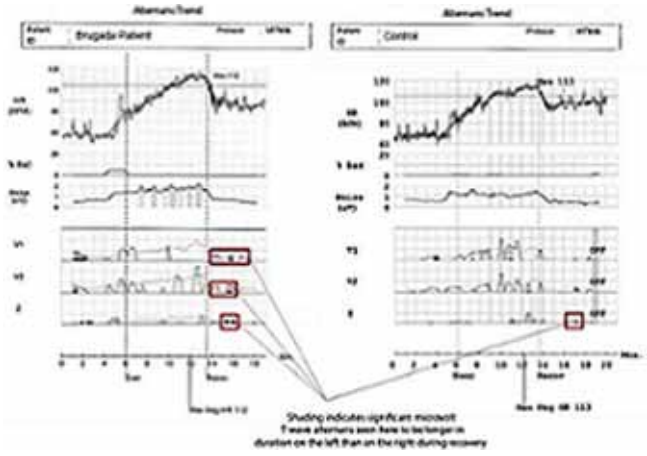
Figure 1. T-wave alternans in Brugada vs control.

measured in V1 V2 leads at the 3ICS and orthogonal lead Z (posterior anterior plane) on recovery from submaximal exercise is more common in BrS.
Methods: 16 males - 8 with Brs and 8 healthy controls (Ctrls) underwent TWA testing with precordial V1 V2 leads at the 3ICS. TWA was measured in V1 V2 and lead Z utilizing spectral methods, focusing on the first 3 minutes of recovery. We considered the alternans amplitude significant if the alternans ratio (AR) (ratio between AA and lead noise) was $\geq$3 in one orthogonal lead or in both V1 and V2 precordial leads.
Results: The mean+SD age for BrS patients and Ctrls were 40.5+12.4 and 29.1+3.0 years (p=0.024). respectively. Both BrS and Ctrls did not have sustained TWA during exercise. Presence of TWA during recovery was more common in BrS patients in V1 V2 and lead Z than Ctrls (7/8 Brs vs 2/8 ctrls. P=0.012). Recovery TWA duration in BrS patients was longer in these leads (median, IQR) 24.3s (14.6-39.4) vs 0s (0-7.0) p=0.05. There was no significant difference in the median AA for Brs vs Ctrls - 1.47μV (1.13-1.81) vs 1.16 μV (0.87-1.44) p=0.46.
Conclusions: BrS patients are more likely to have TWA and have longer TWA time during recovery in higher ICS V1/V2 and Z leads. Further work is required to determine its utility as a diagnostic tool, its correlation with provocative drug test, and its prognostic implications.

P3406 | BEDSIDE
A novel heart rate variability algorithm for noninvasive detection of myocardial ischemia: a prospective clinical trial

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Purpose: Low heart rate variability (HRV) has been shown to be associated with myocardial ischemia and increased risk for all-cause mortality and sudden cardiac death. We hypothesized that the novel HeartTrends HRV algorithm may be superior to conventional EST for the detection of myocardial ischemia in patients without known coronary artery disease (CAD).
Methods: We enrolled 400 subjects without known CAD in a prospective multicenter clinical trial. Study subjects underwent one-hour ECG acquisition for HearTrends HRV analysis prior to EST with myocardial perfusion imaging (MPI), and were subsequently followed-up over a 6-month period. Interpretation of test results was blinded. Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively) were calculated for EST and the HeartTrends HRV analysis, using MPI as the gold-standard for the noninvasive detection of myocardial ischemia.
Results: Mean age of study subjects was 61 ($\pm$10) years, 63% were males, 51% had hypertension, and 25% had diabetes mellitus. The sensitivity of the HeartTrends HRV algorithm for detecting myocardial ischemia was 80% as compared with 29% associated with standard EST (Table). The HeartTrends HRV algorithm showed a negative predictive value of 98% for ruling out significant myocardial ischemia. Consistent with these findings, multivariate analysis showed that the HeartTrends HRV algorithm was associated with a relative incremental value of 4.8 ($p<0.001$) as compared with EST for the detection of myocardial ischemia. Twenty-two patients underwent percutaneous coronary intervention at 6 months of follow-up, of whom 19 (86%) had a positive HeartTrends HRV test and only 8 (36%) had a positive EST.

Diagnostic yield of HeartTrends and EST

	HeartTrends	EST
Sensitivity	80%	29%
Specificity	71%	79%
PPV	22%	15%
NPV	98%	95%

Conclusion: Our data from a prospective clinical trial shows that the novel HeartTrends HRV algorithm provides superior sensitivity compared to conventional exercise stress testing for the noninvasive detection of myocardial ischemia.

ATHEROSCLEROSIS: CLINICAL ASPECTS

P3408 | BEDSIDE
Associations between lipoprotein associated phospholipase A2 levels and plaque burden in young adults

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Purpose: The prevalence of subclinical coronary atherosclerosis in young adults is not negligible. Lipoprotein-associated phospholipase A2 (Lp-PLA2) mass is associated with a poor prognosis as an independent predictor of mortality and morbidity in coronary heart disease. The aim of this study is to investigate the relationships between Lp-PLA2 and subclinical coronary atherosclerosis and plaque burden/structure in young adults.
Methods: A total of 748 subjects under 45 years of age who had undergone coronary computed tomography angiography (CCTA) were evaluated. The 101 patients in whom subclinical coronary atherosclerosis was detected on CCTA were included in the study as a study group and 160 age and gender matched healthy subjects were formed as a control group. Demographic and clinical properties of patients were recorded and blood samples were obtained for Lp-PLA2 and other biochemical analyzes.
Results: The Lp-PLA2 level was significantly higher in the study group compared to the controls (15.42$\pm$11.88 vs. 8.06$\pm$4.32; $p<0.001$). There were positive correlations between the Lp-PLA2 level and the number of involved arteries and the number of plaques in coronary arteries (r: 0.495, $p<0.001$ and r: 0.621, $p<0.001$, respectively). In terms of the plaque formation, Lp-PLA2 correlated significantly with mixed plaques (r: 0.657, $p<0.001$). In multivariate regression analysis, smoking, hs-CRP, uric acid levels, and Lp-PLA2 mass were independently correlated with subclinical coronary atherosclerosis.
Conclusion: In the present study, an independent association between Lp-PLA2 levels and subclinical coronary atherosclerosis was found in young adults, which may implicate the potential use of Lp-PLA2 mass in subclinical coronary atherosclerosis risk prediction.

P3409 | BEDSIDE
Interaction of metabolic syndrome on the relationship between arterial stiffness and adiponectin

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Background: Adiponectin plays a protective role in atherosclerosis. However, the relationship between low adiponectin levels and arterial stiffness has been inconstant. Adiponectin signaling can be affected in high insulin resistance statuses such as metabolic syndrome (MetS). Therefore, we hypothesized an interaction of MetS on the relationship between adiponectin and arterial stiffness.
Methods: A community-based cross-sectional study was performed in 822 subjects. Arterial stiffness was measured using brachial-ankle pulse wave velocity (baPWV). The recommendations of the Third Report of the National Cholesterol Education Program Expert Panel were used for MetS criteria. Multiple linear regression analysis was used for testing the interaction.
Results: Log-transformed adiponectin (LnADPN) and baPWV were not significantly correlated (r =-0.021, p=0.509). In multiple linear regression, LnADPN was negatively associated with baPWV in all subjects (β =-0.103, $p<0.001$), in the subjects without MetS components (β =-0.313, $p<0.001$) and in the subjects with 1 MetS component (β =-0.156, $p<0.05$), whereas not significantly associated with baPWV in the subjects with 2 or more MetS components. The correlation between LnADPN and baPWV was negative in the subjects without MetS components (r =-0.138, $p>0.05$), and was positive in the subjects with 3 or more MetS components (r=0.184, $p<0.05$). After confounding factors were adjusted, the correlation between LnADPN and baPWV in the subjects with 3 or more MetS components was not significant (r=0.051), whereas the negative correlation between LnADPN and baPWV in the subjects without MetS components was stronger (r= -0.377, $p<0.001$). The interaction of the number of MetS components on the relationship between baPWV and LnADPN was significant (p=0.001).
Conclusion: The protective effect of adiponectin on arterial stiffness is attenuated as the number of MetS components increases, which may implicate adiponectin resistance in high insulin resistance states.

P3410 | BEDSIDE
Assessment of carotid artery intima-media thickness and aortic pulse wave velocity in diffuse coronary artery ectasia

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Objectives: It has been shown that carotid intima-media thickness (CIMT) and aortic pulse wave velocity (PWV) constitute important independent risk factors for cardiovascular disease. We hypothesized that CIMT and aortic PWV are increased in patients with diffuse coronary artery ectasia.
Study design: Diffuse coronary artery ectasia (CAE) has been defined as a diffuse dilatation (at least 50% greater than the diameter of the normal portion) in at least one coronary artery and localized or diffuse disease in other coronary artery. Study group consisted of 54 consecutive patients (43 males, 11 females; mean age 65.7$\pm$13.1 years) with diffuse CAE whereas 58 patients (47 males, 11 females; mean age 64.3$\pm$10.9 years) without CAE comprised the control group. CIMT and aortic PWV were measured in two groups of patients who underwent coronary angiography.
Results: Study and control groups were similar in terms of age, sex, body mass index, and the frequencies of hypertension, hyperlipidemia, diabetes mellitus, and smoking ($p>0.05$). The mean CIMK and aortic PWV were significantly higher in the study group compared to the control group (0.81$\pm$0.16 mm and 0.74$\pm$0.13 mm, p=0.021; and 11$\pm$2.4 m/sec and 9$\pm$2.7 m/sec, $p<0.001$, respectively). A significant but a weak relationship was found between CIMK and the presence of diffuse CAE (r=0.219; p=0.021). Compared to CIMT, a more powerful positive correlation was found between aortic PWV and the presence of diffuse CAE (r=0.370; $p<0.001$). Logistic regression analysis showed that the relationship be-

tween diffuse CAE and aortic PWV (OR 1.339; 95% CI 1.135-1.579; p=0.001) was independent of other factors. An aortic PWV ≥9.3 m/sec measured on admission had a 78% sensitivity and 62% specificity in predicting diffuse CAE at ROC curve analysis.
Conclusion: According to the results of the present study, both CIMT and PWV were increased in patients with diffuse CAE. Of note, only the PWV was found to have an independent relationship with the presence of CAE. It may be speculated that, the involvement of media compared to intima is more likely in patients with CAE. This pathophysiology may explain why PWV, compared to CIMT, has more powerful relationship with CAE.

P3411 | BEDSIDE
Hypothyroidism is associated with retinal arteriolar narrowing in a population-based sample

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Objective: Recent studies have shown associations of hypothyroidism with arterial blood pressure, atherosclerosis, and inflammation. Based on these pathways there might also be an association between hypothyroidism and retinal arteriolar narrowing, a marker of micro-vascular damage from hypertension, atherosclerosis, and inflammation. Thus, our aim was to investigate the putative association between serum thyrotropin (TSH) levels and retinal arteriolar narrowing defined by arterio-venous ratio (AVR) from static vessel analysis.
Material and methods: We used data from 3189 individuals from the second cohort of the Study of Health in Pomerania (SHIP-TREND-0). Fundus photography of the central retina was recorded with a non-mydriatic camera, and images were evaluated by one experienced reader. An AVR <0.8 was defined as decreased. Low and high serum TSH levels were defined by the cut-offs 0.3 mIU/L and 3.0 mIU/L Serum TSH levels were associated with AVR by linear and Poisson regression models adjusted for age, sex, cigarette smoking, alcohol consumption, and beta blocker intake.
Results: Serum TSH levels were significantly associated with AVR (β = -0.028; 95% confidence interval (CI) -0.049; -0.007; p=0.009) and with a decreased AVR <0.8 (relative risk 2.05; 95% CI 1.13; 3.73; p=0.019). Individuals with high TSH had a 1.43 higher risk of a decreased AVR (95%-CI 1.04; 1.96; p=0.027) than individuals with serum TSH levels within the reference range. There was no association of low TSH (<0.3 mIU/L) or serum TSH levels within the reference range with AVR or decreased AVR.
Conclusions: Our results substantiate evidence for an association between hypothyroidism and retinal arteriolar narrowing. Potential mechanisms that might explain this association are long-term hypertension, atherosclerotic processes, and inflammation.

P3412 | BEDSIDE
Eicosapentaenoic acid to arachidonic acid ratio is associated with the presence of thin-cap fibroatheroma determined by optical coherence tomography

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Background: A low eicosapentaenoic acid to arachidonic acid (EPA/AA) ratio has been associated with cardiovascular events. However, the relationship between EPA/AA ratio and plaque vulnerability assessed by optical coherence tomography (OCT) has not been fully examined.
Methods: We evaluated 70 patients (including 59 patients with acute coronary syndrome and 11 patients with stable angina pectoris) who underwent percutaneous coronary intervention using OCT and investigated their culprit lesion morphologies. We divided the patients into 2 groups according to their OCT findings: patients with thin-cap fibroatheroma (TCFA) and those without TCFA, and compared EPA/AA ratio.
Results: Thirty-three and 37 patients with and without TCFA, respectively, were identified. Lower levels of EPA/AA ratio were found in patients with TCFA than those without TCFA [0.34 (0.20-0.44) vs. 0.50 (0.325-0.63), p=0.001]. There was a significant positive correlation between EPA/AA ratio and fibrous cap thickness (Spearman ρ=0.37, p=0.002). Multivariate logistic regression analysis showed that EPA/AA ratio was an independent predictor of TCFA (odds ratio 0.061, 95% confidence interval 0.005 to 0.787, p=0.032). Receiver-operating characteristic curve analysis showed that <0.49 of EPA/AA ratio could predict TCFA with 87.9% sensitivity and 54.1% specificity.
Conclusions: Low EPA/AA ratio is associated with vulnerable coronary plaque assessed by OCT.

P3413 | BEDSIDE
Impact of Indoxyl sulfate on the progression of endothelial dysfunction and atherosclerosis in chronic kidney disease patients

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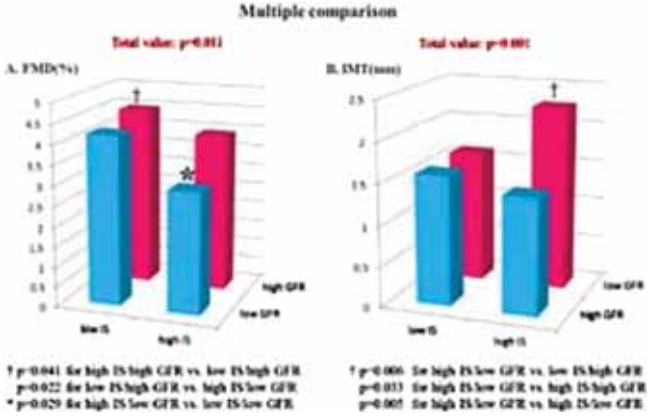
Purpose: Recent data suggest that indoxyl sulfate (IS) induces vascular disorders. However, the IS specific roles are unclear because it is a confounder of renal impairment. We demonstrated this cross-sectional study for the purpose of to investigate the associations of eGFR and IS with the endothelial function and carotid atherosclerosis, and to identify the impact of IS on vascular dysorder independent of renal impairment in pre-dialysis CKD patients.
Methods: Enrolled 100 pre-dialysis CKD patients were evaluated the endothelial function and atherosclerosis by FMD and carotid IMT. Plasma levels of IS and eGFR were also measured, and correlation with FMD and max IMT were elucidated.
Results: Both FMD and max IMT had significant relations with eGFR and IS (p=0.029, 0.005, p=0.02, 0.025, respectively). Multivariate analysis revealed that both eGFR and IS were significant predictors for the endothelial dysfunction and carotid atherosclerosis. To investigate IS specific impact, we divided the participants into 4 groups by the level of IS and eGFR. FMD was significant lower in high IS/high GFR group compare to low IS/high GFR group, also high IS/low GFR group than low IS/low GFR group (p=0.04, 0.02, respectively). Max IMT was significant thicker in high IS/low GFR group than low IS/low GFR group. A multi comparison by ANOVA appeared the endothelial dysfunction and carotid atherosclerosis were progressed in high IS/low GFR group than other groups significantly.



Multipul comparisons of IMT and FMD

Conclusion: Our results appeared that IS is an independent predictor for progression in endothelial dysfunction and atherosclerosis in CKD patients. These results suggest the pivotal role of uremic toxins like IS on vascular damage in CKD patients.

P3414 | BEDSIDE
Association of toll-like receptor 4 on human monocyte subsets and vulnerable characteristics of coronary plaque as assessed by 64-slice multi-detector computed tomography

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Purpose: Although circulating levels of CD14+CD16+ monocyte subsets were related to coronary plaque rupture, it remains unsolved how up-regulation of the monocyte subsets lead to plaque rupture. Recent studies have shown that Toll-like receptor 4 (TLR-4) is involved in monocyte activation of patients with accelerated forms of atherosclerosis. We investigated the relationship between expressions of TLR-4 on monocyte subsets and vulnerability characteristics of coronary plaque assessed by 64-slice multi-detector computed tomography (MDCT) in patients with stable angina pectoris (SAP).
Methods: We enrolled 48 patients with SAP who underwent MDCT. Three monocyte subsets (CD14++CD16–, CD14++CD16+, and CD14+CD16+) and the expression of TLR-4 were measured by flow cytometry. Coronary artery plaques were assessed by 64-slice MDCT. We defined non-calcified coronary plaque vulnerability according to the presence of positive remodeling (remodeling index >1.05) and/or low CT attenuation plaques (<35HU).
Results: A total of 29 (60%) patients had identifiable vulnerable plaque. The circulating peripheral CD14++CD16+ monocytes more frequently expressed TLR-4 than CD14++CD16– and CD14+CD16+ monocytes (p<0.001). The relative proportion of the expression of TLR-4 on circulating peripheral CD14++CD16+ monocytes was significantly greater in patients with vulnerable plaque compared to in those without (10.2 [4.4 to 14.5] vs. 4.5 [2.4 to 7.0] %, p=0.016). In addition, the relative proportion of TLR-4 on circulating peripheral CD14++CD16+

monocytes was positively correlated with remodeling index (r=0.36, p=0.012) and negatively correlated with CT attenuation value (r= -0.41, p=0.004).
Conclusions: The present results suggest that an increased expression of TLR-4 on CD14++CD16+ monocytes is related to coronary plaque vulnerability in patients with SAP. TLR-4 may play an important role in coronary plaque vulnerability.

P3415 | BEDSIDE
Role of adiponectin in early atherosclerosis and incident cardiovascular disease in high-risk european subjects

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Objective: To investigate whether adiponectin has a causal protective influence on subclinical atherosclerosis.
Background: Low plasma adiponectin is generally associated with cardiovascular disease. However, whether adiponectin is a marker of adipose function, reflects other mechanisms implicated in atherosclerosis or exerts direct anti-atherogenic actions remains unknown.
Methods: Plasma adiponectin concentration was tested for association with baseline carotid intima-media thickness (IMT), IMT progression over 30 months and occurrence of cardiovascular events within three years in 3,430 subjects (women, n=1,777; men, n=1,653) with high cardiovascular risk but no prevalent disease. A gene score of adiponectin-raising alleles in six loci, recently identified in a large multi-ethnic meta-analysis, was analysed for influence on IMT.
Results: Adiponectin levels were inversely associated with baseline mean bifurcation IMT (Bif-IMT; beta -0.018, p<0.001) and progression of mean common carotid IMT (beta -0.0022, p=0.047) in men, independent of established risk factors, whereas no association was seen in women. Adiponectin levels were also inversely associated with cardiovascular events (hazard ratio 0.69, p<0.001). An allelic score of adiponectin-raising alleles, not associated with type 2 diabetes mellitus (T2D), diabetes related traits or lipids, was inversely associated with baseline mean Bif-IMT (beta -0.0008, p=0.004: Fig. 1) and incident coronary events (hazard ratio 0.77, p=0.031) in men but not in women.

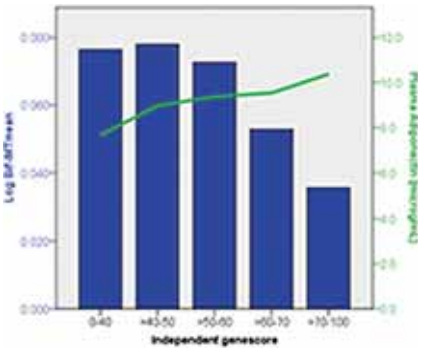

Figure 1. Gene score assoc. with Bif-IMT in men.

Conclusions: The genetic and plasma adiponectin findings presented here are evidence for an unknown adiponectin-associated mechanism which protects against subclinical atherosclerosis with effects being largely confined to men.

P3416 | BEDSIDE
Non-sleepy obstructive sleep apnea: A risk for cardiovascular damages

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Purpose: Obstructive sleep apnea (OSA) is an independent risk for cardiovascular disease. Apnea-hypopnea index (AHI) is a marker for the severity of OSA, and it also reflects the severity of cardiovascular damages. On the other hand, Epworth Sleepiness Scale (ESS) is a marker of clinical symptom of OSA (sleepiness), it has not been fully clarified ESS reflects the severity of cardiovascular damages. The present study was conducted to examine whether ESS is associated with the severity of cardiovascular damages independent of the severity of OSA.
Methods: In consecutive 1724 patients diagnosed as OSA (AHI≧5) by polysomnography, ESS, brachial-ankle pulse wave velocity (baPWV) and left ventricular mass index (LVMI) were measured. Logistic regression analysis of the ESS for baPWV and LVMI was performed.
Results: AHI was positively associated with baPWV and LVMI. On the contrary, ESS was negatively associated with baPWV (Fig. 1, left panel) and LVMI. Multivariate regression analysis showed that ESS was significantly associated with baPWV and LVMI independent of AHI. When patients were divided into two groups: non-sleepy OSA (ESS≦10) group and sleepy OSA (ESS≧11) group, baPWV (15.5±0.4 vs. 14.3±0.3 m/sec, p<0.001) and LVMI (132±34 vs. 123±28 g/m^2, p<0.001) were higher in the non-sleepy OSA group than those in sleepy OSA group (Fig. 1, right panel). These differences were significant even after the adjustments for confounding factors.

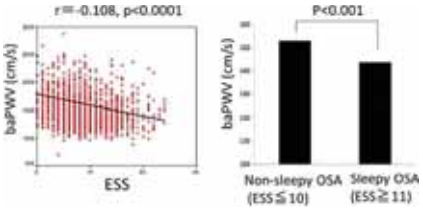

Figure 1. Sleepiness and arterial stiffness in OSA.

Conclusions: Cardiovascular damages were prominent in patients with non-sleepy OSA than sleepy OSA. Thus, in addition to the severity of OSA, absence of sleepiness may be a risk for cardiovascular events in patients with OSA.

P3417 | BEDSIDE
Volume elastic modulus of the brachial artery and coronary artery stenosis in patients with suspected stable coronary artery disease

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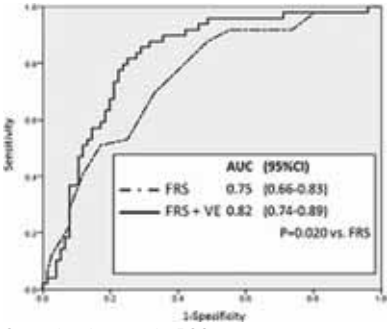
Objective: The aim of the present study was to examine the association between non-invasive measurement of the brachial artery volume elastic modulus (VE), an index of arterial stiffness, and the presence of coronary artery stenosis in patients with suspected stable coronary artery disease (CAD).
Methods: A total of 125 patients with suspected stable CAD underwent oscillometric measurement of the brachial artery VE. Coronary angiography was thereafter carried out to diagnose CAD, defined as having ≥75% stenosis in the epicardial coronary arteries.
Results: The VE was significantly higher in patients with CAD (0.96±0.22 mmHg/%) than in those without CAD (0.82±0.21 mmHg/%, p=0.003). In the multiple logistic regression analysis, the VE was an independent determinant of CAD (odds ratio 1.30 per 0.1 mmHg/% increase, 95%CI 1.05-1.68) even after adjusting for multiple potential confounders including the Framingham Risk Score (FRS), which was calculated based on the conventional cardiovascular risk factors. The area under the curve of the receiver operating characteristic curve analysis for discriminating CAD was significantly increased after the addition of VE to the FRS (0.75 to 0.82, p=0.002) (figure). Continuous net reclassification improvement and integrated discrimination improvement by adding VE to the FRS were 0.47 (95%CI 0.12-0.82) and 0.09 (95%CI 0.04-0.13), respectively.



Comparison between the ROC curves.

Conclusions: The brachial VE was significantly associated with the presence of coronary artery stenosis, and the addition of VE to the FRS improved the ability to identify patients with coronary artery stenosis among those with suspected stable CAD.

ATHEROSCLEROSIS: BASIC ASPECTS

P3419 | BENCH
Ivabradine induces an atheroprotective gene expression profile in the endothelium of ApoE deficient mice before plaque formation

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Purpose: Ivabradine reduces heart rate (HR) by selectively inhibiting the If current in the sinus node. A sub-group of the BEAUTifUL study showed that ivabradine reduces the incidence of myocardial infarction in coronary artery disease (CAD) patients with HR $\geq$70bpm, suggesting a protective effect on the arterial wall. The SIGNifY study is currently testing this hypothesis in more than 19000 CAD patients. In dyslipidaemic mice, ivabradine improves vascular function and reduces aortic plaques area. It has been suggested that ivabradine may exert a protective activity by decreasing low/oscillatory shear stress, which is proinflammatory in the endothelium. This study aims to determine if HR reduction with ivabradine induces an atheroprotective gene expression profile in the endothelium of dyslipidaemic mice before plaque formation.
Methods: 6 week-old ApoE deficient mice (n=6), fed a chow diet, were treated with ivabradine (30 mg/kg/day, in drinking water) for 2 or 4 weeks. Two control groups (n=6) received no ivabradine. Ivabradine reduced HR by 17.4% and 22.9% in mice treated for 2 weeks and 4 weeks respectively. At the end of treatment, endothelium-enriched RNA was isolated from the aortic arch. Gene expression was analyzed by Agilent Whole Mouse Gene Expression Microarray (60k probes). Pathway analysis was performed using DAVID tools. Principal components analysis showed that most of the variability in gene expression can be attributed to ivabradine treatment and was independent of treatment duration. Differentially expressed genes were selected as having a $\geq$1.5-fold expression difference between treated and untreated groups with a p-value $\leq$0.01 at unpaired t-test.
Results: Treatment induced changes in the expression of 930 transcripts. Shear stress-modulated pathways such as MAPK signalling and steroid biosynthesis process (both inhibited by treatment) were among the most significantly affected pathways (p-value = 0.0065 and 0.0009, respectively). We found up-regulation of anti-inflammatory genes and down-regulation of pro-apoptotic and pro-inflammatory genes, the majority of which were NF-kappa B and/or Ang II-regulated genes. Among them, the receptor for oxidized lipoprotein (Olr1) was strongly downregulated (3.2 fold).
Conclusions: In dyslipidaemic mice, short term treatment with ivabradine induces an atheroprotective gene expression profile in the endothelium. Since many of the affected genes are shear stress regulated, our data suggest that shear stress frequency modulation could be part of the molecular mechanisms by which ivabradine protects the endothelium.

P3420 | BENCH
Direct thrombin inhibition with dabigatran improves endothelial function and atherosclerosis in ApoE-deficient mice

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Background: Recently developed oral anticoagulants directly inhibit thrombin (dabigatran). Thrombin is involved in the pathogenesis of atherosclerosis. We investigated the effects of direct thrombin inhibition on atherosclerosis and endothelial function in a hypercholesterolemic mouse model with accelerated atherosclerosis (ApoE–/–-mice).
Methods: Wild type and ApoE–/–-mice were treated with a cholesterol-rich diet for 12 weeks and dabigatran (900mg/kg body weight) or placebo. Wild type (WT, C57/B6) mice served as control. Endothelial function of aortic rings was assessed by pharmacological stimulation with carbachol (endothelium-dependent) using glyceroltrinitrate (endothelium-independent) as control. Atherosclerotic lesion formation was evaluated with oil-red staining and vascular collagen content was determined by Sirius red staining. Modulation of reactive oxygen species (ROS) production was determined by semiquantitative immunohistochemical staining. The amount of NO located intracellularly was evaluated with Diaminofluoreszein diacetate staining. The adjustment of endothelial nitric oxide synthase (eNOS) was determined by semiquantitative immunohistochemical staining.
Results: Treatment with dabigatran attenuated atherosclerotic plaque formation (ApoE–/–-Dabi: 3$\pm$0.7% of ApoE–/–-control, $p<0.001$), decreased collagen content (ApoE–/–-Dabi: 29.4$\pm$5.9% of ApoE–/–-control, p=0.01) and ROS production in DHE-staining (ApoE–/–-Dabi: 50.7$\pm$4.1% of ApoE–/–-control, p=0.014) in parallel to an improvement of endothelial function (ApoE–/–-control 42.6$\pm$2.7 vs. ApoE–/–-Dabi 62.9$\pm$3.3% of phenylephrine-induced contraction, p=0.001) at 100 μM carbachol. Furthermore, by animals treated with dabigatran, the eNOS was upregulated and they had a higher concentration of intracellular NO as a marker for endothelial vitality.
Conclusion: Direct thrombin inhibition improved endothelial function, increased the amount of intracellular NO and eNOS, reduced atherosclerotic lesion size, vascular collagen content and oxidative stress in hypercholesterolemic atherosclerosis. Interference with the coagulation system might provide a therapeutic means to modify atherosclerotic disease progression.

P3421 | BENCH
The effects of beta3-adrenoceptor activation on ApoA1 and SR-B1 in aged ApoE-deficient mice

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Purpose: β3-Adrenoceptors (β3-AR) protects against the progression of atherosclerosis. However, the specific mechanism of this antiatherosclerotic effect is still not clear. Thus, the aim of this study was to determine the molecular basis of the antiatherosclerotic effects.
Methods: Male homozygous apolipoprotein E knockout (ApoE–/–) mice on a high-fat diet and wild-type (WT) C57BL/6J mice on a normal diet were used. Fifty ApoE–/– mice were randomized into five treatment groups: atherosclerotic model, atorvastatin, low-dose β3-AR agonist, high-dose β3-AR agonist and β3-AR antagonist groups. Serum lipids were measured when the treatments ended. mRNA expressions of liver ApoA-1 and SR-B1 were detected by quantitative real-time PCR. Protein expressions of ApoA-1 and SR-B1 in the livers were determined by western blot analysis.
Results: Compared with ApoE–/– control mice, chronic β3-AR agonist treatment significantly increased plasma high-density lipoprotein cholesterol levels. Compared with the age-matched WT mice, the ApoA-1 mRNA and protein expression level in ApoE–/– mice were significantly increased. Compared with ApoE–/– control mice, the ApoA-1 mRNA and protein expression level in liver were significantly increased in the atorvastatin and β3-AR agonist groups. The SR-B1 mRNA expression and protein level in liver of ApoE–/– mice was significantly decreased compared with wild type mice. The SR-B1 mRNA expression and protein in liver were significantly increased in the atorvastatin and β3-AR agonist groups, compared with the ApoE–/– atherosclerotic model mice.
Conclusions: The present study demonstrated that long-term β3-AR activation can regulate lipid metabolic disorders, and reduced progression of atherosclerosis. This effect may be related to ApoA-1and SR-B1.

P3422 | BENCH
MicroRNA expression in peripheral blood monocytes in different stages of atherosclerosis development in humans

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Purpose: Increasing evidence has demonstrated that microRNAs (miRNAs) are involved in vascular inflammation, making them an interesting target to understand macrophages functions as essential regulators of initiation and development of atherosclerosis. The aim of this study is to analyse the miRNA expression profiles in human peripheral blood monocytes in different stages of vascular proliferative diseases.
Patients and methods: Microarrays were used to analyse the global expression of 352 miRNAs in human peripheral blood monocytes from healthy donors (n=30), patients with acute ST-segment elevation myocardial infarction (STEMI, n=30), and during two months of follow-up after STEMI (n=27) as well as patients with transient ischemic attack (TIA) or stroke (n=10). We also assessed miRNA expression profile in human endatherectomy samples from coronary artery (n=10) or carotid artery (symptomatic, n=10 and asymptomatic, n=14) and in healthy arteries as control (mammary artery, n=15). Expression profiles of the miRNAs were verified using TaqMan real-time PCR.
Results: We identified 21 miRNAs, which are significantly dysregulated in blood monocytes from patients with STEMI in comparison to healthy controls and 15 miRNAs, which were aberrantly expressed in endatherectomy samples. Interestingly, most of the highly expressed miRNAs in monocytes of patients with STEMI as well as with TIA or stroke are known as a cardiac-specific (miR-1, miR-21), muscle-enriched (miR-143), inflammation-associated (miR-9, miR19b), and monocytic differentiation-associated (miR-22) miRNAs. In contrast, endothelial enriched miR-92a tends to be lower in patients with cardiovascular diseases. During two months of follow-up the upregulated miR-9 and -21 were close to baseline, whereas miR-1, -19b, -22 and -143 remained higher than controls. Remarkably, reciprocal changes in the expression levels of these miRNAs were found in atherectomy probes, but not in healthy vessels.
Conclusion: MiRNA expression profiles in human monocytes is altered in different stages of atherosclerosis development. The results suggest that miRNAs are novel regulatory RNAs for acute and chronic vascular inflammation and may be a new therapeutic target for vascular proliferative diseases such as atherosclerosis.

P3423 | BENCH
CTCF regulates the formation of apoptosis by conjugating the two opposite pathways in arterial smooth muscle cell

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Purpose: Recent studies revealed apoptosis of arterial smooth muscle cell (SMC) does not necessarily mean the vulnerability of the fibrous cap covering the

atherosclerotic plaque but means a requirement for the cap tissue to be cleaned up and remodeled to be strengthened. The multifunctional chromatin modulator CCCTC binding protein (CTCF) epigenetically promotes or inhibits apoptotic process and becomes the therapeutic target in several types of tumor cells. This study assessed the role of CTCF in the apoptotic process of arterial SMC.
Methods: Human SMC were cultured. CTCF mRNA was either knocked down using specific siRNA or up-regulated by transfection with plasmid loading human CTCF cDNA. The gene expression was investigated by real-time PCR analysis using SYBR-green method. Microarray profiling analysis of mRNAs was performed. The caspase 3/7 activity was measured either by treatment with staurosporine or by reaction of anti-Fas antibody and Fas antigen expressed on the SMC following primed with cytokines. The nuclear DNA fragmentation was revealed by TUNEL reaction.
Results: Knocking down of CTCF mRNA significantly suppressed the increase in the caspase 3/7 activity either by treatment with staurosporine (35+4%, $p<0.01$, n=7) or by Fas-anti-Fas system (56+9%, $p<0.01$, n=6). Moreover in the former case, TUNEL reaction showed significant suppression of the nuclear DNA fragmentation (41+6% of nuclei, $p<0.01$, n=7). On the other hand, overexpression of CTCF mRNA significantly increased the caspase 3/7 activity (35+9%, $p<0.01$, n=6). Real-time PCR analysis following microarray profiling of mRNA revealed knocking down of CTCF significantly up-regulated p53 (82+9%), p53 up-regulated modulator of apoptosis (PUMA) (47+8%) and BAX (81+11%) genes, indicating usual suppressive role of CTCF in the p53-PUMA pro-apoptotic system. While at once, knocking down of CTCF significantly up-regulated the expression of two anti-oxidant enzyme genes: superoxide dismutase 2 (35+4%) and heme oxigenase 1 (85+7%).
Conclusion: Down-regulation of CTCF significantly inhibited apoptosis of SMC. CTCF regulates the formation of apoptosis by conjugating the two opposite pathways in the SMC. These mechanisms may contribute to the vulnerability of the atherosclerotic plaque in the context dependent ways.

P3424 | BENCH
Epigenetic regulation of NADPH oxidase by histone acetylation in human aortic smooth muscle cells

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Purpose: Members of NADPH oxidase (Nox) family are key regulators of cell physiology. Produced in excess, Nox-derived reactive oxygen species (ROS) are highly detrimental in numerous cardiovascular pathologies such as atherosclerosis. The mechanisms of Nox regulation and the specific function of each Nox subtype are yet to be discovered. Post-translational modifications of histones of conserved lysine residues by specialized enzymes results in chromatin conformational changes and influence the DNA accessibility for transcription factors. The precise role of epigenetic mechanisms of Nox regulation by histone modification/histone-modifying enzymes is scantly elucidated. In this study we aimed at investigating the implication of histone acetylation in mediating Nox regulation in human aortic smooth muscle cells (SMCs) exposed to pro-inflammatory conditions.
Methods: Human aortic SMCs were treated with CTPB, a potent activator of histone acetyltransferases (HAT) or interferon gamma (IFNγ) for up to 24h. Lucigenin-enhanced chemiluminescence, dichlorofluorescein assay, real-time PCR, Western blot, and chromatin immunoprecipitation assays were employed to investigate Nox regulation.
Results: CTBP-activated HAT dose-dependently induced up-regulation of intracellular ROS formation, Nox activity, and the mRNA and protein expression levels of the Nox1, Nox4, and Nox5 isoforms. IFNγ treatment mimicked the effect of HAT agonist. It also induced significant increases in HAT1 protein expression level and acetylation of H3K27 (H3K27ac). Pharmacological inhibition as well as silencing of HAT1 reduced significantly but differentially the IFNγ-induced Nox activity and expression. Specific H3K27ac (a marker of positive-acting regulatory regions in the genome) and HAT1 – Nox1/4/5 promoters interactions were identified by chromatin immunoprecipitation assays. Immunofluorescence microscopy indicated an increased expression of HAT1 and H3K27ac in SMCs underlying fibro-lipid and unstable atherosclerotic lesions in human carotid arteries.
Conclusions: The data provide evidence that histone acetylation play a role in mediating Nox expression and function in IFNγ-exposed SMCs. Understanding the complex networking among transcription factors and epigenetic mechanisms converging to Nox regulation may contribute to developing novel pharmacological strategies to reduce the adverse effects of oxidative stress in atherosclerosis.
Work supported by Romanian Academy and Ministry of Education, and Research (PN-II-ID-PCE-2011-3-0548 and PN-II-RU-TE-2011-3-0142).

P3425 | BENCH
Inhibitory effects of eicosapentaenoic acid on arterial calcification in klotho mutant mice, an animal model of typical aging

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Background: The klotho gene was identified as an "aging-suppressor" gene in mice that accelerates arterial calcification when disrupted. We and other investigators have reported that expression levels of serum and local vascular klotho are reduced in patients with chronic kidney disease (CKD) and that the decrease in expression level of klotho is associated with arterial calcification and stiffness in patients with CKD. Intake of eicosapentaenoic acid (EPA), an n-3 fatty acid, reduces the risk of fatal coronary artery disease. However, the effects of EPA on arterial calcification have not been fully elucidated.
Purpose: The aim of this study was to evaluate the effect of EPA on arterial calcification in klotho mutant mice.
Methods: Four-week-old klotho mutant mice (n=24, 12 males & 12 females) and wild-type (WT) mice (n=24, 12 males & 12 females) were given a diet containing 5% EPA (EPA food, klotho and WT: n=12, each) or not containing EPA (control food, klotho and WT: n=12, each) for 4 weeks. Calcium volume score of the thoracic and abdominal aorta was assessed by multi-detector computed tomography before and after 4 weeks of feeding. Arterial smooth muscle cells (SMCs) were obtained by the explanted culture method.
Results: Calcium volume scores were significantly elevated in klotho mice after 4 weeks of control food (before vs after feeding, $P<0.05$), but they were not elevated in klotho mice after 4 weeks of EPA food and in WT mice after 4 weeks of control or EPA food (before vs after feeding, P=NS). Change in calcium volume score in control food-fed klotho mice (Δ calcium volume score: 81 ± 28 mm^3) was significantly greater than that in EPA-fed klotho mice (18 ± 17 mm^3, $P<0.05$) and that in control food-fed WT mice (8 ± 6 mm^3, $P<0.005$) or EPA-fed WT mice (2 ± 11 mm^3, $P<0.005$). Activity of NADPH oxidase (NOX), an enzyme that generates superoxide, and expression level of NOX4 gene were significantly higher in arterial SMCs of klotho mutant mice than in those of WT mice. PCR-array analysis of osteogenesis genes showed that expression of Bmp5 and Csf2 genes was up-regulated and that of Igf1 was down-regulated in SMCs of klotho mutant mice. mRNA of the gene encoding G-protein-coupled receptor 120 (GPR120), a receptor of n-3 fatty acids, was expressed in arterial SMCs. EPA decreased NOX activity and improved altered expression levels of NOX4 and those osteogenesis genes.
Conclusions: Administration of EPA prevents arterial calcification together with reduction of NOX activity and amelioration of osteogenesis gene expression.

P3426 | BENCH
Rivaroxaban, a direct factor Xa inhibitor, attenuates plaque progression and destabilization in ApoE-deficient mice by inhibiting macrophage activation

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Background: Activated factor X (FXa) is a key member in the coagulation cascade responsible for thrombin generation, although accumulating evidence suggests that it also promotes inflammatory responses in many cell types, contributing to the pathogenesis of metabolic syndrome and/or atherosclerosis. In this study, we assessed the hypothesis that rivaroxaban, a direct FXa inhibitor, attenuates plaque progression and destabilization through the inhibition of pro-inflammatory activation of macrophages.
Methods and results: Rivaroxaban (5 mg/kg/day) or vehicle (control) was administered for 20 weeks to 8-week-old apolipoprotein E-deficient (ApoE–/–) mice fed a western-type diet. There were no differences in body weight gain, blood pressure, plasma glucose levels and plasma lipid levels between the groups. Rivaroxaban significantly reduced atherosclerotic lesion progression as determined by en-face Sudan IV staining in aortic arch compared with control group ($20.9\pm5.6\%$ vs. 15.6 ± 2.7; $P<0.01$). Result of Oil red O staining in aortic root demonstrated that rivaroxaban significantly decreased lipid deposition in plaques ($P<0.01$). Histological analyses demonstrated that rivaroxaban significantly reduced MMP-9 expression and increased collagen content in plaques compared with control group ($P<0.05$ and $P<0.01$, respectively). Quantitative RT-PCR analyses using abdominal aorta revealed that rivaroxaban treatment reduced mRNA expression of inflammatory mediators including MMP-9. In vitro experiments using mouse peritoneal macrophages demonstrated that FXa up-regulated mRNA expression of inflammatory molecules (e.g., MCP-1 and MMP-9) compared with non-stimulated control ($P<0.001$). Rivaroxaban attenuated expression of these inflammatory molecules ($P<0.05$). Furthermore, an agonist peptide for protease-activated receptor (PAR)-2, one of the major receptors of FXa, promoted the expression of these inflammatory molecules in this cell type ($P<0.05$).
Conclusion: Rivaroxaban attenuates atherosclerotic plaque progression and destabilization in ApoE–/– mice by inhibiting macrophage activation through FXa-PAR2 pathways at least partially.

P3427 | BENCH
Influence of toll-like receptor 7 in acute and chronic vascular injury

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Background: Atherosclerosis is a chronic inflammatory disease characterized by dysfunction, apoptosis and necrosis of vascular cells. Local cellular damage leads to the release of nucleic acids, which can be detected by endosomal or intracellular pattern recognition receptors (PRR) of the innate immune system. Toll-like-receptor 7 (TLR7), is a PRRs specialized in detecting specific single-stranded RNA motives. We hypothesized that specific activation of TLR7 affects vascular biology in acute and chronic vascular injury mouse model.
Methods and results: 12-week-old C57BL/6J wild-type mice (n=13) were subjected to an electric denudation of the left common carotid artery. Reendothelialisation was quantified 5 days after surgery. 20 μg of the specific TLR7-agonist R848 or vehicle was injected intravenously every 48 hours starting two days prior to the carotid injury. Stimulation of TLR7 impaired reendothelialisation in acute vascular injury of the common carotid artery (43.78±3.23% vs 29.58±2.02%, $p<0.01$). The number of circulating endothelial microparticles (EMP) and endothelial progenitor cells (EPC) were significantly increased in TLR7-stimulated mice ($p<0.05$), and furthermore mediated a systemic inflammatory response by induction of IL-6 ($p<0.0001$), and Rantes ($p<0.0008$). For chronic vascular injury, 10 week old Apolipoprotein E-deficient (ApoE–/–) C57BL/6J mice (n=12) received a high-fat, cholesterol-rich diet for a total of 7 weeks and were injected subcutanously every other day with 20μg of R848. TLR7-stimulated ApoE–/– mice developed significantly larger atherosclerotic plaques in chronic vascular injury than controls (57.41±3.73 vs 39.76±2.08, $p<0.0004$). The production of reactive oxygen species (ROS) in the thoracic aorta ($p<0.01$), and the number of EMPs ($p<0.05$) were elevated in TLR7-stimulated mice.
Conclusion: Systemic stimulation of the pattern recognition receptor TLR7 led to impaired reendothelialisation in acute vascular injury, increased atherosclerotic plaque development in chronic vascular injury, and elevated circulation of endothelial microparticles, endothelial progenitor cells and augmented generation of IL-6 and Rantes. Toll like receptor 7 may therefore play a role in vascular biology following acute and chronic vessel injury by affecting immunoregulatory mechanisms.

P3428 | BENCH
Isolation and characterisation of coronary endothelial outgrowth cells from patients undergoing revascularisation for acute myocardial infarction

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Introduction: Endothelial dysfunction is one of the earliest pathological features in atherosclerosis. Our understanding of endothelial cell biology in man is often derived from the study of human umbilical vein endothelial cells (HUVECs) that provide only limited insight into the pathogenesis of coronary artery disease. We describe a novel method for the isolation of coronary artery endothelial cells from atherothrombectomy specimens obtained during the treatment of patients with acute myocardial infarction.
Methods: Thirty-six patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention and thrombus aspiration were recruited. Atherothrombectomy specimens were manually dissected, plated onto collagen-I coated plates and maintained in endothelial growth media to isolate coronary endothelial outgrowth (CEO) cells. HUVECs were commercially acquired. CEO and HUVECs were characterized by immunostaining, multiparametric flow cytometry (CD31, CD146, V-CAM1, ICAM-1, N-CAM and CD45 expression), growth kinetics (population doubling time), angiogenic potential (tubule-like structure formation on MatrigelÔ) and cellular migration by means of a wound-healing assay.
Results: Coronary endothelial outgrowth (CEO) was obtained from atherothrombectomy specimens in 22/36 patients (61%). CEO cells had typical "cobblestone" morphology, were immunoreactive for the von Willebrand Factor, had high expression levels of CD31 (80%), CD146 (92%), and I-CAM (82%), and were able to expand for an average of 6 passages. CEO had low levels of expression of the pan-leucocyte marker CD45 (~1%). Population doubling times were increased in CEO compared to HUVECs (mean ± SD, CEO 2.3±1.0 versus HUVECs 1.6±0.6 days; $P<0.001$). Whilst the ability to form tube-like structures in CEOs and HUVECs was similar, CEO cells had reduced migratory capacity compared to HUVECs (23±21% versus 93±49%; $P<0.001$).
Conclusion: Coronary endothelial cells can be reliably isolated, expanded and cultured from atherothrombectomy specimens during percutaneous revascularization for acute myocardial infarction. These cells have a mature and stable endothelial phenotype, but have reduced capacity to proliferate and migrate suggesting they retain the functional characteristics of the in situ endothelium. This novel approach to isolate dysfunctional endothelial cells may be useful to provide insight into the cellular and molecular basis of endothelial dysfunction in patients with coronary artery disease.

INFLAMMATION AND THE VESSEL WALL

P3430 | BENCH
Hematopoietic PI3-kinase delta-deficiency aggravates lesional macrophage infiltration and atherosclerosis in LDLR-/- mice

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Atherosclerosis and its consequences such as myocardial infarction and ischemic stroke remains the leading cause of death in western countries. Atherosclerosis is a chronic inflammatory disease of arterial blood vessels, critically involving macrophages, dendritic cells and T lymphocytes. Although different cell types of the innate and adaptive immune system play central pro-inflammatory roles, they exert regulatory functions in different stages of this complex disease as well. Leukocytes highly express the catalytic phosphoinositide 3-kinase isoform p110delta (PI3Kd), a key enzyme involved in the regulation of immune responses. Therefore, PI3Kd represents an interesting target for the modulation of inflammatory processes during atherogenesis.
To investigate the role of PI3Kd in leukocytes for the orchestration of atherogenesis, lethally irradiated LDLR–/– mice were either transplanted with bone marrow from PI3Kd–/– or PI3Kd+/+ mice. After recovery, recipient mice were fed an atherogenic diet for 6 weeks. Hypercholesterolemic PI3Kd–/– recipient LDLR–/– mice displayed a profound reduction of peripheral B and T cells as well as strongly impaired CD4+ T-cell activation, T-helper 1 response and regulatory T-cell numbers in paraaortic lymph nodes and spleen compared with PI3Kd+/+ transplanted recipients. Surprisingly, the profound impairment of the adaptive immune system by PI3Kd-deficiency caused a considerable exacerbation of atherosclerosis in LDLR–/– mice. Atherosclerotic lesion area / aortic root area in PI3Kd–/– recipient LDLR–/– mice was significantly augmented compared with PI3Kd+/+ transplanted controls (0.26±0.07 vs. 0.16±0.04; $P<0.001$). This was confirmed on the level of en face stained whole aortas, displaying significantly higher lesion area / total aortic area in PI3Kd–/– recipients than in PI3Kd+/+ transplanted LDLR–/– mice (0.023±0.009 vs. 0.01±0.005; $P<0.001$). Importantly, atherosclerotic lesions of PI3Kd-deficient LDLR–/– mice were characterized by a lower fraction of CD4+ T cells and a higher proportion of MOMA-2+ monocytes / macrophages compared with PI3Kd+/+ transplanted controls despite unaltered circulating monocyte subsets. Thus, PI3Kd-deficiency in mononuclear phagocytes may contribute to enhanced plaque growth.
In summary, we demonstrate that hematopoietic PI3Kd plays a crucial role in regulating innate and adaptive immune responses within the arterial wall by exerting protective functions during atherogenesis. Current studies aim to dissect PI3Kd-dependent mechanisms that modulate inflammatory processes in multiple stages of atherosclerosis.

P3431 | BENCH
The presence of toll-like receptor 9 protects cardiac function in a diastolic heart failure model

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Purpose: Immune activation is important in the pathogenesis of heart failure (HF). Toll-like receptor 9 (TLR9) activity influences the pathogenesis of various cardiovascular disorders. Studies on TLR9 in HF have employed experimental systolic HF models but the consequence of TLR9 in diastolic HF is unknown. We investigated the role of TLR9 in a murine diastolic HF model caused by cardiomyocyte SERCA2a deletion.
Methods: We engaged in a 3-generation breeding strategy using αMHC-MerCreMer Serca2a flox/flox mice crossed with TLR9–/– mice to generate comparable mouse lines. Diastolic HF was induced both spatially and temporally (Tamoxiphen induced gene-recombination at 8-10 weeks) by KO of cardiac myocyte SERCA2a. Two substudies were undertaken; 1) a 12 week survival study registering death or signs of severe morbidity (leading to euthanasia) and 2) a study with MRI and echocardiography at baseline, 3 weeks and 6 weeks. Finally, tissue and blood was harvested.
Results: All mice depleted of SERCA2a, but none with the SERCA2a gene intact, reached our pre-specified end-parameter within 73 days. The lack of TLR9 in this diastolic HF model led to significant reduction in survival with a median life expectancy of 62.5 days as compared to 58 days (p=0.007). Serial imaging

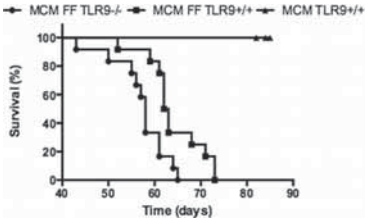

Figure 1. Survival in days after HF induction.

demonstrated an earlier onset of left ventricular restrictive filling abnormalities in the HF group depleted of TLR9. Significantly lower EF and CO, larger left atria, lower end-systolic and end-diastolic left ventricular volumes were detected.
Conclusion: The lack of TLR9 aggravates the development of diastolic HF induced by SERCA2a KO. These findings may add to the understanding of molecular mechanisms governing the progression of diastolic HF.

P3432 | BENCH
Impact of rosuvastatin treatment on reduction of thrombus burden in rat acute inferior vena cava constriction

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Purpose: This study tested the hypothesis that rosuvastatin reduces thrombus burden through inhibiting inflammation and suppressing reactive oxygen species (ROS) generation in an inferior vena cava constriction (IVCCO)-induced deep vein thrombosis (DVT) rat model.
Methods and results: 12-week-old male Sprague-Dawley rats (n=24) were equally divided into sham control (group 1: laparotomy only), IVCCO (group 2: IVC constriction), and IVCCO + rosuvastatin (20 mg/kg/day, orally after induction of IVC constriction) (group 3). IVC diameter was measured by days 0 and 14 and the right hindlimb thickness was measured by day 0, 7, and 14 prior to scarifying the animals. The results showed significantly increased IVC diameter and hindlimb thickness in group 2 than in groups 1 and 3, and significantly increased in group 3 than in group 1 by day 14 after the procedure (all $p<0.001$). Additionally, WBC count and prevalence of helper T cells, cytotoxic T cells, regulatory T cells, and early and late apoptotic mononuclear cells (MNCs) in circulation were significantly higher in group 2 than in group 1, and were significantly suppressed in group 3 after treatment (all $p<0.001$). Furthermore, inflammation at cellular (CD68+ cells) and protein (MMP-9, TNF-α) levels, oxidative stress (oxidized protein) and reactive oxygen species (NOX-1, NOX-2) in IVC also showed similar changes as those of immune cells in circulation among the three groups (all $p<0.01$).
Conclusion: Rosuvastatin treatment significantly reduced IVC thrombus burden through inhibiting inflammatory response and oxidative stress in a rodent model of DVT.

P3433 | BENCH
Activation of invariant natural killer T cells ameliorates the development of angiotensin II-mediated abdominal aortic aneurysm formation in obese ob/ob mice

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Purpose: The infiltration and activation of macrophage as well as lymphocyte within the aorta contribute to the pathogenesis of abdominal aortic aneurysm (AAA). Invariant natural killer T (iNKT) cells are unique subset of T lymphocytes and have a crucial role in atherogenesis. However, it remains unclear whether iNKT cells are involved also in the development of AAA.
Methods: Male obese ob/ob mice were administered angiotensin II (AngII, 1000 ng/kg/min; n=18) or phosphate-buffered saline (PBS; n=10) via osmotic minipumps for 4 weeks and further divided into 2 groups; α-galactosylceramide (αGC, 0.1 μg/g body weight intraperitoneal injection; PBS-αGC, n=8, and AngII-αGC, n=12), which specifically activates iNKT cells, and PBS (PBS-PBS, n=10, and AngII-PBS, n=6).
Results: Maximal abdominal aortic diameter was comparable between PBS-PBS and PBS-αGC, and was significantly greater in AngII-PBS than in PBS-PBS (1726$\pm$288 vs. 833$\pm$69 μm, $P<0.01$). This increase was significantly ameliorated in AngII-αGC (1241$\pm$257 μm, $P<0.01$ vs. AngII-PBS) without affecting blood pressure. Flow cytometric analysis revealed that the proportion of iNKT cells to mononuclear cells was significantly increased in aortic tissues from AngII-αGC compared to AngII-PBS (2.75$\pm$0.17 vs. 1.01$\pm$0.16%, $P<0.05$). The ratio of CD3-positive T lymphocyte or F4/80-positive macrophage area to the lesion area was significantly higher in AngII-PBS than in PBS-PBS (7.7$\pm$0.7 vs. 1.6$\pm$0.2% and 7.0$\pm$0.5 vs. 2.1$\pm$0.5%, both $P<0.001$), and was significantly decreased in AngII-αGC (5.3$\pm$0.5% and 5.1$\pm$0.4%, both $P<0.05$ vs. AngII-PBS). Gene expression of M2-macrophage specific markers, arginase-1 and resistin-like alpha, was significantly greater in aortic tissues from AngII-αGC compared to AngII-PBS by 6.3- and 15.7-folds, respectively (both $P<0.05$), 1 week after AngII administration, and this increase was diminished at 4 weeks. Gene expression of the activation marker of macrophages, major histocompatibility complex (MHC)-class II, was significantly enhanced by 4.6-folds ($P<0.05$) in aortic tissues from AngII-PBS at 4 weeks. Matrix metalloproteinase-2 gene expression was also increased by 5.0-folds ($P<0.01$) in AngII-PBS at 4 weeks.
Conclusions: Activation of iNKT cells by αGC can ameliorate AngII-mediated AAA in ob/ob mice via inducing anti-inflammatory M2 polarized state. iNKT cells may be a novel therapeutic target against the development of AAA.

P3434 | BENCH
Systemic administration of mitochondria alleviates 100% oxygen-induced acute respiratory distress syndrome in rats

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Background: We tested the hypothesis that mitochondria-replacement therapy ameliorated 100% oxygen-induced rat acute respiratory distress syndrome (ARDS).
Methods and results: Adult-Male SD rats (n=24) were equally categorized into group 1 (controls, room air inhalation), group 2 (ARDS: induced by inhalation of 100% oxygen for 48 hrs), and group 3 [ARDS + mitochondrial transfusion (1400 μg/each rat) from intra-venous administration 6 h after ARDS induction]. By 72 h after ARDS induction, the oxygen saturation (O2-Sat) was significantly lower in group 3 and more significantly lower in group 2 than in group 1, whereas pulmonary artery systolic-blood pressure showed a reversed pattern of O2-Sat among three groups (all $p<0.001$). H&E stain for lung crowded score showed an identical pattern of O2-Sat and number of alveolar sacs and lung weight exhibited an opposite pattern of O2-Sat among the three groups. The protein expressions of apoptotic (mitochondrial Bax, cleaved caspase 3 & PARP), fibrotic (Smad5, TGF-β), ROS (NOX-1, NOX-2, NOX-4), oxidative stress (oxidized protein), DNA- & mitochondrial-damaged (γ-H2AX, Ki-67; cytosolic cytochrome-c) and inflammatory (TNF-α, MMP-9, NF-κB) biomarkers, and IHC/IF microscopic findings of inflammatory (CD14+, CD68+), DNA-damaged (γ-H2AX+, Ki-67+) cells exhibited an opposite pattern, whereas the protein expressions of anti-apoptotic (Smad1/3, BMP-2) markers exhibited an identical pattern of O2-Sat among three groups (all $p<0.001$). The anti-oxidant (HO-2, NQO-1), mitochondrial-preserved (mitochondrial cytochrome-c) biomarkers, and cellular levels of anti-oxidants (HO-1, NQO-1, GR, GPx) were significantly higher in group 2 and more significantly higher in group 3 than in group 1 (all $p<0.0001$).
Conclusions: Mitochondria therapy protects against 100% oxygen-induced ARDS.

P3435 | BENCH
Deficiency of MyD88 in myeloid cells attenuates angiotensin II induced vascular dysfunction and arterial hypertension development

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Background: Angiotensin II (ATII), a potent vasoconstrictor, causes hypertension, promotes infiltration of inflammatory cells into the vessel wall, and stimulates both vascular and inflammatory cell NADPH oxidases. In vascular biology research, superoxide and shear stress mediated inflammatory remodeling of conduit arteries was shown to be myeloid differentiation factor 88 (MyD88) dependent, and MyD88 deficiency has been shown to protect from ATII-induced aortic aneurysm formation. The exact mechanisms how MyD88 signaling is promoting vascular dysfunction induced by ATII is unknown.
Objective: The purpose of this study was to determine whether MyD88 contributes to the development of ATII-induced vascular dysfunction and hypertension.
Methods and results: MyD88 deficiency profoundly attenuated ATII-induced (1 mg/kg/d for 7 days) blood pressure increase (measured by radiotelemetry) and vascular dysfunction (assessed by aortic ring relaxation studies). Additionally vascular superoxide and nitrotyrosine formation as well as the expression levels of several inflammation markers like Nox2, VCAM-1 and iNOS were decreased in ATII-infused MyD88–/– mice compared to WT controls. Aortic flow cytometric analysis revealed that ATII-induced infiltration with CD11b+Ly6Chigh inflammatory monocytes was significantly dampened in MyD88–/– mice. In aorta and blood of ATII-infused WT animals we found an increased expression of inflammatory monocytes markers whereas the monocyte phenotype was shifted to M2 in MyD88 deficient mice, indicating together with the FACS results a role of MyD88 in vascular tissue macrophage development. In addition to less monocytes also less IFNgamma+ NK cells were detected in aortic lysates measured by flow cytometry, suggesting that ATII-induced cytokine production is affected by MyD88. To clarify whether MyD88 exerted its effects through cells of hematopoietic lineage, WT mice were lethally irradiated and repopulated with bone marrow-derived cells from MyD88–/– mice. MyD88 deficiency in bone marrow-derived cells profoundly reduced both ATII-induced vascular dysfunction development and infiltration of the vascular wall with CD45+ leukocytes.
Conclusion: We provide first evidence that MyD88 expressed by bone marrow-derived cells plays an essential role in ATII-induced vascular dysfunction and arterial hypertension. Our data indicate that MyD88 might be involved in the ATII-induced differentiation of monocytes into an inflammatory phenotype and is essential for cytokine production.

P3436 | BENCH
Impairment of PD-1 pathway is related with infarct size in ST elevation myocardial infarction

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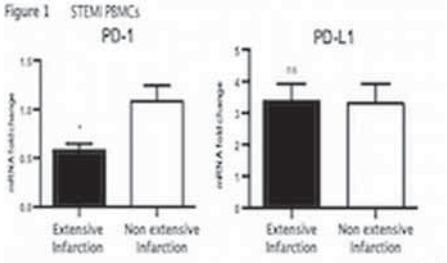
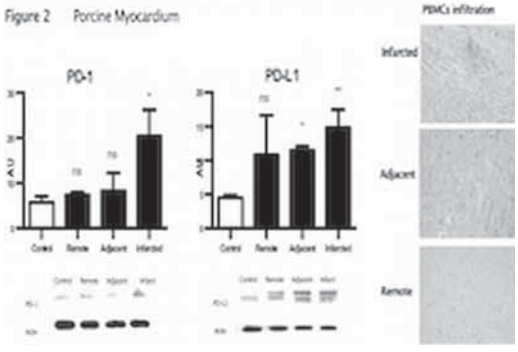
Programmed death-1 (PD-1) and Programmed death-1 ligand (PD-L1) regulate immune response. Previous studies associate an immune deregulation in ST-elevation myocardial infarction STEMI.
We recruited 100 patients with a first STEMI treated with reperfusion. In all patients PD-1 and PD-L1 expression was studied 24 h post-reperfusion in peripheral blood mononuclear cells (PBMCs), by means of flow cytometry and molecular biology. PD-1 and PD-L1 expression was serially analyzed in the first 20 patients before reperfusion and 24h, 96h and 30 days afterwards. Results were compared with 30 age- and sex-matched controls. Cardiac Magnetic Resonance was used to quantify infarct size 1-week after infarction. In a series of 8 swine with induced STEMI, PD-1 and PD-L1 expression was analyzed at baseline, 90 min after balloon inflation, 2 h and 24 h after reperfusion in PBMCs, and in swine hearts. Results were compared to 5 controls.
In patients, in comparison with controls, a significant decrease of PD-1 expression [mRNA fold change 0.8±0.3 vs. 1.2±0.6] and an increase of PD-L1+ expression [mRNA fold change 2.7±2.1 vs. 0.9±0.5] was observed 24h after infarction in PBMCs ($p<0.05$). STEMI patients with large infarct size showed decreased PD-1 expression, PD-L1 did not changed (Figure 1). Both in patients and swine, showed a significant increase of PD-1 and PD-L1 expression before reperfusion. Swine hearts revealed a marked infiltration of PMBCs and a significant increase of PD-1 and PD-L1 expression in the infarcted area compared to controls (Figure 2)





Acute changes in the PD-1 pathway take place in acute STEMI. A lesser expresion of PD-1 in peripheral blood, which could be due to myocardial infiltration in the infarcted area of PBMCs, associates with a larger infarct size.

P3437 | BENCH
Role of TRIF dependent inflammatory signaling in collateral artery growth

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Background: Arteriogenesis (collateral artery growth) is an adaptive mechanism that protects tissue from ischemia in cases of arterial obstruction. The role of TIR-domain-containing adapter-inducing interferon-β (TRIF) dependent inflammatory signaling after Toll-like receptor (TRL) activation in arteriogenesis is unclear.
Methods and results: In organ bath experiments, endothelium-dependent relaxation of aortic rings from C57Bl6J (wildtype, WT) and TRIF –/– mice were comparable. Following ligation of the right femoral artery, hindlimb perfusion was assessed by Laser-Doppler Perfusion Imaging (LDI) before and after, 3 and 7 days after femoral artery ligation. After ligation, perfusion (ratio ligated/non-ligated hindlimb) fell to 7.4±0.7% in WT and to 5.3±0.2% in TRIF–/– mice (p=0.011), indicating that the pre-existing collateral vasculature is comparable. TRIF–/– mice showed decreased perfusion recovery when compared with WT 3d (WT 32±15% vs TRIF–/– 15±4%, p=0.019) and 7d after ligation (WT 33±14% vs TRIF–/– 20±3%, p=0.020).
Immunohistochemistry was used to quantify collateral arteries and surrounding perivascular macrophages in adductor and peroneus muscle 7d after ligation. Collateral arteries as stained by anti-alpha-smooth muscle actin (α-SMA) were reduced to 50.2±8.0% in ligated TRIF–/– mice as compared to WT. Angiogenesis as assessed by staining of CD31-positive capillaries was impaired in TRIF–/– mice: average capillary/fiber ratio in TRIF–/– mice was reduced (adductor: WT 0.62±0.05 vs TRIF–/– 0.28±0.04, p=0.003; peroneus: WT 0.49±0.05 vs TRIF–/– 0.25±0.05, $p<0.001$).
Monocytes and macrophages form peripheral blood (PBMC) and spleen were obtained 7 days after ligation and stimulated with lipopolysaccharide (LPS) and polyinosic-polycytidylic acid (poly I:C) respectively. mRNA expression of classical inflammatory cytokines IL6 and TNFalpha was lower in TRIF–/– PBMC and in spleen mononuclear cells following LPS and polyI:C stimulation. TRIF-dependent cytokines RANTES, CX3CR1, CX3CR1, CXCR3, CXCR4 and CXCL10 were less strongly enhanced in splenic cells following polyI:C-stimulation.
Conclusion: The current data identify TLR-TRIF dependent cytokine signaling to be relevant for arteriole and capillary formation leading to perfusion recovery in hindlimb ischemia. Mononuclear cell cytokine expression appears to mediate the effect. Further analyses including bone marrow transplantation experiments need to prove the causal role of mononuclear cell cytokine signaling in TRIF-dependent decreased arteriogenesis.

P3438 | BENCH
Probucol oxidized products, spiroquinone and diphenoquinone, promote reverse cholesterol transport in mice

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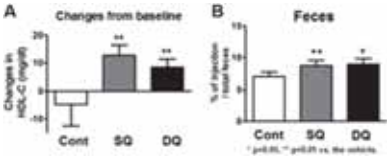
Objective: Oxidized products of probucol, spiroquinone (SQ) and diphenoquinone (DQ), were shown to increase cell cholesterol release and plasma HDL by inhibiting degradation of ATP-binding cassette transporter A1 (ABCA1). We investigated whether these compounds enhance reverse cholesterol transport (RCT) in mice.
Approach and results: SQ and DQ increased ABCA1 protein (2.8 and 2.6 fold, respectively, $p<0.01$) and apolipoprotein A-I (apoA-I)-mediated cholesterol release (1.4 and 1.4 fold, $p<0.01$, $p<0.05$, respectively) in RAW264.7 cells. On the other hand, DQ, but not SQ, enhanced cholesterol efflux to HDL (+12%, $p<0.05$) while both increased ABCG1 protein, by 1.8 and 1.6 fold, respectively. When given orally to mice, both compounds significantly increased plasma HDL-cholesterol (HDL-C), by 19% and 20%, respectively ($p<0.05$, Fig A), accompanied by an increase in hepatic and macrophage ABCA1 but not ABCG1. Finally, in vivo RCT was evaluated by injecting RAW264.7 cells labeled with 3H-cholesterol intraperitoneally into mice. Both SQ and DQ increased fecal excretion of the macrophage-derived 3H-tracer, by 25% and 28% ($p<0.01$ and $p<0.05$, Fig B), respectively.



Conclusions: SQ and DQ increase functional ABCA1 in both macrophages and the liver, elevate plasma HDL-C, and promote overall RCT in vivo. These compounds are promising as therapeutic reagents against atherosclerosis.

P3439 | BEDSIDE
Lipid profiles in women with ApaI, BsmI, TaqI polymorphisms of Vitamin D receptor gene

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Introduction: Observational studies have shown that Vitamin D deficiency is associated with increased risk of major adverse cardiovascular disease events (CVD). It is well known that dyslipidemia is a well-described independent risk factor for CVD. Recent studies showed association between the level of 25(OH)D serum levels and polymorphic variants of vitamin D receptor gene (VDR) with components of the metabolic syndrome. But not only Vitamin D deficiency could play an important role in their pathogenesis, but also vitamin D receptor gene status.
Aim: To study the association between VDR gene (BsmI, ApaI, TaqI polymorphisms) with lipo-proteins levels.
Materials and methods: We studied 449 healthy women who signed informed consent, aged 30 to 50 years (mean 44.2±0.3). The level of serum lipoproteins was measured on COBAS INTEGRO 400/700/800 analyzer, using standard reagents of Roche company (Germany). VDR (ApaI, BsmI, TaqI polymorphisms) genotype was determined by PCR-based method followed by restriction analysis.
Results: We observed that serum total cholesterol, HDL cholesterol, LDL cholesterol levels in carriers of VDR gene BB-, Bb- and bb-genotypes (BsmI poly-

morphism) does not differ compared with women of TT-, Tt-, tt-genotype (TaqI polymorphism) ($p>0.05$). B-allele carriers (BB and Bb genotypes) BsmI polymorphism had lower levels of serum triglycerides (1.32±0.04 and 1.54±0.09 Mmol/L, respectively; $p<0.05$) compared with BB genotype carriers of the gene. In addition, it was found that the AA-genotype carriers (ApaI polymorphism) of VDR gene had a higher total cholesterol and LDL cholesterol levels than that of aa- genotype carriers (5.49±0.15 Mmol/ L and 5.14±0.15 Mmol/L, respectively; $p<0.05$; 3.47±0.13 Mmol /L and 3.25±0.12 Mmol/L, respectively; $p<0.05$). However, serum HDL cholesterol, triglycerides in AA-, Aa- and aa-genotype (ApaI polymorphism) carriers show no difference ($p>0.05$).

Conclusions: The study showed that the carriage of the vitamin D receptor gene polymorphisms (AA-genotype and BB-genotype) in women of reproductive age was associated with atherogenic dyslipidemia (increased serum triglycerides, total cholesterol and LDL cholesterol).

HOW TO BETTER ACCESS CORONARY ARTERY DISEASE WITH ECHO

P3441 | BEDSIDE
Prognostic value of transthoracic coronary flow reserve in medically treated patients with non-culprit stenosis of intermediate severity after acute myocardial infarction

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Introduction: Current guidelines recommend culprit lesion treatment with primary PCI in the setting of ST-elevation myocardial infarction (STEMI), while decision about revascularization of non-culprit lesions should be done later and guided by objective evidence of residual ischaemia. The aim of the current study was to examine the prognostic value of transthoracic coronary flow reserve (CFR) in medically treated patients with non-culprit stenosis of intermediate severity after primary PCI.

Materials and methods: We enrolled 172 patients, 58±11 years of age, with remaining intermediate stenosis (50-70%) on non-infarct related artery (LAD or RCA). All patients were followed for 33±14 months. CFR was defined as the ratio between maximal velocity of diastolic coronary blood flow during maximal hyperemia and in rest, induced by i.v. infusion of adenosine (140mcg/kg/min), with the cut-off value of 2 for detection of significant stenosis. Based on CFR value, which was done in the first week of the hospitalization, patients were divided into two groups: Group 1. CFR >2 and Group 2. CFR≤2. Primary endpoints were: cardiac death, stroke, non-fatal ACS, PCI or by-pass surgery of the examined vessel.

Results: There were 30 events related to the examined vessel. In Group 1: 5 patients had PCI of examined stenosis and 1 patient had AMI. In Group 2: 16 patients had PCI of examined stenosis, 5 patients had by-pass surgery, 1 patient had AMI, 1 patient had cardiac death and 1 patient had stroke. CFR in Group 1 was significantly higher than in Group 2, (2.4±0.3 vs. 1.9±0.3, $p<0.001$, respectively). By Kaplan-Meier method, Group 1 had significantly higher events free survival in follow-up time compared to the Group 2, (96% vs. 20%, $p<0.001$, respectively). Furthermore, patients with CFR≤2 had a 28.9-fold increased in cardiovascular risk compared to patients with CFR>2 (95% CI: 11.7-71.4; $p<0.001$). Negative predictive value of CFR>2 was 96%.

Conclusion: In patients with non-culprit coronary artery stenosis of intermediate severity and CFR>2, deferral of revascularization and continuation of the medical therapy, might be reasonable option since it is associated with good long-term clinical outcome.

P3442 | BEDSIDE
Coronary flow reserve by transthoracic Doppler echocardiography after intravenous infusion of dobutamine for hemodynamic assessment of myocardial bridging

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Introduction: Myocardial bridging (MB) is a congenital anomaly characterized by systolic compression of the tunneled arterial segment, which is located mainly in the medial segment of left anterior descending artery (LAD). Since MB is dynamic stenosis which depends on the degree of extravascular compression, it has been suggested that adequate hemodynamic assessment of MB should be challenged by inotropic stimulation with dobutamine.

Objectives: This study evaluates non-invasive comparative assessment of hemodynamic relevance of MB using coronary flow reserve (CFR) measurements by transthoracic Doppler echocardiography (TTDE) with vasodilatative and inotropic challenge.

Methods: This prospective study includes 42 patients (30 males, mean age 56±9 years) with angiographic evidence of MB of LAD and systolic compression ≥50% diameter stenosis. Patients were evaluated by stress echocardiography test (SEHO) and CFR of the distal segment of LAD during iv. infusion of adenosine (ADO: 140 μg/kg/min) and iv. infusion of dobutamine (DOB: 10-40 μg/kg/min), separately.

Results: Feasibility for determining CFR during ADO was 39/42 (93%) and during DOB 40/42 (95%), respectively. SEHO was positive in only 6/42 (14%). CFR during ADO was significantly higher than CFR during peak DOB (2.84±0.69 vs. 2.45±0.49, $p<0.01$). CFR during peak DOB was significantly lower in SEHO positive vs. negative patients (1,99±0.18 vs. 2.54±0.47, p=0.01), but not during ADO (2.31±0.37 vs. 2.89±0.70, p=0.08), respectively. Using SEHO test as a gold standard for detection of myocardial ischemia, a receiver-operating curve identifies the optimal CFR DOB cut-off 2.26 (AUC 0.86, 95% CI: 0.73-0.99, p=0.01) with a sensitivity and specificity of 100% and 71%, respectively. Univariate logistic regression analysis identified CFR DOB (p=0.036) and age (p=0.054) as variables related to ischemic MB while multivariate logistic regression analysis showed that CFR DOB was the only independent predictors of functional significant of MB (OR 0.355, 95% CI: 0.021-0.751, p=0.036).

Conclusions: Noninvasive CFR measurement by TTDE during dobutamine infusion has an excellent diagnostic efficiency in identifying functionally significant MB.

P3443 | BEDSIDE
Global circumferential strain before cardiac resynchronization therapy is a predictor of long term survival in patients with ischemic cardiomyopathy

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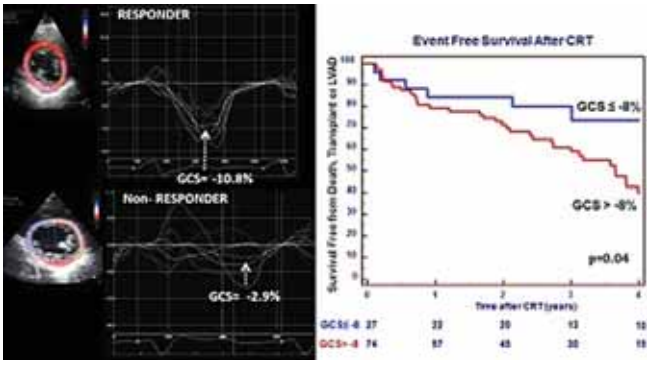
Purpose: One third of the patients receiving cardiac resynchronization therapy (CRT) do not respond, especially patients with ischemic etiology, where viability plays an important role. Our aim was to test the hypothesis that Global circumferential strain (GCS) by speckle tracking echocardiography (STE) has prognostic utility in CRT patients of ischemic etiology.

Methods: We studied 101 heart failure patients with ischemic dilated cardiomyopathy and routine CRT indications according to current clinical guidelines (age 68±9 yrs, QRS width 154±27 ms, left ventricular (LV) ejection fraction (EF) 24±5%). Speckle Tracking Echocardiography determined global strain values from basal and mid-level short axis views (Global Circumferential Strain or GCS). Response was defined as an increase in LV end-systolic volume (ESV) ≥15% at 6-months follow up. Pre-specified outcomes events were death, transplant or LV assist device (LVAD) over 4 years.

Results: Baseline GCS was significantly lower in responders than in non-responders: GCS -7.6±2.5% vs. -5.9±1.7%, p=0.0001), even though baseline basal end-systolic volume was similar (ESV in responders 142±50ml vs. basal ESV 159±56ml in non-responders (p=NS). A cutoff of GCS -8% was specific for CRT response (Sensitivity 44% and Specificity 87%), and a GCS > -8% was significantly associated with the combined endpoint of death, transplant or LVAD over 4 yrs: Hazard ratio 2.37, 95% CI 1.21-4.66, p=0.04.



Conclusion: Quantification of baseline GCS by speckle tracking echocardiography predicts response and important clinical outcomes after CRT in patients with ischemic cardiomyopathy. GCS appears to be a marker for myocardial viability and useful to detect the substrate of response to CRT.

P3444 | BEDSIDE
Validation of tricuspid annular plane systolic excursion and pulsed wave tissue doppler in assessment of right ventricular dysfunction post on-pump vs off-pump coronary artery bypass grafting

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Background: The right ventricle may be selectively impaired following coronary artery bypass graft.

Methods: We tested this hypothesis by prospective study. We examined two groups of patients. Group A (30) patients had Off-pump CABG and group B (30)

Abstract P3444 – Table 1. RV function parameters early after CABG

RV function parameters	n	Significant RCA stenosis (total n=41)			n	Normal RCA (total n=19)			Test for interaction P
		Mean pre	Mean post	Absol. change		Mean pre	Mean post	Absol. change	
Absolute change in TAPSE (cm)									0.28 (NS)
Off-pump CABG	25	1.7±0.45	1.3±0.55	0.4±0.2	5	2.32±0.35	1.72±0.4	0.6±0.3	
On-pump CABG	16	1.71±0.76	1.4±0.71	0.31±0.05	14	2.32±0.5	1.67±0.45	0.65±0.15	
Absolute change in TDTA (cm/sec)									0.95 (NS)
Off-pump CABG	25	11.5±3.01	9.32±2.5	2.2±0.51	5	14.2±0.53	12±1	2.2±0.47	
On-pump CABG	16	11.4±2.01	9.3±3.0	2.1±1.01	14	14.4±1.5	12.4±1.5	2.0	

patients had On-pump CABG. All patients were subjected to preoperative, early post-operative and 6 months follow up, full clinical and ECHO-Doppler studies. All patients had preoperative diagnostic coronary angiography.
Results: There was insignificant difference comparing the clinical picture of right side heart failure in both groups. Preoperative characteristics and RV function by ECHO did not differ significantly between the 2 groups (mean±SD): Tricuspid annular plane systolic excursion was 1.83±0.7 cm, 1.47±0.51 cm and 1.87±0.34 cm in preoperative, early post-operative and 6 months follow up respectively in group A, while in group B was 1.99±0.65 cm, 1.63±0.49 cm and 1.97±0.41 cm. The tricuspid annulus pulsed wave tissue Doppler was 11.98±3.0 cm/sec, 9.77±1.73 cm/sec and 11.9±1.72 cm/sec in preoperative, early post-operative and 6 months follow up in group A, while in group B it was 12.83±3.0 cm/sec, 10.77±2.12 cm/sec and 12.27±1.68 cm/sec. The parameters of RV function including PASP, RV dimension, TAPSE and TDTA were significantly impaired early post-operative in both groups and completely improve after 6 months.
Conclusion: The RV function significantly impaired early post-operative in both modalities of CABG irrespective to the surgical technique and completely improved after 6 months. Both surgical techniques produced equivalent results on the RV function with or without significant disease of RCA.

P3445 | BEDSIDE
Structural and functional carotid arterial markers show similar predictive accuracy for the presence and extent coronary artery disease

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Purpose: Evaluation of carotid artery intima-media thickness (IMT) and carotid atherosclerotic plaques have an incremental value in coronary artery disease (CAD) prediction. Microwave radiometry (MR) allows the in vivo assessment of carotid artery functional properties by measuring internal temperature of tissues. The purpose of this study was to evaluate whether structural and functional carotid arterial characteristics show similar predictive accuracy for the presence and the extent of CAD.
Methods: Consecutive patients (n=287) scheduled for coronary angiography were included in the study. In carotid arteries of both groups the following measurements were performed: 1) Intima-media thickness (IMTmax) and 2) temperature measurements by MR (ΔTmax). We considered the addition of the markers IMTmax and ΔTmax to established risk factors (sex, age, dyslipidemia, arterial hypertension, diabetes, smoking, family history) and we compared the respective prediction models for the presence of CAD and multivessel CAD with the use of Harrel's C-statistic and Net Reclassification Improvement (NRI).
Results: Significant CAD was found in 239 patients (83.3%). Carotid arteries of patients with no CAD (n=96, 16.72%) had lower ΔTmax in comparison to patients with one-vessel CAD (n=206, 35.89%), with two-vessel disease (n=180, 31.36%) and three-vessel disease (n=92, 16.03%) (0.48±0.39°C; 0.68±0.44°C; 0.85±0.49°C; 0.87±0.54°C respectively, p<0.01). In table 1 are summarized the c-statistic and NRI values of the various risk prediction models.

Model	C-statistic	95% CI	p-value	NRI	95% CI
CAD					
IMTmax	0.880*	0.820–0.941	<0.01	0.721	0.022–0.973
ΔTmax	0.880*	0.818–0.941	<0.01	0.546	0.204–1.106
IMTmax + ΔTmax	0.882	0.819–0.945	<0.01	0.797	0.285–1.156
Multivessel CAD					
IMTmax	0.730†	0.672–0.788	<0.01	0.422	0.043–0.604
ΔTmax	0.716†	0.657–0.775	<0.01	0.577	0.254–0.726
IMTmax + ΔTmax	0.732	0.674–0.789	<0.01	0.440	0.237–0.708

*p value for comparison: 0.96; †p value for comparison: 0.47.

Conclusions: Structural or functional markers showed similar predictive accuracy for the presence and extent of coronary artery disease. Potentially the functional assessment in an earlier stage of the disease could increase the predictive value of current imaging modalities.

P3446 | BEDSIDE
Intraprocedural determination of viability by myocardial deformation imaging: a randomized prospective pilot study in the cardiac catheter laboratory

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Aim: Prospective, randomized pilot study to examine the feasibility of an intraprocedural determination of myocardial viability by myocardial deformation imaging in the cardiac catheter laboratory (CLab).
Background: The benefit of revascularization for functional recovery depends on the presence of viable myocardial tissue. At present, patients with a relevant coronary stenosis and analogous severe regional myocardial dysfunction are transferred from the CLab to a determination of myocardial viability by i.e. low-dose-dobutamin-echocardiography (DSE) or cardiovascular magnetic resonance (CMR). The myocardial deformation imaging by 2D Strain analysis allows a reliable determination of layer specific myocardial viability.
Methods: Inclusion of 139 patients (62% men, age 59±8 years) with relevant coronary stenoses and analogous severe regional myocardial dysfunction. After coronary angiogram randomization in 2 groups: Group A: intraprocedural 2D Strain-Analysis in the CLab, determination of myocardial viability by endocardial circumferential Strain (CS) > -20%, in case of positive viability immediate coronary intervention in the same session. Group B: two-step determination of myocardial viability at the next day by CMR, in case of positive viability coronary intervention. After 18 months follow-up analysis of feasibility and efficacy.
Results: Group A with 70 patients (79% with residual myocardial viability), group B with 69 patients (82% with residual myocardial viability), no differences between the two groups concerning localization of the coronary stenosis, comorbidities or medical therapy. Cardiovascular events: group A 2.9% (2 hospitalisation caused by myocardial infarction and acute coronary syndrome) vs. group B 1.4% (1 hospitalisation caused by acute coronary syndrome), p=0.788. Improvement of LV function: group A: +7±2% vs. group B: +7±3%, p=0.963. Costs: group A: 2,096 Dollar vs. group B: 4,543 Dollar, p<0.001.
Conclusion: Intraprocedural determination of myocardial viability by myocardial deformation imaging in the CLab is feasible, safe and cost effective and may become an emerging alternative to the current practice of two-stage viability diagnostics.

P3447 | BEDSIDE
Resting 2D speckle tracking echocardiography for the prediction of myocardial viability after myocardial infarction

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Introduction: Assessment of myocardial viability after ST-elevation myocardial infarction (STEMI) is of clinical importance. Low-dose dobutamine stress echocardiography (LDDSE) is useful in the evaluation of myocardial viability, but requires administration of pharmacologic agents and involves subjective interpretation of wall motion changes requiring experience. The aim of this study was to assess if the quantitative resting assessment of local myocardial function by 2D speckle tracking echocardiography may be helpful in the evaluation of myocardial viability after ST-elevation myocardial infarction (STEMI).
Material and methods: The study group comprised 96 patients (69 male, mean age 58±10 years) with first STEMI treated with successful primary percutaneous coronary intervention. 7-12 days after STEMI, all patients underwent resting echocardiography and LDDSE with visual assessment of contractile reserve which was the reference method for the evaluation of myocardial viability. Subsequently, acquired images were analyzed off-line using 2D speckle tracking algorithm. Measurements included peak systolic longitudinal and transverse strain (SLS and STS) – maximal value before aortic valve closure, peak longitudinal and transverse strain (PLS and PTS) – including possible postsystolic contraction, systolic longitudinal and transverse strain rate (SLSR and STSR) at baseline.
Results: All analyzed longitudinal parameters of strain had a very good diagnostic value (85.5%-91.0%), while transverse parameters had only good (59.2%-76.4%) diagnostic value for predicting myocardial viability defined on the basis of LDDSE. The highest diagnostic accuracy was for SLS, PLS and SLSR-based criterion, the difference was statistically significant for SLS and SLSR, and for PLS and SLSR. All longitudinal parameters had high positive predictive values for the

assessment of myocardial viability meaning that more negative values of longitudinal strain predicted higher probability of contractile reserve corresponding with myocardial viability.
Conclusions: 2D speckle tracking analysis applied during resting echocardiography can be helpful in prediction of myocardial viability in patients after STEMI. Longitudinal strain parameters allow the prediction of local contractile reserve with peak longitudinal strain showing best correlation with LDDSE results. This implies a role of postsytolic shortening in assessment of myocardial viability of reperfused myocardium.

P3448 | BEDSIDE
Different implication of elevated bnp in heart failure with preserved ejection fraction and in that with reduced ejection fraction

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Objectives: We sought to determine the best echocardiographic parameter that described elevated BNP level in patients with heart failure with and without systolic dysfunction.
Background: There have been no reports that show significant direct relationship between echocardiographic parameters and BNP level. This could be due to the heterogeneous pathophysiology of heart failure and a lack of appropriate echocardiographic parameters.
Methods: The study population consisted of 111 consecutive ambulant or hospitalized patients with heart failure undergoing echocardiography (Vivid E9, GE Healthcare) and the same day measurement of plasma BNP level between January 2011 and December 2012. They were divided into the group of patients with heart failure and preserved ejection fraction (HFPEF, n=61) and that with heart failure and reduced ejection fraction (HFREF, n=50). Conventional and new echocardiographic parameters including myocardial strains were measured.
Results: BNP did not reflect any single echocardiographic parameter in patients with heart failure in total. The ratio of early diastolic transmitral flow velocity and mitral annular velocity (E/e') had strong positive correlation with BNP level in the HFPEF group (r=0.84, $p<0.01$) but not in the HFREF group. In the group of HFREF, global longitudinal (r=0.71, $p<0.01$) and circumferential strains (r=0.54, $p<0.01$) were positively correlated. Multivariate analysis revealed that predictors of BNP value in HFPEF and in HFREF were different.
Conclusions: BNP did not reflect any single echocardiographic parameter in patients with heart failure. However, it correlated with E/e' in patients with HFPEF and with myocardial strains in those with HFREF. Therefore, high BNP level may indicate mostly high filling pressure when ejection fraction is preserved and may indicate mostly myocardial dysfunction when ejection fraction is reduced.

P3449 | SPOTLIGHT
3D deformation parameters in patients with acute coronary syndrome: utility in the prediction of adverse remodeling

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Background: Left ventricular (LV) deformation parameters are impaired in acute coronary syndrome (ACS). 2D echocardiography has been employed to assess its prognosis significance regarding LV remodeling. However, the usefulness of 3D LV deformation parameters in these patients has not been studied.
Aims: To evaluate prognosis significance of different 3D LV deformation parameters for midterm LV remodeling in patients with ACS.
Methods: 30 patients admitted with the diagnosis of ACS were included. A standard echocardiographic exam was performed in all cases with LV 3D volume acquisition and 3D LV deformation parameters calculation. All patients underwent coronary intervention of the culprit artery. Follow up was performed 6 months after the acute event with echocardiograph performed with the same protocol. Changes and variations in 3DLV end-diastolic and end-systolic volumes were evaluated.

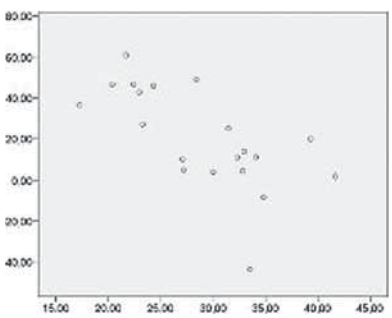

Figure 1. Correlation of 3D GS with LV dilatation.

Correlation between 3D deformation LV parameters in the acute phase and LV volume change during follow up was assessed.
Results: Male 76.6%. Mean age 63.5 years. 22 patients (73, 3%) were classified as ST elevation ACS and 8 patients (22,7%) with non ST elevation ACS. Mean LV ejection fraction was 53,01±11,2. Significant differences were noted in 3D LV end diastolic volume in the ST elevation group (62, 75±19,63 ml vs 84,38±24,32 ml, p=0,011). Global 3D strain and radial strain in the acute phase showed an inverse correlation with the degree of LV dilatation during follow up (radial strain r= -0.713; p=0.002 and 3D global strain r=-608; p=0.018).
Conclusions: 3D global and radial strain in patients with ST elevation ACS correlates with midterm adverse LV remodeling. This parameters may be useful for additional risk stratification and optimization of medical an other therapies in this population.

P3450 | BEDSIDE
Assessing the relationship of aortic structure and myocardial function in the community: an echo strain study

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Background: The ascending aorta dimensions are associated with body size however the relationships of increasing age, gender, and systemic hypertension on aortic dimensions is less clear. Whether there is an association between myocardial contractility and these relationships is untested.
Methods: Participants enrolled in the Olmsted County Heart Function Study; a random selected sampling of community participants (age 50 years and greater) who underwent clinical and echocardiographic evaluation between 2001-2004. A random subset of participants (n=498) had assessment of longitudinal left ventricular (LV) systolic strain by speckle-tracking (Velocity vector imaging, Siemens) and underwent two-dimensional assessment of ascending aortic diameter including sinus of Valsalva, sinotubular junction of proximal ascending aorta as measured by the American Society of Echocardiography guidelines. Eight subjects were excluded as LV ejection fraction was <50%.
Results: Of the 490 participants, 261 (53%) were female. The median age was 65 years with a range of 51 to 93. The average blood pressure was 125±19/69±11 mmHg. 42% of the population had hypertension and 11% had diabetes mellitus. The average body surface area was 1.89±0.23 m^2. The average LV end diastolic dimension was 48±4.2 mm and LV ejection fraction was 70±6.7%. The average LV longitudinal systolic strain was -20±3%. Aortic dimensions were strongly related to body surface area (r2=0.27, $p<0.0001$) and height (r2=0.29, $p<0.0001$). Aortic dimensions adjusted for body surface area, increased with increasing age in both women and men ($p<0.001$). The presence of systemic hypertension was associated with increased ascending aortic dimensions adjusted for body surface area and age in both men and women. Hypertension and age tend to affect Sinus of Valsalva measures more so in women and ascending aorta measures more so in men. 2-D systolic strain was positively associated with indexed ascending aortic dimensions in men and women, after adjusting for age and the presence of systemic hypertension.
Conclusion: Indexed aortic dimensions are larger in men and increase with advancing age. Concomitant systemic hypertension also impacts aortic dimensions with differentiating effects by gender.

P3451 | BENCH
Superiority of real-time three-dimensional versus two-dimensional speckle tracking echocardiography for detection of recovery in patients with acute myocardial infarction

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The ability of 2D strain imaging has been demonstrated to be effective for diagnosis of recovery after AMI, no information is available about the effectiveness of 3D strain in this clinical setting. The present study aimed to assess the diagnostic power of real-time 3DSTE in comparison with 2DSTE in detection of subclinical recovery in patients after AMI.
Methods: The study population included 66 patients (M/F=59/7,mean age=63y) with STEMI– anterior and inferior (26/40) and 20 healthy volunteers (mean age=23y).All the patients underwent standard echo examination within 36 h after revascularization (PCI) and after treatment (4-months follow-up), including 2D EF, 2DSTE with determination of global longitudinal strain (GLS),3D determination of EF and 3DSTE with measurements of 3D GLS, global circumferential (GCS) and radial (GRS) strain and global area strain (GAS). Finally, the infarct size (IS) was estimated based on MRI delayed enhancement and expressed as a percentage of the total LV volume.
Results: After infarct,adverse remodeling (progressive increase in LV size, mass and reduced EF) was found.The radial and circumferential strain decreased in the infarct, perinfarct and remote regions acutely in comparison with controls. The reduction was numerically lower for all types of strain 2D and 3D (radial, circumferential and longitudinal). 2DSTE derived GLS was marginally changed (-8.2±3.7% vs. -11.3±2.9%, $p<0.01$). 3DSTE derived GLS (-9.9±2.0%

vs -12.3±2.5%, p<0.0001), GCS (p<0.001), GAS (-28.1±5.2% vs -31.4±3.4%, p<0.0001) and GRS (p<0.0001) were all significantly reduced at baseline and 4mFU. Also 3D derived EF was lower on baseline (44.1±3.0%) than 4mFU (52.5±3.9%, p<0.0001).The longitudinal 2D and 3D strain only was significantly decreased in infarct regions.There was a significant correlation between the infarct size (31,1±3,4%) and longitudinal 3D strain (r= -0.49, p<0.01), radial 3D strain (r=0.37, p<0,01) and circumferential3D strain (r= -0.39, p<0.05). Among the different 3D strain components, GAS showed the best independent associations with mean IS (β= -0.502, p<0.0001) and LVMi (β= -0.385, p<0.001, R2=0.55, p<0.0001) in the pooled population.
Conclusions: Our study demonstrates the superiority of three-dimensional volumetric echocardiography and 3DSTE in comparison with both standard 2D echocardiography and 2DSTE in detecting subclinical recovery of STEMI patients undergoing PCI.Not only the different 3D-derived strain components but even the simple 3D volumetric EF are in fact significantly reduced after infarction, highlighting the cardiac damage induced by ischemia.

P3452 | BENCH
Myocardial ischemic memory assessed by 3D speckle tracking echocardiography: comparison of circumferential, longitudinal and radial strains

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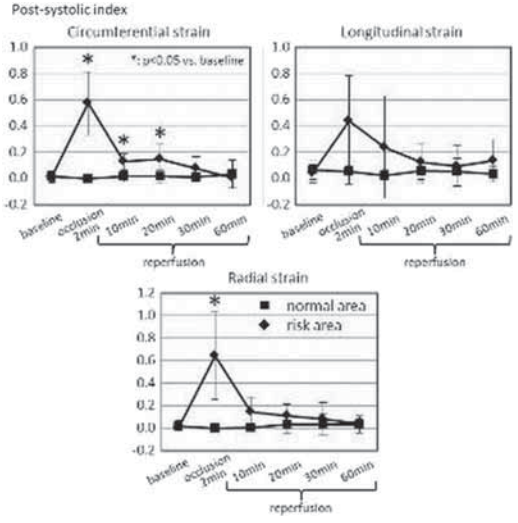
Background: Post-systolic shortening (PSS), a sensitive marker of ischemia, remains for a time after restoration of perfusion (myocardial ischemic memory). Three-dimensional (3D) speckle tracking imaging allows us to assess circumferential, longitudinal and radial strains in the same beat. However, it is unclear whether there is a difference in the assessment of ischemic memory according to the directions of myocardial strain.
Methods: The left circumflex coronary artery was occluded for 2 minutes followed by 60-minute reperfusion in 10 dogs. 3D images were acquired at baseline, during occlusion, 10, 20, 30 and 60 minutes after reperfusion using Vivid E9 (GE) to obtain circumferential, longitudinal, and radial strains in the risk and normal areas. In each direction, peak systolic strain and post-systolic index (PSI) as a parameter of PSS were measured.
Results: In the risk area, peak systolic strain decreased during occlusion but recovered immediately after reperfusion in every direction. In circumferential strain, the increase of PSI significantly persisted in the risk area even 20 minutes after reperfusion. On the other hand, the increase of PSI tended to persist after reperfusion in longitudinal and radial strains but was not significant 20 minutes after reperfusion (baseline vs. 20 minutes after reperfusion: circumferential; 0.01±0.03 vs. 0.15±0.11, p<0.05, longitudinal; 0.04±0.07 vs. 0.13±0.13, p=NS, radial; 0.01±0.01 vs. 0.11±0.11, p=NS).



Conclusion: In the assessment of ischemic memory by 3D speckle tracking echocardiography, circumferential strain may be superior to longitudinal and radial strains.

3D ECHOCARDIOGRAPHY IN VALVULAR DISEASE

P3454 | BEDSIDE
3D echo mitral paraprosthetic leak features. Are they related to hemolysis?

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3D echo mitral paraprosthetic leak features. Are they related to hemolysis?
Background and aim: Hemolysis is a problem associated to mitral paraprosthetic leaks and a prevalent reason for intervention. Nevertheless, variables related to its developments have not been deeply assessed. 3D transesophageal echocardiography may characterize the regurgitant orifice and jet characteristics. Our aim was to evaluate which 3D echo features are associated to hemolysis in patients with paraprosthetic leaks.
Methods: Consecutives patients with mitral paraprosthetic leaks, referred for percutaneous closure, were enrolled. Indications for closure were hearth failure, hemolysis or both. All patient underwent a transesophageal 2D and 3D echocardiogram. Data were stored and 3D data were off-line analyzed by a blinded cardiologist. Nine variables were studied: orifice shape (oval/round, slit like, crescent moon and tunnel) and jet characteristics (fragmentation, collision, acceleration, Free jet and slow deceleration). We also analyzed the number of leaks each patient.
Results: Fifty one patients were enrolled. 43 patients with complete data were included in the final analysis (17 males, mean age 65.83 y). 32 (74.4%) patients suffered hemolysis. Main results are shown in table below.

Table 1

Variable	Hemolysis +	Hemolysis –	p
Oval/round orifice	12 (32.4%)	2 (33.2%)	0.65
Crescent moon	5 (13.5%)	1 (16.7%)	0.62
Slit like	17 (45.9%)	2 (33.3%)	0.45
Tunnel	3 (8.1%)	1 (16.7%)	0.46
Fragmentation	11 (29.7%)	0 (0%)	0.15
Collision	6 (16.2%)	4 (66.7%)	0.02
Acceleration	5 (13.5%)	0 (0%)	0.45
Free jet	10 (27%)	1 (16.7%)	0.51
Slow deceleration	5 (13.5%)	1 (16.7%)	0.62
More than 1 leak	9 (24.3%)	3 (50%)	0.23

Conclusions: Jet collision evaluated by means of 3D transesophageal echocardiography is the only variable associated to hemolysis development. These results provide useful information for the cardiologist in order to forecast the presence of hemolysis early after valvular replacement surgery.

P3455 | BEDSIDE
Two-dimensional flow convergence method compared to three-dimensional echocardiography underestimates the severity of mitral regurgitation caused by a pseudoprolapse of the anterior leaflet

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Purpose: Vena contracta area (VCA) assessed with three-dimensional transesophageal color-doppler echocardiography (3DTCE) is to estimate the effective regurgitant orifice (ERO) in functional mitral regurgitation (FMR). Previous studies have shown that two-dimensional flow convergence method (2DFCM) underestimates the ERO in FMR when the jet is central but there is a lack of information about its performance in patients with an eccentric jet due to a pseudoprolapse of the anterior leaflet. Thus, this study compares both techniques in patients with eccentric FMR.
Methods: We studied 29 patients with eccentric FMR caused by a pseudoprolapse of the anterior leaflet. Using specific software we analyzed the 3DTCE data cropping each volume in mid-systole to obtain the cross-sectional VCA by planimetry (Fig. 1). The ERO was estimated by 2DFCM using the standard transthoracic approach.

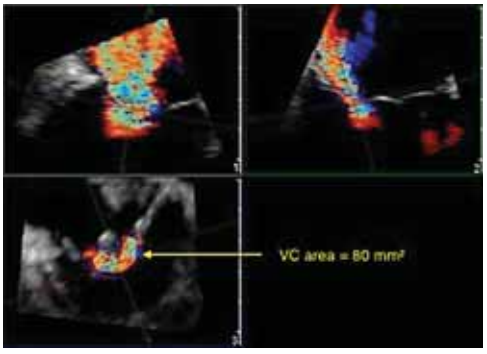

Figure 1. VCA by 3DTCE.

Results: The mean VCA measured with 3DTCE was 60.4 mm^2 (95%CI: 50.8 to 69.9) and the mean ERO calculated by 2DFCM was 48.9 mm^2 (95%CI: 46.0 to 51.8) which represents a significant underestimation by a mean value of 11.5 mm^2 (95%CI: 2.5 to 20.5, p=0.019) when 2DFCM was used. The shape of 3DTCE VCA was elongated and curved (Figure).
Conclusions: In patients with eccentric FMR due to a pseudoprolapse of the anterior leaflet, 2DFCM significantly underestimates the 3D derived ERO size. 3DTCE shows an elongated curved shape of VCA. This new technique could be highly valuable in the evaluation of this group of FMR patients.

P3456 | BEDSIDE
Geometric differences in left ventricular outflow tract with and without upper septal hypertrophy in aortic stenosis: A three-dimensional transesophageal echocardiography study

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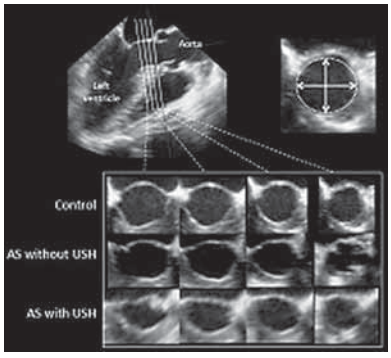
Purpose: 2D echocardiographic continuity-equation derived aortic valve area (AVA) in aortic stenosis (AS) relies on geometric assumptions of left ventricular outflow tract (LVOT) area, which can amplify error, especially in upper septal hypertrophy (USH). This study evaluated LVOT geometry using 3D transesophageal echocardiography (TEE) and assessed the hemodynamic impact of this geometry.
Methods: This prospective study included 124 AS patients and 30 controls who underwent 3D TEE. Multiplanar reconstruction was used to measure LVOT short and long axis diameters at mid-systole (Figure). The LVOT sphericity index (shot/long diameter) and area were also assessed.
Results: Of these, 47 AS patients (38%) had USH. No differences in LVOT short and long diameters, area, or shape were found between the AS patients and controls. AS with USH had shorter LVOT short and long diameters than AS without USH (short, 14.3±2.6 vs. 18.4±4.0mm; long, 22.8±3.6 vs. 24.8±4.9mm; area, 2.6±0.7 vs. 3.7±1.4cm^2; shape, 0.69±0.10 vs. 0.78±0.11; all $p<0.01$). Although no differences in peak velocity, mean pressure gradient, and stroke volume (SV) calculated with the Simpson's method existed between AS with and without USH, AS with USH had greater SV calculated with the Doppler method (77±12 vs. 58±13ml), and AVA (0.56±0.15 vs. 0.50±0.17cm^2, all $p<0.05$) than AS without USH.



Conclusion: USH affected LVOT geometry in patients with AS, which may misleads physicians in assessing AS severity.

P3457 | BEDSIDE
Morphology and clinical impact of the pseudoprolapse of the anterior leaflet in eccentric functional mitral regurgitation: a real-time three-dimensional transesophageal echocardiography study

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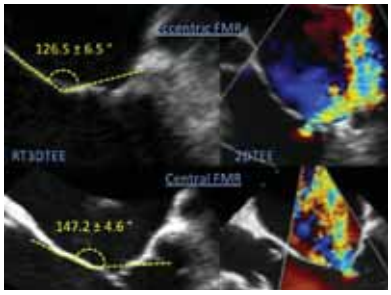
Purpose: A pseudoprolapse of the anterior leaflet (PPAL) has been identified in some patients with eccentric functional mitral regurgitation (FMR), but its cause and implications remain unknown. Real-time three-dimensional transesophageal echocardiography (RT3DTEE) can show its true nature allowing a better understanding of its clinical impact.
Methods: We studied 110 patients with FMR and left ventricular ejection fraction (LVEF) <45%. Specific software was used for RT3DTEE data to measure the mitral valve leaflets and annulus. The 3D volume was cropped to identify the plane where the PPAL was most evident. The smallest angle between the PPAL and the rest of the leaflet was determined in the 3D space (Figure).
We measured the vena contracta (VC) length in the 2D commissural plane and its correlation with the PPAL angle was investigated.
Results: An eccentric posterior jet was found in 49 patients and a central one in 61. The PPAL angle was significantly smaller in the eccentric group than in the central group. There were no significant differences in annulus area and diameters between groups, but there was a larger anterior leaflet length in patients with eccentric FMR than in the central FMR group. No difference in posterior leaflet insertion angle was found between groups. The PPAL angle was inversely correlated with the VC length (R= -0.494, $p<0.0001$). There were no significant differences between both groups in LVEF, nor in other echocardiographical or clinical characteristics.



Pseudoprolapse evaluation with RT3DTEE.

Conclusions: RT3DTEE could quantify the PPAL which was associated with eccentric FMR and its severity. The larger length of the anterior leaflet and the wider VC in patients with eccentric FMR suggest that this group would be in a more advanced stage of the disease.

P3458 | BEDSIDE
Modulating the continuity equation for a more reliable estimation of the left ventricular outflow tract area

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Background: The area of the left ventricular outflow tract (LVOTa) is a major component of the continuity equation (CE), crucial to calculate parameters needed to evaluate various conditions.
Purpose: We investigated whether a formula calculating for an ellipsoid would better address the eccentricity of the LVOT area.
Methods: 53 patients were examined by 2D- and live 3D/xplane-imaging, using TTE and TEE. The axial dimension of the LVOT (length) was measured in the long axis views (LAX), while the medial-lateral dimension (width) and the area planimetry were assessed in the corresponding orthogonal short axis views (SAX) using xplane-mode in TTE and TEE. The LVOTa were assessed as follows: 1) by assuming the conventional circular LVOT, LVOTa-CIRC=π*x2; x=½ of length of LVOT; 2) by planimetry of the LVOT in SAX, LVOTa-TRACE; 3) by assuming an ellipsoid shape of LVOT, LVOTa-ECC=π*0.5x*0.5y; y=½ of width of LVOT. The LVOT eccentricity was calculated as the quotient of length/width.
Results: LVOT measurements were feasible (95%), and intra-observer agreement was high (95%) in TTE and TEE. LVOT-dimensions showed no significant difference between TTE and TEE (p=0.75), and the eccentricity of the LVOT was similar with 0.76 and 0.77 (p=0.61). LVOTa-TRACE, LVOTa-CIRC and LVOTa-ECC were similar between TTE and TEE (p=0.80 to p=0.71 for all). The calculated LVOTa-CIRC showed the anticipated difference to the measured LVOTa-TRACE (TTE: 3.40cm^2 vs. 4.53cm^2 and TEE: 3.47cm^2 vs. 4.46cm^2; $p<0.001$ for all). Furthermore, these differences were similar between LVOTa-CIRC and LVOTa-ECC (TTE: 3.41cm^2 vs. 4.46cm^2 and TEE: 3.51cm^2 vs. 4.50cm^2; $p<0.001$ for each). LVOTa-ECC was not significantly different from the LVOTa-TRACE in TTE and TEE (p=0.81 and p=0.74). As a result, the LVOT-areas were significantly smaller using the circular LVOT formula compared to the LVOTa-TRACE and LVOTa-ECC (bias in TTE: -1.07cm^2 (23%) and TEE: -1.0 cm^2 (22%)). These results were similar in TTE and TEE.
Conclusion: Our results demonstrate the eccentricity of the LVOT and show the systematic underestimation of the LVOT area calculated by the conventional formula in the continuity equation, leading to wrong assumptions, e.g. to too small aortic valve areas or too high flow volumes. This has potentially detrimental effects on clinical decision making. We therefore propose the use of a simple ellipsoid formula for the evaluation of the eccentric LVOT area and its implementation into the continuity equation. Furthermore, our results prove high reliability of LVOT measurements in TTE and TEE respectively.

P3459 | SPOTLIGHT
Automatic measurement of aortic annulus diameter in 3-dimensional transoesophageal echocardiography

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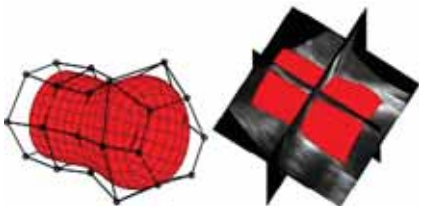
Purpose: Transcatheter aortic valve implantation involves percutaneously implanting a biomechanical Aortic Valve (AV) to treat severe aortic stenosis. In order to select a proper device, precise sizing of the AV annulus is critical.
Methods: We developed a novel and fully automatic segmentation method to measure the AV annulus geometry, operating on 3-dimensional transesophageal echocardiographic (TEE) acquisitions from mid-esophagus with the transducer array aligned with the long axis of the Left Ventricle (LV).
The novel segmentation algorithm can be summarized by the following steps: The

LV Outflow Tract (LVOT) long axis and AV hinge-point plane are automatically estimated. The LVOT, AV and Aortic Root (AR) are then tracked over the cardiac cycle by combining edge detection with a compact geometric representation in a Kalman filter.
The method was validated on 3D TEE recordings of 16 patients with varying severity of aortic disease. Measurements of the AV annulus were done by two independent experienced echocardiologists for comparison. The annulus was traced in mid systole in a plane intersecting the lowest insertion point of all aortic cusps.
Results: The automatic method measured the AV annulus with mean computation time 9.9 s. Comparison against two manual observers showed agreements (mean±SD) of -0.35±1.6 mm (r=0.87) and -0.23±2.3 mm (r=0.74) for perimeter-derived diameters and 0.40±1.6 mm (r=0.86) and 0.46±2.3 mm (r=0.74) for area-derived diameters. The corresponding interobserver agreements were -0.12±2.1 mm (r=0.77) and -0.16±2.1 mm (r=0.76).



Geometric representation of LVOT and AR.

Conclusions: We demonstrated the feasibility of an efficient and fully automatic measurement of the AV annulus in patients with AV disease. The algorithm provided robust measurements indistinguishable from those done by cardiologists.

P3460 | BEDSIDE
Direct measurement of Vena contracta area by 3D colour Doppler: Comparison of multiplanar reconstruction versus single plane method

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Background: Vena contracta area (VCA) quantified by 3D colour Doppler is a relatively new parameter for estimation of mitral regurgitation (MR) severity. The aim of this study was to determine whether a simplified online measurement of VCA using a single plane (VCA_SP) is comparable to multiplanar reconstruction method (VCA_MPR).
Methods: Overall, 114 patients with moderate or severe MR underwent transesophageal echocardiography (TEE). For quantification of VCA_MPR the offline dataset was manually cropped using 3 planes (Fig. 1a). VCA_SP was determined in the same loop using a single cutting plane, moved by the examiner from the left ventricle towards the flow convergence zone of the jet (Fig. 1b).
Results: The time consumption for quantification of VCA by single plane method was significantly lower then for multiplanar reconstruction (0.9±0.6 minutes for VCA_SP vs. 2.5±0.7 minutes for VCA_MPR, p<0.001). Results of the analyze of inter-and intraobserver variability and re-test reliability for both parameters are displayed in Table 1.

Table 1

Parameters	VCA_MPR			VCA_SP		
	ICC	95% CI	SD	ICC	95% CI	SD
Interobserver variability	0.91	0.82 to 0.94	0.083 cm^2	0.92	0.85 to 0.93	0.080 cm^2
Intraobserver variability	0.97	0.94 to 0.98	0.076 cm^2	0.96	0.92 to 0.96	0.078 cm^2
Re-test reliability	0.87	0.76 to 0.87	0.101 cm^2	0.88	0.79 to 0.90	0.092 cm^2

CI, confidence interval; ICC, interclass correlation coefficient, SD, standard deviation of differences.

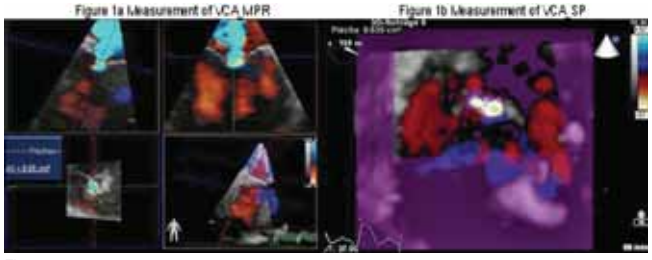

Figure 1

Conclusion: Quantification of VCA using a single cutting plane in the 3D color Doppler dataset is as accurate as multiplanar reconstruction for assessing MR severity.

P3461 | BEDSIDE
Vena contracta area derived by transesophageal 3D colour Doppler: Different cut-off values for the assessment of functional and degenerative mitral regurgitation

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Background: Vena contracta area (3D VCA) is a relatively new parameter for grading MR severity. Aim of the study was to establish 3D VCA cut-off values for grading of functional (FMR) and degenerative MR (DMR), using the European Association of Cardiovascular Imaging recommended 2D integrative approach as a reference.
Methods: Transesophageal echocardiography (TEE) was perfomed in 206 patients with at least moderate MR.
The following 2D parameters were assessed: Vena contracta width calculated as mean of measurements derived from a four chamber and a mitral commissural view (biplane VC width), effective regurgitant orifice area (2D EROA) and regurgitation volume according to proximal isovelocity surface area method. Quantification of 3D VCA was performed by multiplanar reconstruction in a 3D colour Doppler dataset.
Results: The patient population was divided according to the main pathology underlying MR into a group with FMR and a group with DMR. The results of the echocardiographic parameters are displayed in Table 1. In patients with FMR 2D EROA was significantly lower than 3D VCA (p<0.001), whereas both parameters were comparable in the group with DMR (p=0.105).
To define cut-off values for differentiation between moderate and severe MR, receiver operating characteristic curves were calculated with the following results:
– For 2D EROA in FMR group >0.255 cm^2 (Area under curve 0.87; p<0.001; Sensitivity 91%; Specificity 70%)
– For 2D EROA in DMR group >0.355 cm^2 (Area under curve 0.96; p<0.001; Sensitivity 92%; Specificity 86%)
– For 3D VCA in FMR group >0.385 cm^2 (Area under curve 0.95; p<0.001; Sensitivity 91%; Specificity 83%)
– For 3D VCA in DMR group >0.415 cm^2 (Area under curve 0.94; p<0.001; Sensitivity 94%; Specificity 92%)

Table 1

	Moderate FMR (n=41)	Severe FMR (n=77)	Moderate DMR (n=38)	Severe DMR (n=50)
Biplane VC width (mm)	5.9±1.7	8.1±1.5*	5.5±1.5	7.0±1.9*§
Reg volume (ml)	38±15	64±20*	46±22	92±39*§
2D EROA (cm^2)	0.24±0.09	0.38±0.10*	0.27±0.08	0.68±0.34*§
3D VCA (cm^2)	0.32±0.09	0.55±0.14*	0.31±0.10	0.67±0.27*§

*p<0.05 vs. moderate MR, §p<0.05 vs. FMR.

Conclusion: Especially in patients with FMR 2D EROA significantly underestimates the regurgitation orifice compared to 3D VCA. The 3D VCA method improves accuracy of MR grading with a lower variation of cut-offs for prediction of severe regurgitation in different types of MR.

P3462 | BEDSIDE
Proximal isovelocity surface area by single-beat three-dimensional color Doppler echocardiography applied for tricuspid regurgitation quantification

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Introduction: Two-Dimensional (2D) Proximal Isovelocity Surface Area (PISA) method has known technical limitations, mainly the geometric assumptions of PISA shape required to calculate Effective Regurgitant Orifice Area (EROA). Recently developed single-beat real-time Three-Dimensional (3D) color Doppler imaging has been validated for mitral regurgitation assessment. Our aim is to validate this novel method in patients with chronic Tricuspid Regurgitation (TR).
Methods: Ninety patients with chronic TR were included. EROA and Regurgitant Volume (RV) were assessed by transthoracic 2D and 3D-PISA methods. Quantitative Doppler method and transthoracic 3D-planimetry of EROA were used as reference methods.
Results: Mean age was 74±12 years and 37 patients (41%) were men. The etiology of TR was of organic cause in 9 patients and functional in 81. The jet was central in 69 patients (77%) and eccentric in 21 patients (23%). Both EROA and

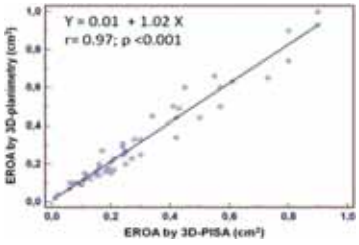

Figure 1

RV assessed by 3D-PISA method had better correlation with the reference methods than conventional 2D-PISA (Figure). A consistent significant underestimation of EROA and RV using the 2D-PISA was observed, particularly in the assessment of eccentric jets. Based on 3D-planimetry of EROA 35 patients had severe TR (EROA≥0.4 cm^2). Of these 35 patients, 25.7% (9 of 35) were underestimated as having non severe TR by 2D-PISA method. In contrast 3D-PISA method had 94.3% (33 of 35) agreement with 3D-planimetry in classifying severe TR. Good intra- and interobserver agreement for 3D-PISA measurements was observed, with an intraclass correlation coefficient of 0.94 and 0.90 respectively.
Conclusions: TR quantification using PISA by single-beat real-time 3D color Doppler echocardiography is feasible in the clinical setting and more accurate than conventional 2D-PISA method.

P3463 | BEDSIDE
Proximal flow convergence method by three-dimensional color doppler echocardiography for mitral valve area assessment in mitral stenosis

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Introduction: Two-dimensional (2D) proximal isovelocity surface area (PISA) method has important technical limitations for mitral valve orifice area (MVA) assessment in mitral stenosis (MS), mainly the geometric assumptions of PISA shape and the requirement of an angle correction factor. Recently developed single-beat real-time three-dimensional (3D) color Doppler imaging allows direct measurement of PISA without geometric assumptions nor the requirement of an angle correction factor (Figure). This novel method has been recently validated for valvular regurgitation quantification. Our aim is to validate this method in patients with rheumatic MS.
Methods: Sixty-three consecutive patients with MS were included. MVA was assessed by transthoracic 2D and 3D-PISA methods. 3D color Doppler transthoracic planimetry of MVA and pressure half-time method (PHT) were used as reference methods.
Results: 3D-PISA method had better correlation with the reference methods (with 3D-planimetry: r=0.89, p<0.001; and with PHT: r=0.85, p<0.001) than conventional 2D-PISA method (with 3D-planimetry: r=0.66, p<0.001; and with PHT: r=0.68, p<0.001). In addition a consistent significant underestimation of MVA using conventional 2D-PISA method was observed. A high percentage (30%) of patients with non-severe MS by 3D-planimetry were misclassified by 2D-PISA method as having severe MS (EROA<1 cm^2). In contrast 3D-PISA method had 94% agreement with 3D-planimetry. Good intra- and interobserver agreement for 3D-PISA measurements were observed, with an intraclass correlation coefficient of 0.95 and 0.90 respectively.

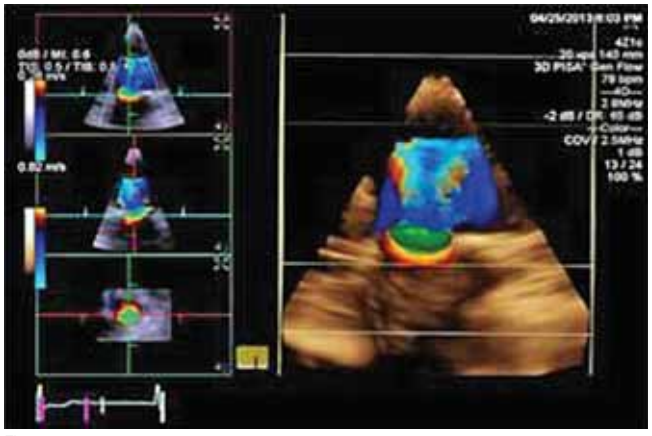

Figure 1

Conclusions: MVA assessment using PISA by single-beat real-time 3D color Doppler echocardiography is feasible in the clinical setting and more accurate than conventional 2D-PISA method.

IMAGING OF CORONARY PLAQUE

P3465 | BEDSIDE
Usefulness of iterative reconstruction algorithms for plaque detection in coronary CT angiography: Comparison between 120 kV and 100 kV acquisition protocols

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Purpose: Iterative reconstruction algorithms are used to reduce image noise and allow data acquisition using low-dose acquisition protocols. We evaluated the influence of iterative reconstruction in comparison to filtered back projection on the intra- and interobserver agreement for coronary atherosclerotic plaque detection using segment involvement score in standard 120 kV versus 100 kV acquisition protocols.
Methods: Dual Source CT angiography data sets (Siemens Definition Flash, Siemens Healthcare, Forchheim, Germany) of 100 symptomatic patients were acquired using prospectively ECG-triggered acquisitions (0.28s rotation, 2x128x0.6mm). Tube voltage was set at either 120 kV or 100kV. Images were reconstructed with filtered back projection (FBP) and iterative reconstruction (ITR, SAFIRE, Siemens Healthcare, Forchheim, Germany). Data sets were visually assessed for the presence of any atherosclerotic plaque per coronary segment using the 18 segment coronary model recommended by the society of cardiovascular CT. A segment involvement score (SIS) was calculated as the total number of coronary artery segments exhibiting plaque, irrespective of the degree of stenosis (minimum score 0, maximal score 18). Intraobserver and interobserver agreement between the two reconstruction algorithms was assessed.
Results: Mean patient age was 56±13 years (55 males, 55%). Mean effective radiation dose was 2.5±1.8 mSv. The mean heart rate during examination was 59±10 bpm, mean BMI was 28±4.5 kg/m^2, and the mean contrast agent was 65 ml. Fifty data sets were acquired using 100 kV and 50 using 120 kV. Comparing FBP and ITR, intraobserver agreement for the SIS was excellent for both 100 kV and 120 kV acquisition protocols (Kappa 0,92, 95% CI 0,88-0,97 versus 0,78, 95% CI 0,71-0,84 for 100 kV versus 120 kV acquisitions, respectively, p<0.0001). In a subgroup of 25 patients (12 patients acquired using 100 kV and 13 patients using 120 kV), interobserver agreement for SIS was good for FBP and ITR reconstruction algorithms (Kappa 0,68, 95% CI 0,59-0,77 versus 0,63, 95% CI 0,53-0,73 for FBP versus ITR, respectively, p<0.0001).
Conclusions: Agreement for plaque detection using the segment involvement score is comparable for FBP and ITR in 120 kV and 100kV acquisition protocols. Iterative reconstruction algorithms would probably influence plaque detection in extremely low-dose CT acquisition protocols (<100 kV).

P3466 | BEDSIDE
The Determinant of Coronary artery plaque progression by serial coronary computed tomography angiography (ACCORSS study)

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Background: Coronary computed tomography angiography (CCTA) has emerged as a non-invasive method for accurate detection of coronary artery stenosis. In addition to luminal narrowing, CCTA enables assessment of coronary atherosclerotic plaque surrounding lumen. Furthermore, CCTA can assess all the plaque in all the coronary vessels. In this study, we are using CCTA to evaluate the serial change of plaque.
Method: In this multi-center, retrospective registry, named ACROSS (Assessment of Change in AtheROSclerotic Plaque by Serial Coronary CT Angiography) study, 100 patients with suspicious coronary artery disease underwent CCTA from May 2005 to Jun 2010, and serial imaging was performed after a median interval of 3.4 years. All patients received contemporary medical treatment and all available vessels (239 lesions) were examined in every subject. Vessel volume, lumen volume, plaque volume, and plaque burden were evaluated and the progression of atherosclerosis assessed by means of the change in plaque volume and plaque burden per year.
Result: The mean measured coronary length was 21.0±13.6 mm. The vessel and the plaque were increased but the lumen was decreased in post-CCTA compared with pre-CCTA. The mean annual plaque progression rate were 3.7±4.5%/year. Age (β=0.153, p=0.024), diabetes mellitus (β=0.140, p=0.021) and hypertension (β =0.162, p=0.014) were the determinant for plaque progression by univariate analysis and in multivariate analysis, age (β =0.223, p=0.003), hypertension (β=0.147, p=0.045), diabetes mellitus (β=0.107, p=0.039) and smoking ((β=0.236, p=0.002) showed major determinant of plaque progression.
Conclusion: CCTA enable to quantitatively assess the serial change of plaque and we found the major determinant of plaque progression were age, hypertension, diabetes and active smoking using the serial CCTA. CCTA might be usable for personalized treatment by assessing the plaque progression rate.

P3467 | BEDSIDE
The association between coronary artery atherosclerosis and CHA2DS2-VASc score in nonvalvular atrial fibrillation patients who underwent catheter ablation

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Purpose: The major complication of atrial fibrillation (AF) is thromboembolism. The risk factors of thromboembolism includes advanced age, diabetes, and hy-

pertension, which are the common risks for coronary atherosclerosis. This study aimed to investigate the association between the severity of coronary artery disease (CAD) and CHA_2 DS_2-VASc score, as a simple estimation for embolic risk, in patients with AF prior to pulmonary vein (PV) isolation (PVI).
Methods: One-hundred and forty consecutive patients with AF (paroxysmal, n=101; persistent, n=39) refractory to antiarrhythmic treatment underwent multidetector computed tomography (MDCT) examination for the assessment of PV anatomy and CAD before PVI. Presence of ≥50% stenosis in at least one of coronary arteries on MDCT angiography was defined as significant CAD.
Results: Of 140 patients, 45 patients (32%) had any degree of CAD and 20 patients (14%) had significant CAD. As the CHA_2 DS_2-VASc scores increased, the presence of CAD also increased ($p<0.001$) (Fig. 1A). No CAD was observed in patients with CHA_2 DS_2-VASc score of 0, whereas significant CAD was observed in 20% of patients with CHA_2 DS_2-VASc scores ≥3 (Fig. 1B). Case example in patient with CHA_2 DS_2-VASc score of 4 is presented in Fig. 1C. Significant stenosis was observed in proximal segment of left anterior descending coronary artery (arrows).

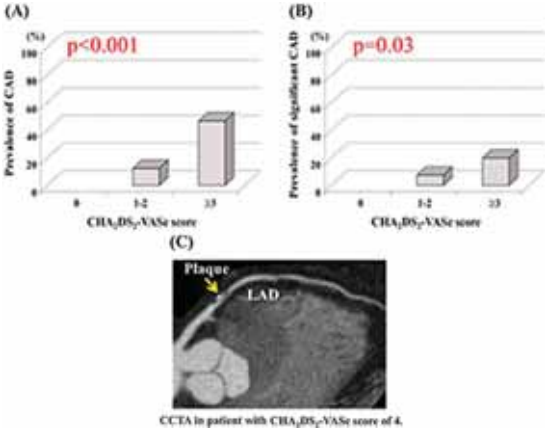

Figure 1

Conclusions: This study demonstrated that CHA_2 DS_2-VASc scores were predictive of the presence and severity of CAD in patients with AF who underwent catheter ablation. MDCT provided simultaneous assessment of PV anatomy and CAD, which is useful especially in patients with higher CHA_2 DS_2-VASc score.

P3468 | BEDSIDE
Coronary plaque detection in low-dose CT: comparison of iterative reconstruction and filtered back projection

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Purpose: In coronary CT angiography, iterative reconstruction algorithms have been used to improve image noise and allow data acquisition with reduced radiation exposure. Our aim was to evaluate the impact of iterative reconstruction in comparison to filtered back projection on the interobserver agreement for coronary atherosclerotic plaque detection with a low-dose acquisition protocol.
Methods: Coronary Dual Source CT angiography data sets (Siemens Definition Flash, Siemens Healthcare, Forchheim, Germany) of 95 symptomatic patients were acquired in low-dose prospectively ECG-triggered technique (0.28s rotation, 2x128x0.6mm, 80 or 100kV tube voltage, 160mAs tube current). Images were reconstructed with filtered back projection (FBP) and iterative reconstruction (ITR, SAFIRE, Siemens Healthcare, Forchheim, Germany). Data sets were visually assessed for the presence of calcified, non-calcified and partially calcified atherosclerotic plaque per coronary segment and per vessel by two independent observers. Segments containing stents were excluded. Agreement between the two reconstruction algorithms and their differences regarding interobserver variability were assessed.
Results: Mean patient age was 64±10 years (66 males, 69.5%). Mean effective dose was 0.49±0.18 mSv. In FBP, observer 1 found any coronary plaque in 227/380 vessels (59.7%), whereas observer 2 found any coronary atherosclerotic plaque in 215/380 vessels (56.6%, p=0.42). In ITR, observer 1 found any coronary plaque in 247/380 vessels (65.0%), whereas observer 2 found any plaque in 241/380 vessels (63.4%, p=0.70). There was no significant difference in atherosclerotic plaque detection between FBP and ITR for observer 1 (p=0.15) and observer 2 (p=0.06). Agreement between observers 1 and 2 was reached in 1448/1710 segments (85%) for FBP and in 1427/1710 segments for ITR (83%, p=0.35). Dividing coronary plaque according to the composition (calcified, non-calcified, partially calcified plaque), a significant difference for non-calcified plaque detection was found between the observers using FBP and not ITR with detection of non-calcified plaque in 55 and 34 vessels (14.5% vs. 8.9%, p=0.02) in FBP in comparison to 54 and 42 vessels (14.2% vs. 11.0%, p=0.23) in ITR.
Conclusions: Iterative reconstruction allows accurate coronary plaque detection in low-dose coronary CT angiography. Interobserver agreement regarding coronary plaque detection is comparable to filtered back projection. Iterative reconstruction algorithm seems to be better for evaluation of non-calcified plaque with a better interobserver agreement.

P3469 | BEDSIDE
Combined CT angiographic assessment of area stenosis, lesion length and approach score is superior in prediction of functionally significant coronary stenosis than individual indices alone

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Background: Computed tomography (CT) angiographic evaluation of diameter stenosis modestly predicts functionally significant coronary-artery-stenoses defined by fractional flow reserve (FFR≤0.8) in lesions of intermediate stenosis severity. Our aim was to 1) identify CT indices independently associated with FFR≤0.8, 2) derive a novel (STELLA) score which combines CT indices most predictive of FFR≤0.8 and 3) to evaluate the diagnostic accuracy of the score in prediction of FFR≤0.8.
Methods: We prospectively assessed consecutive patients who underwent CT coronary angiography and FFR assessment, with a discrete lesion with intermediate (30% to 70%) stenosis on CT as determined by visual assessment. Quantitative CT measurements were performed using dedicated software. The following CT indices were evaluated: plaque burden, minimal luminal area and diameter, diameter stenosis, area stenosis (AS), lesion length (LL), remodelling index, plaque morphology, calcifications severity and APPROACH score, which approximates size of myocardium subtended by lesion. The score was derived using the modified Akaike's information criterion (AIC).
Results: Our cohort consisted of 85 patients (mean age 64.2; 66% male, 124 lesions). Thirty-eight (30.6%) lesions were FFR≤0.8. Based on multivariate analysis, area stenosis, LL and APPROACH score remained significant predictors for FFR≤0.8, and were used to derive the STELLA score. The optimism-adjusted Harrell's c-statistic for STELLA score was 0.82 which was superior to visual diameter assessment (0.74), AS (0.74), LL (0.75) and APPROACH score (0.71) ($P<0.001$ for trend). The incremental discrimination improvement indices (P value) are 0.17 (<0.001) for AS, 0.11 (<0.001) for LL, and 0.19 (<0.001) for APPROACH score suggesting that the score improves reclassification of estimated FFR compared with any one angiographic index. A STELLA score of ≥7 provided 76.3% sensitivity, 76.7% specificity, 59.2% positive predictive value, 88.0% negative predictive value and 76.6% overall accuracy.
Conclusion: The STELLA score which accounts for CT derived area STEnosis, Lesion Length and APPROACH score may improve prediction, beyond individual indices and visual diameter assessment, of functionally significant coronary stenoses in lesions with intermediate stenosis severity.

P3470 | BEDSIDE
Non-invasive prediction of hemodynamically significant coronary artery stenoses by contrast density drop in coronary CT angiography

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Objectives: Coronary computed tomography angiography (CTA) allows the detection of obstructive coronary artery disease. However, its ability to predict the hemodynamic significance of stenoses is limited. We assessed differences in plaque characteristics and contrast density drop between hemodynamic significant and non-significant stenoses, as defined by invasive fractional flow reserve (FFR).
Methods: Coronary CTA data sets of 75 consecutive patients (96 lesions) in whom invasive FFR was performed in at least one coronary artery following cardiac CTA with diagnosis of moderate to high grade stenoses were evaluated by two experienced observers concerning the lesion characteristics. Coronary CTA data sets were acquired on a dual source CT scanner (2x128x0.6 mm collimation, temporal resolution 75 ms, 100 kV/350 mAs or 120 kV/400 mAs, 60-70 ml intravenous contrast agent). Plaque composition (low-density non-calcified, non-calcified, calcified), remodeling index as well as contrast density drop (defined as the percentage decline in luminal contrast density over the lesion) were assessed for hemodynamic significant and non-significant stenoses using an automatic software (Autoplaq). Hemodynamically significant lesions were defined by invasive FFR ≤0.8.
Results: Mean patient age was 65±11 years with 55 males (73%). 23 out of 96 coronary artery lesions (24%) were hemodynamically significant according to invasive FFR. Mean invasive FFR for these lesions was 0.66±0.19 and 0.9±0.05 for hemodynamically non-significant lesions. No significant differences were found for plaque characteristics between hemodynamic significant and non-significant lesions. The only independent predictor for hemodynamic significant stenoses was the contrast density drop (26.4±20.3% for hemodynamically significant vs. 16.2±10.8% for non-significant lesions; p=0.002 in multiple regression

analysis). No significant difference concerning the attenuation before and after the stenotic lesion was obtained between hemodynamically significant and non-significant stenoses (mean attenuation before 368.6±95.1 HU vs. 369.2±60.6 HU, p=n.s. and after 349.9±79.3 HU vs. 350.9±57.3 HU, p=n.s., for hemodynamically significant vs. non-significant stenoses). At a threshold of ≥40%, 50% of all coronary lesions were hemodynamically significant by FFR (specificity 96%, sensitivity 17%, PPV 57%, NPV 79%).
Conclusions: Measurement of the contrast density drop across coronary lesions in coronary CTA data sets allows the non-invasive identification of hemodynamically significant stenoses.

P3471 | BEDSIDE
Impact of carotid plaque score in patients achieved LDL cholesterol management goal for primary prevention of coronary artery disease

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Purpose: Lipid-lowering treatment focused on LDL cholesterol (LDL-C) was recommended in high risk patients for primary prevention of coronary artery disease (CAD). However, it was also demonstrated that LDL-C was not the best predictor of CAD risk. Atherosclerosis of carotid artery is associated with cardiovascular event. The aim of this study was to evaluate the utility of carotid ultrasound measures of atherosclerosis for CAD in patients achieved LDL-C management goal for primary prevention of CAD.
Methods: The study population consisted of consecutive 112 patients aged 30-74 years old with suspected CAD. Coronary CT angiography (CTA) was performed using a 64 MDCT. CAD was defined visually as ≥50% luminal narrowing in at least one major vessel in CTA and/or coronary calcium score ≥400. Carotid IMT and plaque score (CPS) were evaluated within 1 month after CTA. The carotid ultrasound scan protocol requires the visualization of the near and far wall of the right and left common carotid, internal carotid artery, and bifurcation. Carotid plaque was defined as a focal region with IMT >1.0mm by high-resolution B-mode ultrasound. CPS was defined as the sum of all plaque heights measured by carotid ultrasound in bilateral carotid arteries. Carotid ultrasound findings and presence of CAD were compared. Carotid IMT, CPS and clinical parameters (age, gender, family history of coronary artery disease, smoking, hypertension, and diabetes mellitus) were used in a logistic regression model with CAD.
Results: Of 112 patients, 82 patients (73.2%) (Male 51.2%, 62±9 years) who achieved LDL-C management goal according to Japan Atherosclerosis Society Guideline were included in this study. Statin treatment was performed for 28 patients (34.1%). Despite of good management goal for LDL-C level, 16 patients (19.5%) had CAD. Carotid IMT and CPS were higher in patients with CAD compared to those without CAD (1.4±0.7 vs. 1.0±0.5, P=0.016; 7.8±5.0 vs. 2.5±2.5, P=0.001, respectively).
In multiple regression analysis, CPS was only significant predictor of CAD (OR, 1.47; 95% CI, 1.2 to 1.8; p<0.001). ROC analysis revealed that CPS ≥4 was best cutoff value for detection of CAD (AUC 0.80).
Conclusions: Despite of good management goal for LDL-C level, nearly 20% of study patients had CAD. CPS is useful tool to confirm whether primary prevention of CAD is managed in patients achieved LDL-C management goal.

P3472 | BEDSIDE
Low backscattering detected by optical coherence tomography may be valuable in predicting prognosis of patients after PCI

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Background: Morphologic characteristics of stent restenosis by optical coherence tomography (OCT) ranges among patients. Low backscattering is an infrequent but poorly understood morphology pattern in OCT images. We investigated whether factors influencing low backscattering can be identified and whether clinical outcome is different.
Methods: Patients presenting stent restenosis documented by OCT reexamination after percutaneous coronary intervention (PCI) were included from February 2009 through September 2011. Backscattering of restenotic tissue was qualitatively analyzed and classified into two patterns, namely, low backscattering and high backscattering. White blood cells, platelet, glycated hemoglobin (HbA1c), hsCRP, Serum total cholesterol (TC), triglyceride, low density lipoprotein (LDL) and creatinine were analyzed in order to assess their contribution to backscattering characteristics. Follow-up were performed in patients who didn't receive revascularization during OCT reexamination. We prospectively evaluated the relationship between morphologic patterns and prognosis of the patients.
Results: 128 patients undergoing OCT reexamination 2.2±2.6 years after stent implantation were included. Low backscattering was detected in 22 (17.2%) patients. The incidence of low backscattering was positively correlated with stent implantation time (p<0.001). Higher serum TC (OR 2.592, 95%CI =1.239-5.423, p=0.011) and LDL (OR 2.686, 95%CI=1.158-6.230, p=0.021) were associated with more frequent low backscattering. No significant correlationship was found between low backscattering and other baseline characteristics. 84 patients who didn't undergo revascularization during reexamination were followed-up for 3.7±0.5 years. Major adverse cardiac events (MACEs) occurred in 7 (7.3%) patients with a predominance of target-vessel revascularization 7 (7.3%) while showed no correlation with OCT morphology patterns. 16 (16.7%) patients experienced unstable angina (UA) and showed great significance with low backscattering (RR 3.48, 95%CI=1.033-11.722, p=0.044).
Conclusion: OCT detected low backscattering is positively correlated with stent implantation time. Higher serum TC and LDL are associated with higher incidence of low backscattering, which is associated with more frequency of UA. Low backscattering should be paid more attention in the future, and it may be valuable in predicting prognosis of patients after PCI.

P3473 | BEDSIDE
Coronary plaque characteristics of signal high intensity on T1-weighted magnetic resonance imaging associated with myocardial injury after percutaneous coronary intervention

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Objectives: Non-contrast T1-weighted imaging (T1WI) has emerged as a novel noninvasive imaging modality for vulnerable coronary plaque, exhibiting a signal of high intensity plaque (HIP). However, the impact of HIP for percutaneous coronary intervention (PCI) has not been fully evaluated. We investigated the association between the presence of HIP and the incidence of myocardial injury after PCI.
Methods: A total of 88 lesions from 70 patients (68±9 years) with stable angina who were scheduled for PCI were imaged with non-contrast T1WI with a 1.5-T magnetic resonance imaging before PCI. We defined HIP as a signal intensity of coronary plaque to cardiac muscle ratio ≥1.3. Cardiac troponin-T (cTnT) was measured at baseline and 24 hours after PCI to assess myocardial injury related procedure.
Results: HIP was identified in 39% (34/88) of plaque. In the IVUS assessment, vessel volume and plaque volume were significantly greater in HIP group than in non-HIP group (229±122 vs 143±82 ml3, 173±91 vs 98±57ml3 for vessel and plaque volume, respectively). The frequency of ultrasound attenuation and positive remodeling were significantly higher in HIP group as compared to non-HIP group (91% vs 11%, 82% vs 15% for ultrasound attenuation and positive remodeling, respectively). Although baseline cTnT was not significantly different between both groups, cTnT was significantly elevated in HIP group as compared to non-HIP group (0.014±0.013 to 0.032±0.024, 0.032±0.024 to 0.190±0.311ng/ml, P<0.001, respectively).
Conclusion: HIP on non-contrast T1WI was characterized as vulnerable coronary plaque on IVUS and was associated with the incidence of myocardial injury after PCI.

P3474 | BEDSIDE
Relationship between segmental peri-coronary epicardial adipose tissue volume and coronary plaque characteristics: a magnetic resonance imaging study

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Background: Epicardial adipose tissue (EAT) has been proposed to modulate underlying coronary plaque features. No prior studies have correlated segmental peri-coronary EAT (sEAT) volume with underlying plaque characteristics in the corresponding coronary segment.
Purpose: To determine the relation between sEAT volume, assessed by cardiac magnetic resonance (CMR), and underlying coronary plaque characteristics, as estimated by multidetector computed tomography (MDCT).
Methods: The study included 32 male patients (median age: 54 y; diabetes: 14 pts) with stable angina and angiographic evidence of significant (≥50%) coronary artery disease (CAD). Eleven age-matched healthy male volunteers served as control group. All patients were not on statins. For each CAD patient, sEAT volume around 8 coronary segments (3 in left anterior descending artery, 3 in right coronary artery, and 2 in left circumflex artery) were quantified by CMR using the summation of slices method. Total EAT volume around both ventricles indexed to body surface area (EAT-i) was similarly measured. By MDCT, plaques in each coronary segment were characterized in terms of plaque volume, type (calcified vs. mixed vs. non-calcified), and severity of luminal stenosis. Total and segmental coronary artery calcium (CAC) scores were calculated. Serum levels of lipoproteins, adiponectin, leptin, and resistin were measured.
Results: EAT-i volume was significantly higher in CAD patients than control group (57.1 vs. 24.5 cm^3/m^2, p<0.001). EAT-i volume showed significant linear correlations with total CAC score (r=0.51, p=0.003) and plaque volume (r=0.45, p=0.01) in CAD patients. Among all studied biomarkers, only serum resistin level showed significant correlation with EAT-i volume (r=0.69, p<0.001). Analysis of 265 coronary segments showed larger sEAT volume with increasing luminal stenosis of the corresponding segment (mild: 8.2 cm^3; moderate: 11 cm^3; severe: 11.8 cm^3, p<0.001). sEAT volume was larger in segments with mixed than those with calcified or non-calcified plaques (12.1 cm^3 vs. 10.2 cm^3 vs. 9.5 cm^3 respectively, p=0.015). sEAT volume correlated significantly with segmental CAC score (r=0.38, p=0.006) and plaque volume (r=0.32, p=0.002).

Conclusions: When coronary arteries are segmentally analyzed, a significant relation was detected between peri-coronary epicardial adipose tissue volume and underlying coronary plaque characteristics. Increased epicardial adipose tissue volume is associated with increased serum resistin level.

RIGHT VENTRICULAR FUNCTION

P3476 | BEDSIDE

The risk assessment of the acute pulmonary embolism by computed tomography parameters

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Purpose: The aim of this study is to evaluate the association between computed tomography parameters and clinical course in patients with acute pulmonary embolism.
Methods: 132 patients with acute pulmonary embolism verified by CT pulmonary angiography were retrospectivelly analyzed from hospital database. The following parameters were assessed: pulmonary artery diameter to aorta diameter ratio (PA/Ao), normalized pulmonary artery diameter (nPA), right ventricular to left ventricular diameter ratio from CT (RV CT/LV CT), normalized end-diastolic right ventricular diameter (nRVD echo) and right to left ventricular end diastolic diameter ratio (RV echo/LV echo) from echocardiography. The relation between these parameters and tachycardia/hypotension, administration of thrombolysis, troponin-T, NT-proBNP and necessity for intensive care unit (ICU) hospitalization was assessed.
Results: Multivariate logistic regression analysis showed a significant association between PA/Ao and thrombolysed (0.97) to non-thrombolysed (0.88) patients, OR=1.56, p=0.008, and also RV CT/LV CT and thrombolysed (1.5) to non-thrombolysed (0.94) patients, OR=1.30 P<0.001. Patients with NT-proBNP levels over 1000ng/l had higher nPA (15.7 vs 13.5mm.m-2, OR=7.65, p=0.005) and RV CT/LV CT (1.47 vs 0.91, OR= 3.25, p=0.004) The significant difference was also found in intensive care unit hospitalization necessity, for RV CT/LV CT (1.39 vs 0.91, OR=1.23 P=0.003), and RV echo/LV echo (0.78 vs 0.64, OR=1.83 P=0.033.
Conclusion: From the CT pulmonary angiography parameters, the most predictive value showed RV CT/LV CT. A significant association was found between this parameter and thrombolysis administration, higher NT-proBNP levels and ICU hospitalization. The PA/Ao had relation only to thrombolytic therapy as well as nPA only to NT-proBNP levels.

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Use of dual-energy CT-scan compared to V/Q-scintigraphy in the diagnostic workout of chronic thromboembolic pulmonary hypertension

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Purpose: Computed Tomography (CT) and Ventilation/Perfusion scintigraphy (V/Q scintigraphy) have been used for the diagnosis of pulmonary embolism (PE). Recently, Dual-Energy CT (DE-CT) is increasingly being used for detection of PE and Chronic Thrombo-embolic Pulmonary Hypertension (CTEPH). This study aims to assess the sensitivity, specificity, positive and negative predictive value of these 2 modalities in the diagnosis of CTEPH.
Methods: Twenty-nine patients referred to us between 2008 and 2013 for diagnostic imaging of chronic pulmonary hypertension were investigated in a retrospective study. Patients who had had pulmonary CT-angiography (pCTA) as well as DE-CT imaging for lung perfusion were included. Images of DE-CT and pCTA were scored by a dedicated thoracic radiologist. Planar images of V/Q-scintigraphy were scored separately by a nuclear physician. Each lung segment was scored as either having a perfusion defect or not. The statistical analysis was performed using Statistical Package for Social Sciences (SPSS), using the McNemar test to compare data with the golden standard pCTA.
Results: Comparing the segmental images obtained with DE-CT (n=476), using CT angiography as golden standard, we calculated a sensitivity of 66.3% and a specificity 89.3% of for DE-CT. Positive and negative predictive value were 55.8% and 92.9%, respectively. There were missing data for one patient, which therefore was excluded from the analysis. For the V/Q scintigraphy (n=136), we calculated a sensitivity of 59.2% and a specificity of 74.7%; positive predictive value was 56.9% and negative predictive value was 76%, respectively.
Conclusion: Our results suggest that Dual-Energy CT might be more sensitive than planar V/Q-scintigraphy in the diagnosis of chronic thromboembolic pulmonary hypertension. Larger studies with multicenter patient populations are warranted. Dual-Energy CT is a very promising diagnostic tool for chronic thromboembolic hypertension. However, more prospective research is needed before any recommendation can be made to use Dual-Energy CT as the basic diagnostic tool for Chronic Thromboembolic Hypertension.

P3478 | BEDSIDE

Doppler derived estimation of pulmonary vascular resistance in patients with adult congenital heart disease with left to right shunting

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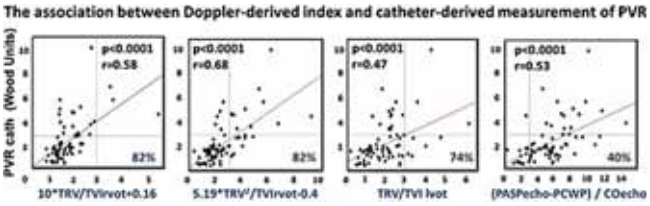
Background: Pulmonary vascular resistance (PVR) is a critical and essential parameter of the assessment and selection of treatment in patients with adult congenital heart disease accompanied by pulmonary hypertension. Cardiac catheter is the gold standard methods, however is invasive method for PVR measurement.
Methods: Our study population consisted of 70 subjects with secundum atrial septal defect (ASD) who underwent transthoracic echocardiography (TTE) and right heart catheterization in the evaluation of the indication for percutaneous closure with an Amplatzer closure device. They underwent complete cardiac catheterization study including measurements of PVR, Qp/Qs and cardiac output was calculated using the method of Fick. All the patients underwent Doppler echocardiographic study within 48 hours of catheter study.
The association between Doppler-derived index and catheter-derived measurement of PVR were evaluated:
Doppler-derived index defined as the ratio of the tricuspid regurgitation velocity (TRV) to the velocity time integral (VTI) of the right ventricular outflow tract (RVOT); TRV/TVIrvot, TRV*TRV/TVIrvot, TRV/TVI lvot, systolic pulmonary artery pressure (sPAP) /Heart Rate*TVIrvot, PEP/Act/TT (pre-ejection period/acceleration time/total systolic time) and mean PAP-pulmonary capillary wedge pressure (PCWP)/cardiac output estimated by Doppler echocardiography.
Results: There were significant but modest correlations between catheter based PVRs and Doppler-derived estimation of PVRs.



Conclusions: In conclusion, Doppler-derived estimation of PVR in patients with adult congenital heart disease with left-to-right shunting may help to differentiate subjects in whom pulmonary systolic pressure may be exaggerated by high stroke volume or pulmonary vascular lesion.

P3479 | BEDSIDE

Long term right ventricular and pulmonary reverse remodelling one year after pulmonary endarterectomy PEA for chronic thrombembolic pulmonary hypertension CTEPH by cardiac MRI

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Background: Pulmonary Endarterectomy (PEA) offers a cure for patients with chronic thrombembolic pulmonary hypertension (CTEPH) with complete restoration of pulmonary hemodynamics only hours after surgery. We could show early right ventricular (RV) and pulmonary arterial (PA) reverse remodelling within ten days of PEA. It was the purpose of this study to examine the longterm effects of reverse remodelling one year after PEA.
Methods: 90 patients were examined on a 1.5 T Scanner 2 days prior as well as 10 days and 365±73 after PEA. Complete volumetric coverage of the RV from apex to base was performed by SSFP Cine sequences in standard fashion, ejection fraction (EF), enddiastolic (EDV) and endsystolic (ESV) volumes as well as RV-mass (RVM) were derived. Phase contrast gradient echo flow measurements were performed in the pulmonary trunk, pulmonary peak velocity (PPV) and pulmonary artery distensibility (PAD) (as relative PA area change) were recorded.
Results: While RV volumes decreased, ejection fraction improved significantly, both effects were slightly less pronounced but sustained after one year. (EF 24.4 vs. 43.8 vs. 35.9%, p<0.001; EDV 185 vs. 131 vs. 144 ml, p<0.001; ESV 142 vs. 83 vs. 85 ml, p<0.001). Of note RVM decreased significantly after one year (RVM 63 vs. 58 vs. 43 g, p<0.05). Reverse remodeling of the RV was paralleled by changes in PA flow. Peak velocity increased significantly (PPV 61 vs. 73 vs. 74 cm/s, p<0.05). Interestingly the distensibility in the PA trunk decreased immediately after surgery and improved again in the long run (PAD 28 vs. 21 vs. 24%, p<0.05).
Conclusion: Pulmonary hemodynamics return to normal very early after PEA and are paralleled by RV and PA reverse remodeling despite severely reduced RV function at baseline. Our current data show, that positive reverse remodeling is a long term effect and persists one year after surgery with a relevant reduction in RV mass.

P3480 | BEDSIDE

Improvement of non-invasive estimation of pulmonary vascular resistance by echocardiography in comparison with right heart catheter measurements

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Purpose: The diagnosis of pulmonary arterial hypertension (PAH) requires an elevated pulmonary vascular resistance (PVR) documented at right heart catheterization (RHC). Response to treatment also necessitates serial invasive measurements. The traditional echocardiographic (TTE) method for estimation of PVR ([PVR1 = ((TR Vmax / RVOT VTI) x 10) + 0.16]) has poor correlation when the PVR is markedly increased. Improved accuracy and agreement was achieved when the correction for left atrial pressure (Ratio of mitral inflow E velocity to annular tissue velocity E') was included ([PVR2 = (RVSP – E/e') / RVOT VTI]; where RVSP = (4 x TR Vmax^2) + RA pressure). We aimed to validate a novel TTE-based measure of PVR3 against invasive RHC data.
Methods: The study cohort included pulmonary hypertension patients who underwent both RHC and TTE on the same day. PVR1 and PVR2 were estimated with the above equations. PVR3 was calculated with a modified equation that more closely simulated the RHC method [Transpulmonary gradient/Cardiac output]. Mean pulmonary artery pressure (mPAP) was estimated using [mPAP = (0.61 x RVSP) + 2mmHg] and cardiac output (CO) by the Doppler technique [CO = 0.785 x LVOTd^2 x LVOT VTI]. Therefore, [PVR3 = (mPAP – ((1.24 x E/e') + 1.9))/CO].
Results: 100 patients (65±14years; 86% female) were included. The mean PVR on RHC was 6.9±3.5 Wood Units. The means of PVR1, PVR2, and PVR3 were 3.4±1.2, 5.0±2.5, and 5.8±3.1 Wood Units respectively. PVR3 demonstrated the best agreement (Intraclass correlation (ICC) 0.87) and consistency (Cronbach's alpha 0.9) in comparison to the gold standard RHC measurements. PVR2 was a reasonable alternative (ICC 0.71; Cronbach's alpha 0.80) but PVR1 estimations remained relatively poor (ICC 0.33; Cronbach's alpha 0.56).
Conclusion: This novel non-invasive TTE-based technique is more reliable than the other contemporary TTE methods for the evaluation of PVR. PVR3 correlates well with RHC measurements and may potentially reduce the need for serial invasive assessments.

P3481 | BEDSIDE

Assessment of echocardiography estimate precision of right atrial pressure in patients with acute decompensated heart failure

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Purpose: Several methods that estimate right atrial pressure (RAP) from echocardiography parameters have been proposed. However, their precision, i.e., how much they decrease RAP estimation uncertainty, is unknown. In this prospective study, we aimed to evaluate and compare the precision of previously proposed RAP estimates of in-patients with acute decompensated heart failure.
Methods: We acquired echocardiography and invasive hemodynamic data in 75 patients with acute decompensated heart failure. Measurements were made at the start and 48-72h after the beginning of treatment. RAP was estimated by Method 1, using the cut-offs defined by inferior vena cava diameter (IVCd) and IVCd percent change (IVCd%change) during inspiration, and by Method 2, using IVCd%change and systolic to diastolic hepatic flow ratio (S/Dhep). Method 3 was used in patients with sinus rhythm, using the ratio of early tricuspid inflow and early diastolic Doppler tissue tricuspid annulus velocities (E/E'ta). RAP was also estimated by resting IVCd, IVCd during inspiration, IVCd%change, right ventricular regional isovolumetric relaxation time (rIVRT), E/E'ta, right atrial volume index (RAVI), S/Dhep, RV Tei index, RV E/A, and RA emptying fraction (RAEF). Precision gain was measured as the difference between standard deviation of RAP and standard error of the estimate of RAP.
Results: Method 1 (r=0.48, p<0.05), IVCdinsp, (r=0.49, p<0.0001), IVCd %change (r=0.41, p<0.0001) and IVCd (r=0.40, p<0.0001) had the highest correlation with RAP. The highest gain in precision was also observed with the above methods (9%, 13%, 9%, 8%, respectively). All other parameters had poor correlation with RAP.
Conclusion: In patients with advanced heart failure, none of the tested RAP prediction methods resulted in a clinically relevant improvement of RAP estimate. Estimating RAP from a single IVCd measurement is at least as precise as using complex prediction methods.

Correlation and precision gain of parameters to the RAP

	r value initial	p	r value 48–72hrs	p p	Cumulative r value	p	Precision gain
IVCdinsp	0.39	<0.01	0.42	<0.01	0.49	<0.0001	13%
IVCd % change	–0.37	<0.01	–0.55	<0.01	–0.41	<0.0001	9%
IVCd	0.45	<0.001	0.57	<0.001	0.40	<0.0001	8%
rIVRT	0.44	>0.1	0.05	>0.1	0.27	0.01	4%
RV E/E'ta	0.18	>0.1	0.21	>0.1	0.19	0.04	2%

P3482 | SPOTLIGHT

Biventricular dysfunction in patients with liver cirrhosis

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Objective: Patient with liver cirrhosis is associated with left ventricular (LV) myocardial dysfunction. However, studies on the right ventricular (RV) function in these patients are limited. The aim of this study thus was to evaluate both LV and RV function in patients with cirrhosis.
Methods: A total of 103 cirrhosis patients (age 54.9±7.3 years, 74.8% male) and 48 age- and gender-matched healthy controls were included. Detail transthoracic echocardiography were performed in all subjects. Conventional echocardiography parameters including LV dimension, LV ejection fraction, RV dimension and RV systolic function assessed by tricuspid annular plane systolic excursion (TAPSE) were measured. In addition, advanced speckle-tracking derived strain analysis to detect subtle LV and RV systolic dysfunction were measured. Global LV strains were assessed from three orthogonal directions: longitudinal (LS), circumferential (CS), and radial strain (RS). Global RV longitudinal strain (RV-LS) including the RV free wall and septum were measured.
Results: Both LV and RV dimension were comparable between patients with cirrhosis and controls. Despite similar LV ejection fraction (65.1±4.8% vs. 64.1±4.4%; P=0.193) and TAPSE (2.37±0.43 vs. 2.34±0.24; P=0.592), patients with cirrhosis had impaired global LS (-18.5±2.9% vs. -20.1±2.8%, P<0.01), CS (-16.6±2.4% vs. -21.6±3.6%, P<0.01), RS (39.9±13.1% vs. 44.9±14.3%, P<0.05) and RV-LS (-21.2±4.4% vs. -23.0±2.6%, P<0.01) compared with controls. Upon multivariable adjustment with age, gender and cardiovascular risk factors, both global LV and RV strains remained significantly impaired in patients with cirrhosis.
Conclusions: In addition to impaired LV systolic function, the present study firstly demonstrated that patients with cirrhosis had concomitant RV systolic dysfunction assessed by speckle tracking derived strain. This data thus suggested patients with cirrhosis had biventricular myocardial dysfunction.

P3483 | BEDSIDE

Improvement in right ventricular function evaluated by two-dimensional strain after cardiac resynchronization therapy

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Background: Several studies have stressed the effect of cardiac resynchronization therapy (CRT) on left ventricular function. Nonetheless, little is know about the effects of CRT on right ventricular (RV)function.
Objectives: To evaluate the effects of CRT on RV function by 2D strain.
Methods: The population consisted of 50 consecutive HF patients referred for CRT (64±6 years old, 41 men, 78% with ischaemic aetiology, 2.2% with non-ischaemic aetiology, QRS duration QRS >120msec, LVEF <35%). All patients were in sinus rhythm and with optimal pharmacological therapy. Conventional echocardiography, Tissue Doppler Echocardiography and Speckle-tracking Echocardiography was performed preoperatively and at 12-month follow-up using a commercially available system (Vivid 9 systems). All parameters were analyzed off-line using EchoPac softwere (GE-Vingmed). Standard echocardiographic parameters, tricuspid annular plane systolic excursion (TAPSE, mm), peak systolic velocity of tricuspid annular motion (St, cms^{-1}) were measured.The software automatically divided RV myocardium into six segments (basal, mid, and apical segment of the septum and the RV free wall). The global longitudinal strain (GLS) was calculated by averaging all segmental longitudinal strain curves. Response to CRT was defined as ≥15% reduction in LV end-systolic volume at 6 months follow-up.

Abstract P3483 – Table 1

RV remodeling	All (n=50)			Responders (n=38)			Non responders (n=12)	
Anulus RV (mm)	39.1±3.3	34.1±	<0.001	38.1±3.3	31.1±2.8	<0.001	40.1±3.3	40.1±3.9
RA area (cm^2)	25.3±2.6	24.1±3.9	0.03	25.6±3.6	24.5±3.6	<0.001	26.9±3.5	25.1±7.5
TAPSE (mm)	12.0±0.9	14.7±2.3	<0.001	13.6±1	16.2±2.1	<0.001	11.1±1.9	11.0±1.8
S'	8.6±1.3	11.8±0.2	<0.001	9.37±1	12.87±1.43	<0.001	7.7±0.9	8.2±0.9
E'	5.4±0.4	7.8±0.3	<0.001	5.8±0.6	8.8±0.10	<0.001	4.9±0.2	5.1±0.5
PAPS (mmHg)	38.7±3.2	31.0±0.9	<0.001	39.1±3.0	25.7±3.1	<0.001	39.1±3.9	36.1±4.4
RV fractional area change (%)	30±1.4	39.4±2.7	<0.001	33.3±2.4	41.2±2.5	<0.001	30.6±3.8	29.7±0.8
TI	2.5±1	1.5±0.5	0.01	1.9±1.3	1.3±0.5	0.01	2.8±0.9	2.1±1.3
Global strain (%)	–14.4±2.8	–20.2±1	<0.001	–15.0±2.3	–22.0±3.5	<0.001	–11.9±1.8	–12.3±6.4

Results: After 1 year, LVEF had increased significantly (from 29.7±7.3 to 39.7±11.6; P<0.01) and there was an improvement in RV function (Table 1).
Conclusion: Significant improvements in RV function were observed in CRT patients.

P3484 | BEDSIDE
Right atrial appendage structure and function in non-valvular atrial fibrillation

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Background: Non-valvular atrial fibrillation (NV-AF) is associated with structural changes and dysfunction of left atrial appendage (LAA). There is lack of evidence regarding evaluation of right atrial appendage (RAA) and its relation to parameters of LAA in patients (pts) with NV-AF.
Purpose: To evaluate parameters of RAA structure and function according to the risk of LAA thrombus formation (TF) in pts with NV-AF.
Methods: The study included 121 pts with NV-AF (mean age [median and interquartile range] 62 (56-69) ys; 82 men (67,8%) and 39 women (32,2%)). According to degree of spontaneous echo contrast (SEC) or LAA thrombus pts were divided into 3 groups: group 1 (G1) – no SEC or SEC 1-2 degree (n=73), group 2 (G2) – SEC 3-4 degree (n=28), group 3 (G3) – LAA thrombus (n=20). The groups were comparable by age and gender. Assessment of LAA structure (maximal area (Smax)) and function (ejection velocity (Evel), spectral tissue Doppler imaging (TDI) apex (Avel) and basis (Bvel) movement velocities) and RAA structure and function (Smax, Evel, Bvel) was performed by transesophageal echocardiography. Groups G1 (relatively low TF risk) and combined G2 and G3 (relatively high TF risk) were used as binary outcomes in ROC-analysis. Data operational characteristics (sensitivity (Se), specificity (Sp)) were presented with 95% confidence intervals (CI). Data were analyzed by non-parametric methods with p-value <0,017 as statistically significant.
Results: It was found, that increasing of LAA TF was associated with both LAA and RAA impairment (G1 vs. G3): increasing LAA and RAA Smax by 36,7% (p<0,001) and 27,1% (p<0,017), respectively, decreasing LAA and RAA Evel by 51,9% (p<0,001) and 36,4% (p<0,001), respectively; Avel by 34,8% (p<0,001); LAA and RAA Bvel by 29,0% (p<0,001) and 31,9% (p<0,001), respectively. The strongest correlations were observed between RAA Bvel and LAA Evel (Spearman's r=0,74, p<0,001) and LAA Avel (r=0,73, p<0,001). Evel was the most sensitive and specific LAA state parameter for discriminating G1 and (G2+G3): Se 75,0% (95% CI 60,1-85,9), Sp 97,3% (95% CI 89,6-99,5). Bvel was the most accurate RAA state parameter: Se 77,1% (95% CI 62,3-87,5), Sp 78,2% (95% CI 66,4-87,0).
Conclusion: RAA and LAA structural and functional changes are interrelated in NV-AF. Despite being less accurate than LAA parameters for LAA TF risk assessment, RAA parameters should be considered in NV-AF management.

P3485 | BEDSIDE
Relation between duration of surgery and postoperative electrocardiographic changes in non-cardiac patients undergoing major abdominal surgeries

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Background: Patients undergoing abdomino-pelvic surgeries may have postoperative cardiac events. In patients above age of 40, ECG is frequently performed preoperatively to screen for asymptomatic coronary artery disease. Many perioperative factors may play role in precipitating silent myocardial ischemia, that's only presented by postoperative ECG changes.
Objectives: To evaluate the association between different perioperative factors and postoperative ECG changes suggestive of silent myocardial ischemia.
Patients and methods: The study included 200 non-cardiac patients, above the age of 40, with a normal preoperative ECG, who underwent major elective non-vascular abdomino-pelvic or laparoscopic surgeries. A twelve-lead ECG was performed pre-, immediately post- and 3 days postoperative. Patients, who showed any postoperative ECG changes, were tested for their CK-MB, Na, K, Mg and ionized Calcium serum level.
Results: Six patients (3%) showed postoperative T-wave inversion, none of them experienced cardiac symptoms, elevation of CM-MB, or abnormal electrolyte level. Three patients (50%) underwent abdominal, 2 (33.3%) laparoscopic and 1 (16.7%) pelvic surgery. Two patients (33.3%) experienced intraoperative hypotension. ECG changes were significantly related to the mean duration of surgery (5.0 + 2.5 Vs 3.6 +1.5 hours, p=0.02) but were not related to patients' age (p=0.6), preoperative heart rate (p=0.2), preoperative systolic (p=0.7) or diastolic blood pressures (p=0.6).
Conclusion: The long duration of major non-vascular abdomino-pelvic surgeries may cause serious cardiovascular hemodynamic effects leading to silent myocardial ischemia. Postoperative ECG changes may be the only tool to detect postoperative silent myocardial ischemia.

PERIPHERAL ARTERIAL DISEASES: ASSESSMENT AND PROGNOSIS

P3487 | BEDSIDE
Gadofosveset trisodium-enhanced MRI for the diagnosis of deep vein thrombosis; comparison with duplex ultrasound

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Objective: The intravascular contrast agent for MRI gadofesveset trisodium is suitable for venous angiography for the detection of deep vein thrombosis (DVT) of the lower extremities, mainly due to a long vascular half-life of approximately 30 minutes. In this study we compared the results of gadofosveset trisodium-enhanced MRI and compression duplex ultrasound (DUS) in 42 patients (mean age 57,6±17,2 years; 26 male) with suspected DVT concerning the detection rates in vein segments and the absolute lengths of detected DVTs in the legs with suspected DVT and the contra lateral legs.
Material and methods: MRI was performed with a 1.5-T system in supine position after a single injection in an antecubital vein. The DUS comprised color flow and pulsed wave doppler for the pelvic veins and compression ultrasound for the deep and the saphenous veins of the thigh and the lower leg.
Results: Three patients refused the MRI after inclusion in the study. All of the 5 MRI-detected thrombi in the iliac veins were suspected via indirect signs in the DUS, herewith 3 additional DVTs were suspected without pathologic signs in the MRI (Cohen's coefficient 0.74; p<0.001). The Cohen's coefficient was 0.81 for the veins of the thigh and 0.690 for the veins of the lower leg (both p<0.001), comparing MRI and direct visualization of the thrombi via DUS. In the segmental comparison MRI detected thrombi in more segments of the legs; this was due to pathologic signals in the tibial anterior vein in the MRI in 12 patients with normal findings in the DUS, with excellent visualization of the veins with DUS in this area. There was no significant difference concerning the number and the lengths of detected DVT in the posterior veins of the lower leg.
Conclusions: The two methods DUS and gadofosveset trisodium-enhanced MRI show comparable results in the detection and localization of DVT of the lower extremities except in the tibial anterior veins.

P3488 | BENCH
Reproducibility of vascular strain analyses at different arterial sites in healthy subjects

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Background: Vascular strain analysis by duplex ultrasound (DUS) allows the detection of premature alterations of vascular elasticity. Whether and to which extent vascular strain differs between various sites of the vascular tree is not known. Further, data on the reproducibility of vascular strain analysis are scarce. The aim of this study was to compare vascular strain between various parts of the arterial tree and to assess its reproducibility.
Methods: The common carotid arteries (CCA), common femoral arteries (CFA), popliteal arteries and the abdominal aorta of healthy volunteers were investigated using DUS. To assess inter- and intraday-reproducibility cross-sectional DUS clips of the respective arteries were obtained on three consecutive days, three times each day. Vascular strain was determined offline and the inter-/intraday reproducibility as well as the components of variance of vascular strain were calculated.
Results: In total 93.5% of the DUS clips acquired in ten healthy subjects (m:f=7:3, mean age 28.3±3.2 years) could be analysed. Vascular strain was highest in the abdominal aorta (7.2±3.0%) lower in the CCA (5.7±2.1%) and lowest in the CFA (2.1±1.1%) and popliteal artery (1.9±1.1%). Intraday reproducibility of vascular strain in the CCA and CFA was lower than interday reproducibility. In the popliteal artery and abdominal aorta similar strain values were observed within one day and between days (see Table). A variance component analysis showed that the variance of vascular strain mainly depended on the investigated vessel and subject, while individual clips of one vessel, the day of examination and the body side (right/left) only had low impact on the variance of vascular strain. The variance components were similarly distributed in the CCA, CFA, popliteal artery and abdominal aorta.

Coefficients of variation

	Intraday coefficient of variation [%]	Interday coefficient of variation [%]
Common carotid artery	3.9	8.4
Common femoral artery	3.3	10.0
Popliteal artery	6.1	4.6
Abdominal aorta	6.2	5.9

Conclusion: Vascular strain can reliably be determined at various arterial sites with an acceptable reproducibility. Importantly, vascular strain varies considerably between different arteries.

P3489 | BEDSIDE

Doppler ultrasound diagnosis of renal artery stenosis: a retrospective analysis of 1113 examinations in hypertensive patients (2001 - 2013)

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Aims: 1) to perform a retrospective analysis of all hypertensive patients studied with Doppler ultrasound over a 12 years period, in the vascular laboratory of our Institution; 2) to assess the prevalence of >60% renal artery stenosis (RAS); 3) to establish the agreement between positive ultrasound (US) examination and angiography (AGX), resonance angiography (MRA) or computed tomography angio (CTA); 3) to ascertain long-term outcomes of the two treatment options (medical therapy alone vs renal PTA/stenting) in patients with RAS. After giving their informed consent to the inquiry patients filled in a questionnaire on the clinical status, the cardiovascular outcome and the renal function by phone interview.
Methods: 1072 hypertensives underwent 1113 renal US examinations between June 2001 and May 2013. A >60% RAS was diagnosed if renal artery peak systolic velocity (PSV) was >200cm/s, renal aortic velocity ratio (RAR) (i.e. renal PSV/aortic PSV) >3.5 and the interlobar acceleration time (AT) >80ms. Three subgroups were distinguished according to the site of stenosis: 1) proximal monolateral - group I; mid renal artery monolateral - group II; bilateral - group III.
Results: 99 patients (9.2%) met US criteria for RAS: 63 group I patients (5.9%), 10 group II patients (0.9%), 26 group III patients (2.4%).Twenty-five out of the 99 patients with RAS underwent further investigation (AGX, CTA and MRA). AGX and US were consistent in 8 out of 9 patients (88.9%), MRA and US in 5 out of 6 patients (83.3%), CTA and US in 14 out of 16 patients (87.5%). A PSV >200 cm/s showed the strongest relation with radiological results (always present in AGX or CTA positive patients). A >0.80 hilar resistive index and a <10 mm cortical thickness were the strongest predictors of death and were beyond the normal limits in all patients who had died by the end of the follow up. Patients with baseline >1.2mg/dl serum creatinine had the highest mortality rate and the higher number of PTA/stenting procedures (t=3.379; p=0.001 and t=-2.46; p=0.017). In eight out of the 18 patients treated with renal PTA/stenting (44.4%) serum creatinine decrease averaged 8.63% (from >1.2 to <1.2 mg/dl; χ^2=5.315, p=0.021).
Conclusions: A 9.2% >60% RAS prevalence was found in the 1072 hypertensives consecutively screened with Doppler; PSV was the most sensitive parameter to diagnose RAS and was shown to have good agreement with other diagnostic imaging techniques. A >0.80 RI was related with poorer cardiovascular and renal outcome. The PTA/stenting lead to improvement of the renal function in 44.4% of the treated patients.

P3490 | BEDSIDE

The use of iodinated contrastmedia can be reduced by using carbon dioxide contrast media for endovascular therapy regardless of renal function

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Purpose: Iodinated contrast medium (ICM) is harmful to the kidneys. Contrast-induced nephropathy (CIN) is one of the most important clinical complications associated with endovascular therapy (EVT) and is known to be related to ICM volume. Large amounts of ICM are often used in the treatment of complex lesions, especially TransAtlantic Inter-Society Consensus (TASC)- II C and D lesions. In addition, CIN sometimes occurs regardless of renal function. Therefore, we recommend that ICM volume be reduced as much as possible for all patients. Carbon dioxide (CO2) contrast is used as an alternative contrast medium and contributes to the reduction of ICM volume. In this study, we evaluated the effects on renal function of reducing ICM volume by using CO2 contrast in the treatment of complex lesions.
Methods: From July 2012 to October 2013, EVT was performed in 102 consecutively enrolled patients with peripheral artery disease (145 limbs). Patients were divided into 2 groups, the ICM group and the CO2 group. In the ICM group, 51 patients (72 limbs) underwent intravascular ultrasound (IVUS)-guided EVT with only ICM. In the CO2 group, 62 patients (73 limbs) underwent IVUS–guided EVT with CO2 contrast and a small amount of ICM. CO2 was injected by hand using a simple homemade delivery system. Lesions were classified according to TASC II classification.
Results: The overall technical success rate was 100% in both groups, and there were no major complications. The use of CO2 contrast prevented worsening estimated glomerular filtration rates (eGFR) postprocedure, unlike the use of ICM (ΔeGFR: -1.17±10.7mL/min/1.73 m^2 in the ICM group vs +2.6041±12.0mL/min/1.73 m^2 in the CO2 group, P=0.936). In addition, ICM volume was significantly reduced by using CO2 contrast for the treatment of TASC C and D lesions (92.7±40.6 mL in the ICM group vs 38.6±27.1 mL in the CO2 group, P=0.011), especially below the knee lesions (88.0±35.1mL in the ICM group vs 28.9±19.2mL in the in the CO2 group, P=0.046).
Conclusions: The use of ICM in endovascular therapy can be reduced by using CO2 contrast regardless of renal function, especially for the treatment of complex lesions. We suggest that CO2 contrast can be used as a main contrast agent in endovascular therapy.

P3491 | BEDSIDE

Are intermediate ankle-brachial index values important? Insights from a large cohort of never-treated hypertensives

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Purpose: Ankle brachial index (ABI) is a diagnostic tool for peripheral arterial disease; moreover it has a prognostic value for future events. However, the role of intermediate ABI values (0.9 to 1.3) is still unclear. We investigated the interplay of intermediate ABI values with indices of subclinical organ damage in a large cohort of newly diagnosed, never treated hypertensives.
Methods: 1,127 newly diagnosed, never-treated hypertensives were recruited. ABI was measured with the oscillometric method; subjects with ABI <0.9 or >1.3 were not included. Carotid-femoral pulse wave velocity (cfPWV), central (aortic) blood pressures, augmentation index (AIx), left ventricular mass index (LVMI) and C-reactive protein (CRP) were measured. Chronic kidney disease stage was determined according to eGFR values. The 10-year risk for cardiovascular disease (CVD) was calculated using the Framingham Risk Score.
Results: The cohort had mild-moderate hypertension (systolic BP: 151±18 mmHg, diastolic BP: 90±11 mmHg) and mean ABI value 1.15±0.08. LV hypertrophy was detected in 42.2% of patients; the 10-year risk was 15.9±9.6%. ABI correlated with cfPWV, central systolic BP, AIx, LVMI and CRP (r: -0.182, -0.268, -0.195, -0.075, -0.152 respectively, p<0.01 for all). The 10-year risk increased with lower ABI values (r=-0.077, p<0.01). After adjusting for confounders, patients with LVH had higher levels of ABI; lower ABI values were observed with worsening renal function (Fig. 1).

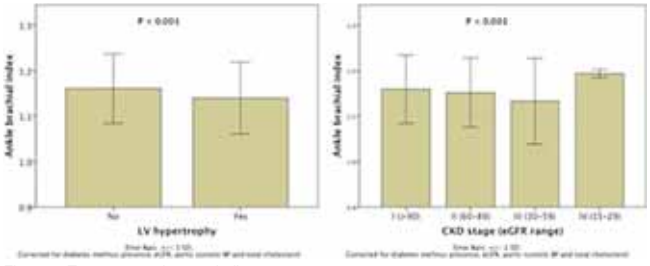

Figure 1. Target organ damage indices

Conclusions: Intermediate ABI values carry prognostic information in never-treated hypertensives, as they are related to large artery stiffness, impaired central hemodynamic indices, LVH, renal function impairment and 10-year risk of CVD. ABI measurements should be part of an integrated approach for both diagnostic and prognostic reasons.

P3492 | BEDSIDE

Ankle-brachial index in patients with coronary artery disease: is it useful?

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Purpose: The usefulness of an ankle-brachial index (ABI) <0.9 in predicting atherosclerotic disease in other vascular territories and in evaluating cardiovascular risk has been questioned and higher values of ABI (<0.99) have been recently evaluated. In coronary artery disease (CAD) patients the prevalence of peripheral arterial disease (PAD) is not consensual and the utility of ABI in this population is questionable.
This study aims to evaluate ABI utility as predictor of subclinical PAD, in relation with CAD severity, in a non-selected population of patients submitted to coronariography.
Methods: ABI was evaluated in 284 consecutive patients (mean age 57.6±15.5 years, 60.6% males) submitted to coronariography because of acute coronary syndrome or stable angina and in 35 control-patients without known CAD. ABI was calculated as the least ratio between ankle and ipsilateral arm arterial pressure, measured with a Doppler probe. ABI <0.99 was considered diagnostic of PAD.
Results: An ABI <0.90 and <0.99 was observed, respectively in 31 (10.9%) and 53 (18.7%) patients. ABI mean value was 1.04±0.06 in control group; 1.03±0.13 in the group without CAD; 1.06±0.16 in the group with 1 vessel CAD; 0.99±0.17 in the group with2 vessels CAD; 1.00±0.17 in the group with 3 vessels CAD (p=ns). When compared with patients without CAD or 1vessel CAD, patients with

multivessel CAD tended to present higher prevalence of ABI<0.99 in univariate analysis (17.2% vs 27.2%, OR 1.84; CI95 0.95-3.58, p=0.053), but not in multivariate analysis including age and other cardiovascular risk factors (p=0.094). ABI <0.99 was related to age (62.0±14.4 vs 56.6±15.7 years, p=0.02) and diabetes (OR 2.96; CI95 1.49-5.90; P=0.02), but not with dyslipidaemia, hypertension, and smoking (p=ns). In multivariate analysis the association of ABI<0.99 with age (OR 1.04, CI95 1.01-1.08, p=0.011), diabetes (OR 2.36 CI95 1.12-4.97, p=0.024) and smoking (OR 2.56, CI95 1.11-6.00, p=0.028) persisted.
Conclusions: In CAD patients, the prevalence of subclinical PAD assessed by ABI is low and is not associated with CAD severity. Routine evaluation of the ABI in this population has little utility, even using a more sensitive diagnostic value (ABI <0.99). However this technique may be useful in a subgroup of highest risk CAD patients (elderly, diabetics and smokers).

P3493 | BEDSIDE
Predictive value of toe brachial index for CV mortality of patients on hemodialysis with normal ankle brachial index

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Background: Ankle brachial index (ABI) is not only an established marker of peripheral artery disease but also reflects systemic atherosclerosis. However, the diagnostic accuracy is often disturbed in patients with advanced atherosclerosis such as those with diabetes or end-stage renal disease. We investigated whether toe brachial index (TBI) could more accurately predict cardiovascular (CV) and all-cause mortality compared to ABI in patients on chronic haemodialysis (HD).
Methods: A total of 553 outpatients on maintenance HD therapy underwent both ABI and TBI measurement. They were prospectively followed-up for up to 5 years. Normal levels were defined as 0.9 to 1.3 for ABI, and ≥0.6 for TBI, respectively.
Results: Abnormal ABI (<0.9 and ≥1.3) and declined TBI (<0.6) were seen in 146 (26.4%) and 222 (40.1%) patients, respectively. Of patients with normal ABI (≥0.9 and <1.3), 117 (28.7%) patients had declined TBI. Furthermore, diabetes patients significantly frequently had both normal ABI and declined TBI compared to non-diabetes patients (37.0% vs. 22.5%, p=0.0024). During follow-up period (median: 32 months), 100 (18.1%) patients died including 47 (8.5%) with CV causes. Both abnormal ABI (adjusted hazard ratio (HR) 1.90, 95% confidence interval (CI) 1.01-3.54, p=0.046) and declined TBI (adjusted HR 2.59, 95%CI 1.39-4.83, p=0.0027) were independent predictors for CV mortality, respectively. However, even in patients with normal ABI, 5-year Kaplan-Meier event-free survival for CV mortality was significantly lower in patients with TBI<0.6 than those with TBI ≥0.6 (76.1% vs. 91.0%, adjusted HR 2.36, 95%CI 1.08-5.18, p=0.031). Furthermore, the CV mortality risk was similar between patients with abnormal ABI and those with normal ABI but TBI<0.6 (HR 1.32, 95%CI 0.64-2.73, p=0.44). Similar results were observed in all-cause mortality.
Conclusion: Declined TBI was frequently seen, and could independently predict CV- and all-cause mortality even in HD patients with normal ABI. TBI measurement should be recommended in this advanced atherosclerotic population.

P3494 | BEDSIDE
Combination of ankle brachial index and geriatric nutritional risk index improves the prediction of cardiovascular mortality in chronic hemodialysis patients

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Background: Ankle brachial index (ABI) is a marker of systemic atherosclerosis in hemodialysis (HD) patients. Protein-energy wasting (PEW), currently considered to be due to inflammatory process rather than poor nutritional intake, is also highly prevalent in this population. We investigated whether combining of ABI and geriatric nutritional risk index (GNRI) as a simplified marker of the PEW improve the prediction of cardiovascular (CV) mortality in HD patients.
Methods: A total of 1036 HD patients were divided into three groups according to ABI levels; normal group: 0.9-1.4 (n=682), high group: >1.4 (n=150) and low group: <0.9 (n=204). They were also divided into tertiles according to GNRI levels; tertile 1 (T1): <90.8, T2: 90.8-97.3 and T3: >97.3. They were followed up for 8 years.
Results: Declined GNRI levels were independently associated with abnormal ABI (<0.9 or >1.4) (odds ratio 0.97, 95%CI 0.96-0.99, p=0.0009). Both GNRI and ABI were independent predictors for CV mortality, respectively. In the combined setting of ABI and GNRI, the risk of CV mortality was higher in the low ABI group with T1 of GNRI (adjusted HR 4.27, 95%CI 2.06-8.86) and in the high ABI group with T1 of GNRI (adjusted HR, 3.28, 95%CI 1.60-6.76), compared to the normal ABI group with T3 of GNRI, respectively. As regarding model discrimination, C-index, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were greatest in a model consisted of traditional risk factors plus both ABI and GNRI compared to the other models, respectively (Table). Similar results were also obtained in all-cause mortality.
Conclusion: Abnormal ABI and declined GNRI were closely linked, and the combination of both markers more accurately predicted CV and all-cause mortality in HD patients, compared to either variable alone.

Discrimination of each predicting model

	C-index	P value	NRI	P value	IDI	P value
Established risk factors	0.699	Reference		Reference		Reference
+ ABI alone	0.725	0.036	0.370	<0.0001	0.012	0.020
+ GNRI alone	0.734	0.023	0.303	0.0003	0.019	0.0020
+ ABI and GNRI	0.756	0.0004	0.466	<0.0001	0.037	<0.0001

P3495 | BEDSIDE
Mortality rates and mortality predictors in patients with symptomatic peripheral artery disease stratified according to age and diabetes

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Purpose: Atherosclerotic peripheral arterial disease (PAD) is one of the most prevalent, morbid, and mortal diseases. The aim of this study was to evaluate mortality rates of patients with atherosclerotic PAD stratified according to age and diabetes and to determine predictors of death.
Methods: We studied 487 patients with symptomatic PAD consecutively admitted to hospital. This cohort included the following four patient subgroups: (i) 216 PAD patients <75 years of age without diabetes mellitus; (ii) 115 PAD patients <75 years of age with diabetes mellitus; (iii) 102 PAD patients ≥75 years of age without diabetes mellitus; and (iv) 54 PAD patients ≥75 years of age with diabetes mellitus. Control subjects without atherosclerotic disease were matched to the patients with PAD in a 1:1 design by sex, age (±2 years), and diabetes mellitus status. Outcome measure was all-cause mortality at 5 years.
Results: Mortality rates at 5 years were: 10% in non-diabetic PAD patients <75 years [vs. 5% in controls; risk ratio (RR), 2.15; 95% confidence interval (CI), 1.60-4.34]; 23% in diabetic PAD patients <75 years (vs. 7% in controls; RR, 3.53; 95% CI, 1.80-6.91); 38% in non-diabetic PAD patients ≥75 years (vs. 22% in controls; RR, 2.08; 95% CI, 1.26-3.44); and 52% in diabetic PAD patients ≥75 years. Applying multivariate Cox proportional-hazards regression analyses (with cardiovascular risk factors, co-existing atherosclerotic disease, clinical stage of PAD, and several biochemical markers as predictor variables), we found the following independent predictors of outcome: in the 216 non-diabetic PAD patients <75 years, high-sensitivity C-reactive protein (hs-CRP) (RR, 3.04; 95% CI, 1.48-6.26); in the 115 diabetic PAD patients <75 years, amino-terminal pro-B-type natriuretic peptide (NT-proBNP) (RR, 2.63; 95% CI, 1.65-4.19); in the 102 non-diabetic PAD patients ≥75 years, critical limb ischemia (RR, 3.70; 95% CI, 1.82-7.52) and NT-proBNP (RR, 1.93; 95% CI, 1.32-2.82); and in the 54 diabetic PAD patients ≥75 years, hs-CRP (RR 2.61, 95% CI 1.45-4.67) and NT-proBNP (RR 3.31, 95% CI 1.96-5.60).
Conclusions: Mortality rates at 5 years varied considerably among PAD patients stratified according to age and diabetes. Predictors of death differed among the four patient subgroups in this study and included critical limb ischemia, hs-CRP and NT-proBNP. Our results might help to develop future strategies for optimized treatment of hospitalized patients with symptomatic PAD.

P3496 | BEDSIDE
Wave reflection analysis for assessment of augmentation index: comparison between tonometry (SphygmoCor), oscillometry (Vascular Explorer) and finger plethysmography (EndoPAT)

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Objective: Augmentation index (AIx) calculated from wave reflection analysis is an established marker of arterial stiffness contributing to cardiovascular risk assessment and is usually assessed using applanation tonometry (AT) as non-invasive gold-standard. In recent years, various devices have emerged allowing for rapid clinical assessment of AIx using upper arm oscillometry (AO) or finger plethysmography (FP), but these techniques have rarely been compared to AT.
Methods: AIx was assessed in 97 male individuals (mean age 44±9 years) free of cardiovascular disease using three different devices representing the different techniques: AT (SphygmoCor), AO (Vascular explorer) and FP (EndoPAT). Measurements were performed consecutively in the morning after >12h of fasting and >30min resting; blood pressure was unchanged during assessment. Agreement between the devices was analyzed using bivariate correlations and Bland-Altman plots.
Results: Mean AIx for AT, AO and FP were 16.6±12.5%, 13.1±9.6% and 2.9±14.9%, respectively. Strong and highly significant correlations to AT were observed for both AO (r=0.839; p<0.001) and FP (r=0.717; p>0.001) and also between FP and AT after normalization of AIx to a heart rate of 75/min (r=0.682;

p>0.001; AO: normalization not provided). However, Bland-Altman plots comparing means and differences of either AT/AO or AT/FP measurements, although symmetrically distributed, revealed large variations between absolute values in particular for FP (95%-limits of agreement AT/AO -3.0-15.4%; AT/FP -5.8-25.4%), resulting in clinically relevant differences of AIx measurements. These differences were observed independent of age, height, weight and heart rate.
Conclusion: In this cohort of male individuals free of cardiovascular disease, AIx assessed by AO or FP strongly correlates to AT, but absolute values in particular for FP show substantial differences. This may readily be explained by methodological differences, but, when implementing AIx measurements into cardiovascular risk assessment, device-specific reference values will have to be determined beforehand.

P3497 | BEDSIDE
The relationship between carotid plaque area and cardiovascular outcomes

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Purpose: To determine cardiovascular outcomes both mortality and morbidity in patients where carotid plaque area and plaque score had been measured.
Methods: Males 40-70 years and females 50-70 years were selected. Patients with a minimum of 1 year of follow up were included. Patients with diabetes, taking a statin or a history of prior vascular disease were excluded. The first carotid examination was used for analysis. Patients or their surviving relatives were contacted by phone and any vascular events were confirmed by reviewing local hospital records, office records, or coroner's records. As patients often had multiple vascular events, only the first vascular event was used in this analysis. In the case of cardiovascular death, the death was taken as the only event for that patient. Plaque area was measured offline using commercially available GE software in the carotid bulbs and internal carotid arteries. Patients were divided into 4 quartiles according to their total plaque area. The quartiles were as follows, 0mm^2, 0-10.4mm^2, 10.6-37.1mm^2 and ≥37.2mm^2. Statistical analysis was performed using ANOVA and Chi-squared analysis. A P value of <0.05 was considered significant.
Results: See Table 1. There were 1,253 patients who were studied and followed for an average of 4 years (1-8 years). These 1,253 patients experienced 58 cardiovascular events, including 7 cardiovascular deaths. The majority of events (46, 79.3%) including 6 cardiovascular deaths occurred in the 3rd and 4th quartiles. A plaque area <10.4mm^2 is associated with a low cardiovascular event rate, approximately 0.48% per year compared to 1.83% per year for patients' with a plaque area of >10.4mm^2 and 2.39% per year for patients with a plaque area >37.2mm^2.

Table 1

Quartiles	Number	Age (years)	Plaque area (mm^2)	Plaque score (0–6)	Maximal CCA IMT (mm)	CV deaths	CV events	Total events
1	313	58.0±7.4	0	0	0.94±0.24	1	5	5
2	313	58.8±7.1	0.84±3.34	0.39±0.75	0.94±0.24	0	7	7
3	313	59.7±6.7	23.42±7.35	1.94±0.95	1.10±0.40	2	14	16
4	314	62.3±6.2	72.82±33.78	3.31±1.22	1.36±0.63	4	26	30
P value		<0.0001	<0.0001	<0.0001	<0.0001	0.1712	<0.0001	<0.0001

Conclusions: Plaque burden as represented by total either plaque area in the carotid bulb and internal carotid artery or plaque score are both good predictors of future adverse cardiovascular events.

P3498 | BEDSIDE
Assessment of endothelial microparticles and their relation to functional imaging in patients with systemic sclerosis and raynauds phenomenon

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Objectives: Microparticles (MP) are small membrane vesicles, released from activated, damaged and apoptotic cells. Endothelial MP (EMP) can be characterized by the presence of endothelial-specific surface antigens. They do not only reflect ongoing damage or activation of endothelium but also actively modulate processes in inflammation, coagulation and vascular function. Systemic sclerosis (SSc) is a systemic, autoimmune connective tissue disease characterized by vasculopathy and microvascular changes. The aim of the present study was to investigate the number of EMP in relation to inflammation and functional vascular imaging.
Methods: EMPs were quantified in plasma samples of 25 patients (1 male, age: 41±9 years) with SSc using flow cytometry. EMP was defined as CD31+/CD42- MP, and CD62+ MP. Perivascular inflammation was assessed using fluorescence optical imaging (FOI) of the hand (Xiralite). Macrovascular endothelial function was non-invasively estimated using the Endopat system.
Results: Plasma levels of CD31+/CD42- EMP and CD62+EMP were lower in patients with SSc compared to controls (both p<.05). While there was no significant correlation between both EMP and endothelial function, there was a strong association between CD62+EMP and perivascular soft tissue inflammation as assessed by FOI global score (Spearman, p=0.002, r=0.61).
Conclusions: Circulating EMP concentrations are decreased in patients with SSc and raynaud's phenomenon. However, higher counts for EMP representing endothelial activation (CD62) within the patient cohort are associated with perivascular inflammation and vascular leakage.

CHRONIC LIMB ISCHAEMIA

P3500 | BEDSIDE
Elevated blood urea nitrogen is associated with CLI in PAOD patients

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Background: Impairment of renal function is often found in atherosclerosis patients. However, it also accelerates atherosclerosis per se, thus leading to a vicious cycle. We therefore investigated the association of blood urea nitrogen (BUN) with the co-existence of critical limb ischemia in peripheral arterial occlusive disease (PAOD) patients.
Methods and findings: In our retrospective study we included 1521 PAOD patients with normal and impaired renal function treated at our institution from 2005 to 2010. Patients on renal replacement therapy were excluded from analysis. The cohort was divided into tertiles according to the serum BUN levels. An optimal cut-off value for the continuous BUN was calculated by applying a receiver operating curve analysis to discriminate between CLI and non-CLI.
In our cohort occurrence of CLI significantly increased with an increase in BUN (13.1% in the first tertile, 18.7% in the second tertile, 29.0% in the third tertile, p for trend <0.001). As an optimal cut-off a BUN of 17.7 mg/dl was identified. Two groups were categorized, one containing 636 patients (BUN<17.7) and a second group with 885 patients (BUN>17.7). CLI was more frequent in BUN>17.7 patients (342 (38.6%)) compared to BUN<17.7 patients (134 (21.1%)) (p<0.001), as were prior myocardial infarction (45 (5.1%) vs. 15 (2.4%), p=0.007) and congestive heart failure (86 (9.7%) vs. 31 (4.9%), p<0.001). A BUN>17.7 was associated with an OR of 1.6 (95%CI 1.3-1.9, p<0.001) for CLI even after adjustment for other established vascular risk factors like age>75 years and type 2 diabetes.
Conclusions: An increased BUN is significantly associated with a high risk for CLI and other vascular endpoints. The BUN is an easily determinable, broadly available and cheap marker, which could be used to highlight patients at high risk for vascular endpoints.

P3501 | BEDSIDE
Endovascular infrapopliteal interventions guided by an angiosome-based concept will improve clinical outcome in critical limb ischemia

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Background: Primary successful infrapopliteal endovascular interventions show a high variability in the healing process of critical limb ischemia. This might be due to angiosomal variability, differences in collateralization, the unknown role of a revascularization of boundary angiosomas and a missing pedal arch. The aim of this retrospective study was to assess the success rates of limb salvage in respect of an angiosome-based revascularization.
Patients and methods: Between January 2009 and April 2012 we performed 75 infrapopliteal interventions in 72 patients (pts.;35 female, 37 male, mean age: 77±12 years). 97% of the patients had at least one occluded infrapopliteal artery. Patients were placed in two different strategy groups. Group 1 (n=36 pts.) included endovascular interventions guided by an angiosome-based concept of wound healing. In Group 2 (n=39 pts.) infrapopliteal interventions were aimed to achieve at least one straight line flow to the foot. Clinical follow-up was assessed 6 months after intervention. Successful revascularisation was defined by clinical parameters such as wound healing and avoidance of amputation.
Results: In Group 1 successful revascularization by balloon angioplasty (PTA) was performed in three (n=5 pts.), in two (n=18pts.) and one (n=13 pts.) infrapopliteal arteries. Furthermore revascularisation of the pedal arch was done in 15 pts. In Group 2 successful PTA was performed in three (n=2 pts.), in two (n=15 pts.) and one (n=20) infrapopliteal arteries. Technical success rate to reconstitute the patency of at least one tibial artery was 92%. Additional drug-coated balloon angioplasty was performed in 17% of pts. (8% in group 1 and 9% in group 2, respectively). Interventional results yielded in complete wound healing after 6 months in 27 of 36 in Group 1 (75%). Group 2 revealed less complete wound healing (24 of 39 pts; 62%). Amputation rate was 22% in Group 1 and 31% in Group 2, respectively.
Conclusion: Infrapopliteal endovascular interventions which are targeted for direct angiosome revascularization demonstrate increased success rates of limb salvage and an improved clinical outcome. Further analysis is required to assess the importance of the angiosomal variability.

P3502 | BEDSIDE
Development and validation of a new scoring system for predicting wound healing in critical limb ischemia with tissue loss following endovascular therapy

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Background: This study was conducted to design a scoring system for predicting wound healing in critical limb ischemia (CLI) treated with endovascular therapy (EVT). Although the Wagner and the University of Texas wound classification systems are available for diabetic foot ulcer, there is no scoring system for CLI patients.
Methods: Between April 2007 and October 2012, 184 CLI patients (217 limbs) with tissue loss were treated by EVT. In these limbs, 236 individual wounds existed and were divided into a development (n=118) and a validation cohort (n=118). Predictors of wound healing were analyzed using Cox hazard analysis.
Results: Multivariate Cox hazard analysis revealed that Texas grade≧2 (HR 0.531, 95%CI 0.292-0.965, p=0.038), infectious wound (HR 0.529, 95%CI 0.295-0.950, P=0.033), dependence on hemodialysis (HR 0.469, 95%CI 0.264-0.833, P=0.010), no direct blood flow to wounds (HR 0.340, 95%CI 0.139-0.832, P=0.018) and not toe wounds (HR 0.316, 95%CI 0.160-0.624, p=0.001) were adverse predictors of wound healing. Each predictor was assigned score based on their regression coefficients and total scores were calculated. Total score 0 to 1 were considered low-risk, 2 to 3 intermediate-risk, and 4 or greater high-risk for wound un-healing. The area under the receiver operating characteristics curve was 0.922 in the development cohort and 0.808 in the validation cohort. Rates of wound healing at 1 year in low-, intermediate-, and high-risk were 94.6%, 67.6%, and 9.1%, respectively, in the development cohort (P<0.001), and 92.3%, 70.5%, and 31.3%, respectively, in the validation cohort (P<0.001).
Conclusions: This scoring system is useful to predict wound healing in CLI.

P3503 | BEDSIDE
Prognosis of critical limb ischemia with tissue loss after complete wound healing

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Background: Wound healing is important for critical limb ischemia (CLI) with tissue loss, however their prognosis after successful wound healing remains unclear.
Methods: We treated 187 of CLI patients with tissue loss by endovascular therapy from April 2007 to January 2013. Of these 113 patients were achieved wound healing and enrolled in this study. The primary end point was overall survival. The secondary end points were major amputation rates and the recurrence rates of CLI.
Results: The mean follow-up period was 23±17 months. At 1,2, and 3 years, the overall survival rates were 85%, 80%, and 77%, respectively; major amputation rates were 0%, 0%, and 0%, respectively; and the rates of recurrence of CLI were 1.8%, 4.4%, and 6.2%, respectively. In Cox hazard proportional analysis, body mass index<18.5 (HR 2.69, 95% CI 1.10-6.59, P=0.03), dependence on hemodialysis (HR 3.46, 95% CI 1.56-7.68, P=0.02), non-ambulatory status (HR 2.36, 95% CI 1.05-5.31, P=0.039) and age>75 (HR 4.07, 95% CI 1.62-10.2, P=0.003) were independent predictors of all cause death after complete wound healing.
Conclusions: Prognosis of CLI patients with tissue loss after successful wound healing was acceptable, and recurrence of CLI was low. BMI<18.5, dependence on HD, non-ambulatory status, and age>75 can be the predictors of death after complete wound healing.

P3504 | BEDSIDE
Prevalence of coronary artery disease in critical limb ischemia patients undergoing endovascular therapy in asian population

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Background: Peripheral vascular disease (PVD) is known to be a risk factor of significant coronary artery disease (CAD). The aim of this study was to analyze the prevalence of CAD in patients of critical limb ischemia undergoing endovascular therapy (EVT) in a series of Asian population.
Methods: A total of 286 consecutive critical limb ischemia (CLI) patients (pts) were treated by EVT. A total 252 pts [male 76.1%, age 67.4±10.4] who underwent coronary angiography (CAG) before or after EVT were enrolled between November 2004 and October 2012. CAD was defined as angiographic stenosis ≥50% and significant CAD as ≥70% stenosis.
Results: At baseline, the incidence of hypertension was 70.6%, diabetes 73.0%, dyslipidemia 12.6%, cerebrovascular disease 17%, chronic kidney disease 23.0% and atrial fibrillation 9.1%. Among the study population, 58% of pts had wounds (including DM foot, 49.2%), gangrene 9.1%, claudication 11.9%, resting ischemic pain 21.4% and Buerger's disease 3.1%. CAG results showed that the prevalence of CAD was in 71.0% (179/252)and significant CAD in 57.5% (145/252). Left main disease was in 8.3% (21/252), multi-vessel disease 35.7% (90/252), and chronic total occlusion 11.5% (29/252). Among pts with significant CAD, 16.2% (41/252) of pts had history of previous percutaneous coronary intervention (PCI) and 28.9% of Pts (73/252) received PCI during admission for EVT. A total 78.6% (114/145) of significant CAD pts with CLI underwent PCI.
Conclusion: In this study, 57.2% of pts with CLI undergoing EVT had significant CAD and 78.6% of them underwent PCI, showing that advanced PVD was highly associated with significant CAD.

P3505 | BEDSIDE
Clinical impact of complete wound healing within 6 months after endovascular therapy in octogenarians with ischemic tissue loss

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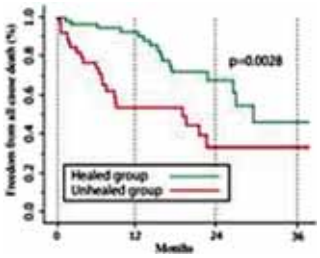
Introduction: It has been reported that patients aged 80 or older with critical limb ischemia (CLI), especially with ischemic limb ulcer or gangrene has poor prognosis. We assessed the hypothesis that complete wound healing after endovascular therapy (EVT) improves the prognosis of octogenarians with ischemic tissue loss.
Patients and methods: Octogenarians with ischemic tissue loss were selected from Japanese prospective multicenter registry, in which CLI patients presenting with pure isolated below-the-knee lesion were included, and were divided into two groups; complete wound healing was obtained (Healed group) and was not (Unhealed group) within 6 months after their initial EVT. Mortality was defined as the primary outcome and analysed by Kaplan-Meier estimation and Cox proportional hazards model.
Results: From 2005 to 2012, in 14 institutes, below-the-knee intervention was performed on 100 octogenarians with ischemic tissue loss. Median follow-up period was 433 days. 39 patients were died within the follow-up period; 33% were died from infectious disease and 23% were from cardiovascular reasons. Wound healing was obtained in 60 patients and incomplete in 40 patients. Patient characteristics except for hemodialysis (28.3% in Healed group vs. 50.0% in Unhealed group, p=0.047)did not differ significantly between two groups. At 1, 2 years, the survival rate were significantly higher in Healed group; respectively 90.1%, 66.9% (Healed group); 52.6%, 32.0% (Unhealed group) (p<0.01). Multivariate analysis also revealed that complete wound healing is a predictor of mortality (HR 0.34, 95%CI 0.16-0.86, p=0.02).



Conclusion: Even in octogenarians with ischemic tissue loss due to CLI, complete wound healing within 6 months after initial EVT surely improves their prognosis.

P3506 | BEDSIDE
Skin perfusion pressure after endovascular therapy and wound healing rate of patient with critical limb ischemia

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Objectives: Skin perfusion pressure (SPP) has been proposed as a method for predicting wound healing in critical limb ischemia (CLI). However, the association between SPP after endovascular therapy (EVT) and wound healing in CLI remains to be clarified. This study aimed to determine the predictive value of SPP for wound healing after EVT.
Methods: We retrospectively analyzed a multicenter database (Japanese BElow-the knee Artery Treatment: J-BEAT). From April 2004 to December 2012, 1097 consecutive patients with CLI, 1332 limbs underwent EVT at 14 cardiovascular centers in Japan. Of these patients, 751 limbs were measured SPP value immediately after EVT.
Results: The wound healing rate was 62.5% (n=487). SPP values after EVT were significantly higher in patients with than in those without wound healing (43.3±16.9 mmHg vs. 36.3±18.6 mmHg, p<0.001). ROC analysis of SPP after EVT to predict wound healing had an area under the curve of 0.62 (95%CI: 0.576-0.663, p<0.001). Binary logistic regression analysis demonstrated SPP af-

ter EVT to be an independent predictor of wound healing ($p<0.001$). The probability of wound healing with SPP values greater than 30 mmHg, 40 mmHg, and 50 mmHg were 56.6%, 62.3%, and 67.8%, respectively.

Figure 1. Probability of wound healing.

Conclusions: SPP after EVT is an predictor of wound healing in patients with CLI. In our study, an SPP value of 50 mmHg was objective goal for prediction of wound healing after EVT.

P3507 | BEDSIDE
Clinical outcome of endovascular therapy for patients with critical hand ischemia

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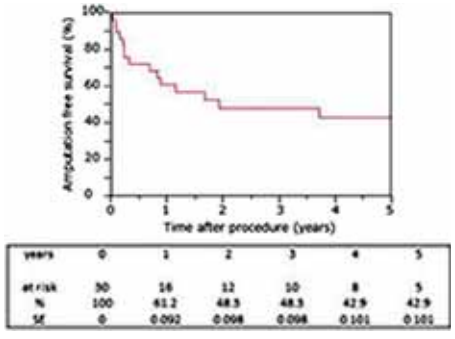
Background: Although atherosclerotic obstructive disease of the upper limb is less common than that of the lower limb the patients with critical hand ischemia are increasing along with increases of the hemodialysis patients. Little is known about clinical outcome of endovascular therapy for CHI. The purpose is to investigate the clinical outcome of endovascular therapy (EVT) for CHI.
Methods: This was a multicenter retrospective study. From January 2001 to December 2012, 30 consecutive patients (33 limbs; mean age 65.8±8.9 years; 56.6% male) who underwent EVT for de novo upper limb artery disease with CHI were retrospectively analyzed. Initial success was defined as <30% of residual stenosis without complications. The primary end point was amputation-free survival (AFS) at 5 years. Secondary end point was freedom from major adverse limb events (MALE: any repeat revascularization for limb and major amputation [defined as above-the-wrist amputation]) at 5 years.
Results: Mean follow – up duration was 26.6±27.8 months. Forty-seven percent of the patients had diabetes, and 63% were on hemodialysis. Initial success was achieved in 97.0%. The 5-years AFS rate was 42.9%, with hemodialysis (P=0.002) associated with a poor prognosis for AFS. The 5-years freedom from MALE was 42.9%, with age (P=0.03), female gender (P=0.03), hemodialysis (P=0.007), and use of warfarin (P=0.002) associated with a poor prognosis for major adverse limb events.



years	0	1	2	3	4	5
at risk	30	16	12	10	8	5
%	100	61.2	48.5	48.5	42.9	42.9
SE	0	0.092	0.098	0.098	0.101	0.101

Conclusions: EVT for upper limb artery disease with CHI was feasible, but the prognosis was poor.

P3508 | BEDSIDE
Long-term clinical outcome after infrapopliteal bypass surgery in chronic hemodialysis patients with critical limb ischemia

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Background: As an established procedure to treat critical limb ishemia (CLI), bypass surgery has been widely performed even in chronic hemodialysis (HD) patients, however, poor prognosis is consistently a clinical problem in this population. Although infrapopliteal occlusive disease is frequently seen in HD patients with CLI, the clinical outcome still remains unclear. We investigated long-term outcomes after infrapopliteal bypass surgery in chronic HD patients with CLI.
Methods: A total of 226 CLI patients with 236 limbs who electively underwent bypass surgery for treatment of infrapopliteal disease were enrolled. Patients were divided into two groups; those on HD (n=177) and those not (n=49), and were followed up for 5 years. Amputation-free survival (AFS), defined as freedom from major amputation or all-cause death, was primarily evaluated. Incidence of target vessel revascularization (TVR) was also analyzed.
Results: Of all patients, 206 patients (91.2%) patients had ulcer/gangrene and 233 limbs (98.7%) were treated using autogenous vein. Age was lower (67±9 years vs. 72±9 years, p=0.0011) and ulcer/gangrene was more prevalent (93.8% vs. 81.6%, p=0.0080) in HD patients than in non-HD patients. During follow-up period (median 28 months), 33 major amputation (14.6%) and 28 TVR (12.4%) occurred, and 65 (28.8%) patients died. Five-year AFS was significantly lower in HD patients than in non-HD patients (43.6% vs. 78.8%, p<0.0001). Adjusted hazard ratio (HR) of HD was 2.36 [95% confidence interval (CI) 1.13-4.92, p=0.022]. Similarly, HD patients had independent risk for major amputation (72.4& vs. 92.5%, adjusted HR 4.36, 95% CI 1.04-18.3, p=0.045) and for mortality (56.9% vs. 83.2%, adjusted HR 2.81, 95% CI 1.30-6.09, p=0.0085), respectively. However, freedom from TVR was comparable between two groups (84.3% vs. 86.8%, p=0.89). In HD patients, body mass index (HR 0.86, 95% CI, 0.76-0.96, p=0.014) and C-reactive protein (HR 1.06, 95% CI 1.01-1.11, p=0.014) were identified as independent predictors for major amputation. Elevated C-reactive protein levels was also associated with mortality (HR 1.04, 95% CI 1.01-1.09, p=0.047).
Conclusion: Despite clinical outcome after infrapopliteal bypass surgery was obviously poorer in HD patients with CLI compared to non-HD patients, the outcome might be acceptable. The comorbid condition such as malnutrition or chronic inflammation was associated with the poor outcome in this population.

P3509 | BEDSIDE
Progression from intermittent claudication to critical limb ischemia after endovascular therapy for femoropopliteal disease

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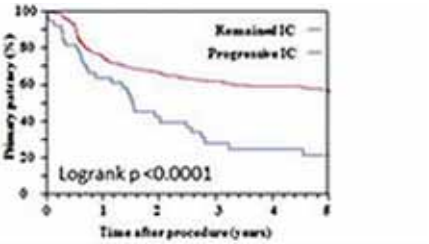
Objective: The purpose is to investigate the outcomes and predictors of progression from IC to CLI after EVT for FP disease.
Methods: From January 2004 to April 2013, 716 consecutive patients (939 limbs, mean age 72.9±8.4 years; 73.0% male) who underwent successful EVT for de novo FP lesions with IC were retrospectively analyzed. The patients were divided into remained claudication group and progression from IC to CLI group. The outcomes of this study were primary patency (PP), secondary patency (SP), overall survival (OS), amputation free survival (AFS), major adverse cardiovascular events (MACE), and MALE (repeat revascularization for the limb or major amputation [defined as above-the-ankle amputation]).
Results: The mean follow-up period was 42.3±28.7 months. 39 patients were progression from IC to CLI after EVT for FP disease. The rate of progression from IC to CLI was 8.5% at 5 years. At 5 years, PP, SP, OS, AFS and freedom from MALE were significantly lower in progression from IC to CLI group (21.7% vs. 56.3%, P<.0001; 57.3% vs. 88.0%, P<.0001; 50.5% vs. 74.4%, P=0.02; 54.0% vs. 75.6%, P=0.01; 22.6% vs. 63.4%, P=0.01, respectively). Freedom from MACE was numerically lower in progression from IC to CLI group (41.5% vs. 62.5%, P=0.06). On multivariate analysis, body mass index (BMI) (HR, 0.87; P=0.03), hemodialysis (HD) (HR, 4.28; P=0.003), medical history of cerebrovascular disease (CVD) (HR, 2.54; P=0.02), and use of statin (HR, 0.41; P=0.049) were the independent predictors of progression from IC to CLI after EVT for FP disease.



years	0	1	2	3	4	5
at risk						
Remained IC	677	441	306	212	168	120
Progressive IC	39	26	16	11	8	6
%						
Remained IC	100	78.1	66.4	61.9	59.4	56.3
Progressive IC	100	64.0	39.8	28.4	28.3	21.7
SE						
Remained IC	0.000	0.017	0.020	0.021	0.022	0.024
Progressive IC	0.000	0.077	0.080	0.076	0.073	0.071

Conclusion: The rate of progression from IC to CLI after EVT for FP disease was low, but the outcomes were extremely poor. BMI, HD, medical history of CVD, and use of statin use were the independent predictors of progression from IC to CLI.

CEREBROVASCULAR DISEASE AND STROKE

P3511 | BEDSIDE
Does gender have an impact on the outcome of patients undergoing carotid artery stenting in clinical practice? Results of the multidisciplinary GECAS Registry

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Background: Severe carotid artery stenosis is known as one major risk factor for stroke. The therapeutic role of carotid artery stenting (CAS) for symptomatic and asymptomatic carotid artery stenosis is still a matter of scientific debate. To date only sparse data exists evaluating gender-related differences of patients undergoing CAS in daily clinical practice.
Methods: We analysed data of the prospective, multicenter and multidisciplinary GECAS-Registry, which was founded in 2011 for continuing quality control in CAS in clinical practice in Germany.
Results: In the GECAS-Registry 1275 CAS procedures were performed in 1210 patients at 51 participating hospitals between January 2011 and December 2012. 318 (26.3%) of all patients were female. 51 hospitals participated in the GECAS Registry in 2011, whereas only 35 hospitals participated in the GECAS Registry in 2012. Table 1 show patient's characteristics, procedural details and the in-hospital event rate.

Table 1

	Women (n=318, 26.3%)	Men (n=892, 73.7%)	p-value
Age (years, Median)	72 (65–78)	71 (64–77)	
Sympt. carotid stenosis	33.9%	30.8%	0.32
Coronary artery disesase	54.2%	63.7%	<0.01
Peripheral arterial disease	22.8%	30.9%	<0.01
Embolic protection system used	91.8%	92.5%	0.70
In-hospital events			
Death	1.6% (5/311)	0.8% (7/881)	0.32
Death or stroke	2.9% (9/311)	2.6% (23/881)	0.79
Major stroke	0.6% (2/309)	0.5% (4/878)	0.65
Minor stroke	1.0% (3/308)	1.6% (14/879)	0.58
Myocardial infarction	0.0% (0/306)	0.2% (2/877)	1.0

Conclusions: One quarter of all CAS procedures are performed in women in clinical practice in Germany today. Women are older and show significantly lower rates of concomitant vascular diseases like coronary artery disease or peripheral arterial disease. The rate of symptomatic carotid stenosis and the rate of in-hospital events did not differ significantly between women and men undergoing CAS in clinical practice. The present data support CAS as a safe and effective treatment option of severe carotid artery stenosis in clinical practice today.

P3512 | BENCH
Long-term outcome of patients with atrial fibrillation or flutter undergoing carotid artery stenting

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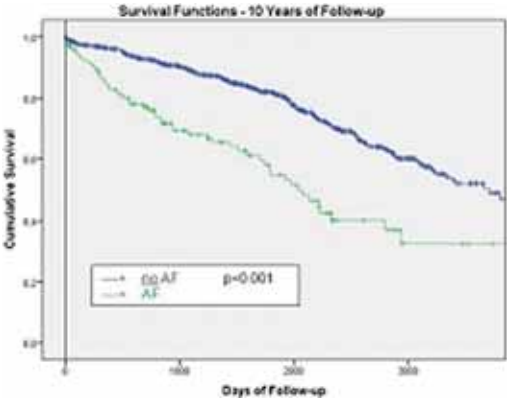
Background: Atrial fibrillation or flutter (AF) is an additional stroke risk factor in patients scheduled for carotid artery stenting (CAS) and is suspected to have an impact on peri- and post-interventional cardiovascular event rates.
Methods: Until October 2013, a total of 884 consecutive patients underwent carotid artery stenting as part of the GECAS-Registry, thereof 120 patients (13.6%) had AF. Comorbidity was higher in patients with AF concerning age (p=0.013), symptomatic status (p=0.04), renal impairment (p<0.001), LVEF <40% (p=0.001) and COPD (p=0.009).



Results: The combined endpoint, consisting of stroke and death after 30 days, was found in 2.9% of all non-AF and 5% of all AF patients (p=0.22). Neurological subentities - i.e. TIA, amaurosis, minor/major stroke - also showed no significant differences. Adversely, Kaplan-Meier analysis of the long-term risk for MACCE (figure) substantiated a highly significant difference in event-free survival disfavoring patients with AF. This difference was mainly driven by a higher percentage of cardiovascular deaths (p<0.001); however also the rate of ipsilateral (p=0.030) and the total number of major strokes (p=0.026) was found to be higher in AF patients. During 10 years of follow-up, no relevant difference has been observed for the rate of TIA, minor stroke (total and ipsilateral), neurological death, and restenosis.
Conclusion: Our consecutive patient data corroborate the hypothesis that patients with AF and severe carotid stenosis have a higher mortality and are at higher risk of sustaining a major stroke during long-term follow-up after CAS. The periprocedural stroke risk seems not to be affected by AF. Thus, emphasis has to be put on optimal long-term management of additional cardiovascular risk factors in AF patients.

P3513 | BEDSIDE
Plaque neovascularization is increased in human carotid atherosclerosis related to prior neck radiotherapy: a contrast enhanced ultrasound study

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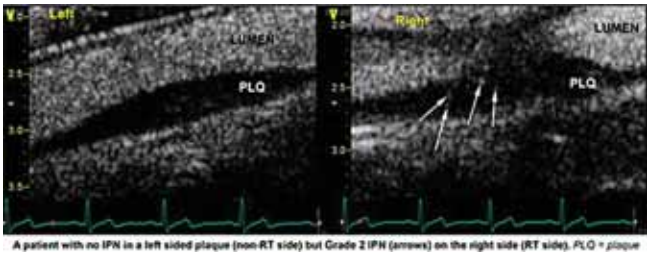
Purpose: Irradiation of the carotid artery during radiotherapy (RT) for head & neck cancer (HNC) increases the risk of stroke. However, the effects of RT upon plaque composition are unknown. Intraplaque neovascularization (IPN) is a pre-cursor to intraplaque haemorrhage and a widely believed marker of plaque instability. Contrast-enhanced ultrasound (CEUS) is a novel method of assessing IPN in vivo.
Methods: B-mode and CEUS carotid ultrasonography were performed in HNC survivors who had received RT >2yrs previously. Long and short axis views of the ipsilateral (RT side) and contralateral (non-RT side) carotid arteries were recorded, first in B-mode and then CEUS, using a continuous contrast infusion. IPN was graded semi-quantitatively as absent (Grade 0), limited to the plaque base (Grade 1) or extensive and/or extending into the plaque body (Grade 2) by a cardiologist blinded to the side of RT.
Results: Of the 49 patients enrolled, the mean age was 57±8yrs and 69% were male. The mean time duration from RT to carotid imaging was 5.3±2.6yrs. Plaques were found in 38 (78%) patients, of whom 36 had plaques on the RT side vs. 17 on the non-RT side (73% vs. 35%, p<0.001). IPN was seen in 29/36 patients with RT-side plaques vs. 7/17 patients with non-RT side plaques (81% vs. 41%, p=0.004). Grade 2 IPN was seen in 14/36 patients with RT-side plaques vs. 2/17 patients with non-RT side plaques (39% vs. 12%, p=0.04). Presence of IPN was not predicted by age, gender, prior chemotherapy or time since RT. The only predictor of IPN was laterality of RT.



A patient with no IPN in a left sided plaque (non-RT side) but Grade 2 IPN (arrows) on the right side (RT side). *PLQ = plaque*

Conclusions: IPN is significantly increased in plaques from irradiated arteries, suggesting that the increased risk of stroke in such patients may be due to RT-mediated proliferation of IPN, thus increasing plaque vulnerability.

P3514 | BEDSIDE
Carotid artery stenting before coronary artery bypass grafting in neurologically asymptomatic patients: data from the TARGET-CAS registry

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Purpose: The role of carotid revascularization in neurologically asymptomatic patients with severe internal carotid artery (ICA) stenosis previous to coronary artery

bypass grafting (CABG) remains undefined. The aim of this study was to evaluate safety and efficacy of carotid artery stenting (CAS) performed before CABG in patients with severe, asymptomatic carotid stenosis coexisting with multivessel coronary artery disease requiring CABG.
Methods: Between 2009 and 2013, among 65 patients with severe, concurrent carotid and coronary artery disease from the TARGET-CAS registry, who had a revascularization by CAS combined with CABG, there was 36 (55%, age 68.7±7.1y, range 53-79y, 77.8% male) neurologically asymptomatic patients with ICA stenosis of 86% ± 8.1%, range 75-99%. Each patient was assessed individually in a multidisciplinary team including cardiac surgeon, invasive cardiologist, vascular surgeon and neurologist. Contralateral ICA occlusion was present in 4 (11%) cases. All CAS procedures were done according to the TARGET-CAS study algorithm, which idea is mandatory use of the neuroprotection system device (NPD) and selection of the NPD (proximal or distal) and stent type to the lesion severity, morphology and neurological symptoms. Closed cell stent was implanted in 32 (89%) patients and proximal NPD was used in 18 (50%) of patients. Left main stenosis was found in 14 (39%) patients. Mean operation risk according to euroSCORE was 2.4±1.2%, range 0.85-6.58%. CABG was either simultaneous or staged with CAS, according to the coronary symptom status. Patients with CCS class 4/unstable angina/NSTEMI were scheduled for hybrid procedure – CAS was immediately followed by CABG (24, 66%), while the others with severe, but stable angina had two sequential procedures: CAS in the first stage and CABG about 5 weeks later (12, 34%). Off- pump CABG was performed in 4 (11%) cases and total arterial myocardial revascularization was done in 7 (19%) patients.
Results: There was no neurological complications (stroke, transient ischemic attack) and no myocardial infarcts in-hospital and on 30-day observation. One (2.7%) death as a result of multi-organ failure occurred on the second postoperative day in the patient with euroSCORE 6.58%.
Conclusion: Our results suggest that strategy of CAS before CABG (hybrid or staged) seems to be an effective method to prevent possible perioperative stroke. This strategy may be a safe and feasible alternative to the surgical methods for neurologically asymptomatic patients with severe ICA stenosis coexisting with multivessel coronary artery disease.

P3515 | BEDSIDE
Main air pollutants and stroke: a systematic review and meta-analysis

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Purpose: Exposure to high levels of air pollution may trigger stroke but this association remains unclear. Our study goal was to assess and quantify the association between short-term exposure to main air pollutants (ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, and particulate matter ≤10 μm (PM10) and ≤2.5 μm (PM2.5) in diameter) and stroke risk.
Methods: An exhaustive electronic search of several databases was conducted (from 1948 and January 1, 2014) for studies investigating the association between short-term exposure (for up to 7 days) to 1 or more air pollutants and subsequent stroke risk. Two independent reviewers selected and extracted data from eligible studies. Using a random effects model, relative risks (RRs) and 95% CIs were calculated for each increase of 10 μg/m^3 in pollutant concentration, except for carbon monoxide (1 mg/m^3). The population attributable fractions (PAFs) were calculated from RRs with the assumption that the prevalence of air pollution exposure was 80% in industrialized countries.
Results: After a detailed screening of 268 citations, 19 studies were identified involving 607,581 stroke cases. All the main air pollutants, except for ozone, were significantly associated with an increase in stroke risk (carbon monoxide: 1.034, 95% CI [1.004-1.065]; nitrogen dioxide: 1.014, 95% CI [1.003-1.025]; sulfur dioxide: 1.008, 95% CI [1.001-1.016]; PM10: 1.008, 95% CI [1.001-1.015]; and PM2.5: 1.002, 95% CI [1.001-1.004]). For ozone, the RR was 0.994, 95% CI [0.984-1.005]. Moreover, PAFs ranged between 0.12% and 2.72%, depending on the air pollutant.

Stroke risk per 10 μm/m^3 air pollutant concentration increase (1 mg/m^3 for carbon monoxide)

Air pollutants	N studies	RR	I-squared	Egger's test
Ozone	9	0.994, 95% CI [0.984–1.005], P=0.281	70%	P=0.34
Carbon monoxide	6	1.034, 95% CI [1.004–1.065], P=0.024	86%	P=0.08
Nitrogen dioxide	8	1.014, 95% CI [1.003–1.025], P=0.015	66%	P=0.09
Sulfur dioxide	8	1.008, 95% CI [1.001–1.016], P=0.05	73%	P=0.15
PM10	10	1.008, 95% CI [1.001–1.015], P=0.031	76%	P=0.02
PM2.5	7	1.002, 95% CI [1.001–1.004], P=0.037	25%	P=0.41

Conclusion: All the main air pollutants, with the exception of ozone, were significantly associated with a near-term increase in stroke risk. Although the RRs were relatively low, the PAFs were not negligible.

P3516 | BEDSIDE
Grade 1 hypertension is associated with an increase in cerebral infarction in octogenarians without atrial fibrillation; analysis from 2473 autopsy cases

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Background: HYVET study showed the efficacy of antihypertensive treatment in healthy octogenarians, but target blood pressures (BP) for the very elderly remain to be examined. The Hisayama study suggested that the risk of vascular events rose with increasing BP above 180 mmHg in octogenarians. Moreover, complication of atrial fibrillation (AF) might affect the results.
Methods: We studied 2473 consecutive autopsy cases including brain autopsy (1235men, mean 80.6±0.2yrs) at a general geriatric hospital. We related office systolic BP and the age of death to cerebral infarction (CI) and severity of CI. The atherosclerosis of the intra-cranial artery (A-CA) was semi-quantitatively evaluated. Complication of AF was examined with electrocardiogram and the medical record.
Results: Office BPs were 141±1/78±0mmHg. Antihypertensive drugs were prescribed in 35% of the cases. CI was detected in 66%. The age of death was associated with systolic BP (r=0.12, *p<0.001), pulse pressure (r=0.16*), left kidney weight (r= -0.41*), and A-CA (r=0.30*). Moreover, systolic BP (r=0.16, *p<0.001), diastolic BP (r=0.10*), pulse pressure (r=0.12*), left kidney weight (r= -0.14*), A-CA (r=0.39*), and complications of AF (r=0.22*) were related to severity of CI. In the logistic regression analysis, the hazard of CI after adjustment for age and sex was 2.56 (95%CI, 1.95 to 2.19*) for the highest (≥156mmHg) versus the lowest systolic BP quartile (<120mmHg), and 1.69 (95%CI, 1.30 to 2.19*) for the second highest (140-155mmHg). The hazard of CI among the cases <80 yrs old (n=1043) was similarly significant. The hazard of CI among the cases ≥80 yrs old (n=1430) was 1.80 (95%CI, 1.23 to 2.63; p=0.003) only for the highest quartile. However, after excluding those with AF the hazard of CI was 2.03 (95%CI, 1.34 to 3.06; p=0.001) for the highest, 1.60 (95%CI, 1.07 to 2.39; p=0.023) for the second highest quartile.
Conclusion: With the advancing age, kidney atrophies, BP increases, and systemic atherosclerosis progresses. Grade 1 hypertension is associated with an increase in cerebral infarction for octogenarians without AF, as well as for the subjects under the age of 80.

P3517 | BEDSIDE
Risk of stroke in patients with high on clopidrogel platelet reactivity to ADP after percutaneous coronary intervention: systematic review and meta-analysis

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Background: Several prospective studies have shown that high on clopidogrel platelet reactivity (HPR) in patients undergoing percutaneous coronary intervention (PCI) is a risk factors for ischemic events. All studies were insufficiently powered to detect differences in stroke between patients with HPR and those without. Therefore we performed a systematic review and meta-analysis of available publications aimed at determining whether patients undergoing PCI with HPR are also at increased risk of stroke.
Methods: We searched for prospective studies enrolling patients undergoing PCI and treated with aspirin and clopidogrel that reported on clinical relevance of HPR to adenosine diphophate (ADP). Study endpoint was the rate of stroke. We also investigated whether there was an interaction on the relative risk of stroke between HPR, clinical presentation, duration of follow up or laboratory methods.
Results: Fourteen studies including 11959 patients were deemed eligible. On pooled analysis, the risk of stroke was higher in patients with HPR as compared to patients with no-HPR (1.2% vs. 0.7%, Relative Risk on fixed effect=1.84; 95% Confidence Intervals: 1.21-2.80). There was no heterogeneity among the studies

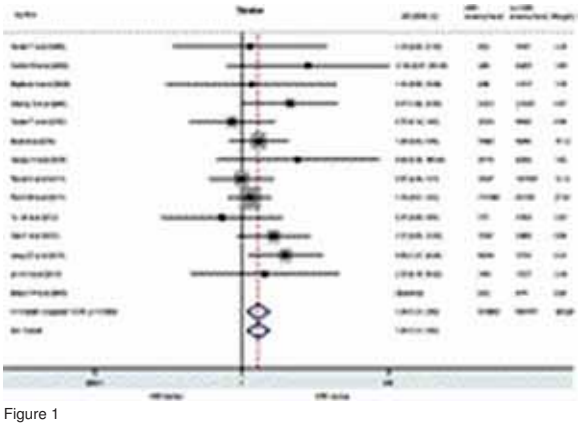

Figure 1

(I2 = 0.0%, P=0.5) [figure]. Clinical presentation (p=0.39 for interaction), duration of follow up (p=0.87 for interaction) and labotarory method for detection of HPR (p=0.99 for interaction) did not affect the relative increase in the risk of stroke in patients with HPR as compared to patients with no-HPR.
Conclusions: In patients with coronary artery disease undergoing PCI the presence of HPR to ADP is a risk factor for stroke.

P3518 | BEDSIDE
Within-individual day-by-day blood pressure variability during subacute stage predicts functional and long-term survival outcomes in ischemic stroke patients: Fukuoka Stroke Registry

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Purpose: In the Fukuoka Stroke Registry (FSR), a large-scale multicenter registry enrolling stroke patients, higher blood pressure (BP) during the acute stage was associated with poorer 3-month functional prognosis in patients after acute ischemic stroke. However, prognostic significance of within-individual BP variability remains unknown in patients after acute ischemic stroke. Thus, we investigated the impact of in-hospital day-by-day BP variability during the subacute stage (4-10 days after the onset) on 3-month functional prognosis and long-term survival prognosis.
Methods and results: Among consecutive 7571 patients in the FSR (median follow-up of 740 days), we investigated 2540 patients with the first-ever ischemic stroke within 24 hours after onset, who had been functionally independent before onset. Within-individual day-by-day variability of systolic BP (SBP) was assessed by standard deviation and coefficient of variance of SBP (SD-SBP and CV-SBP, respectively). After adjustments for SBP levels and confounding factors, large SBP variability was significantly and independently associated with poor 3-month functional prognosis with modified Rankin scale of 3 or more (e.g. top-quartile odds ratios for SD-SBP: 1.46 [1.04-2.07], $p<0.05$ and for CV-SBP: 1.50 [1.07-2.09], $p<0.05$). Kaplan-Meyer curves showed that long-term prognosis, a composite of all-cause death and stroke recurrence, was poorer in the top-quartile of SD-SBP and CV-SBP than other quartiles (Log-rank test: $p<0.001$ for both). After adjustments for SBP levels and confounding factors, SBP variability was an independent predictor of long-term prognosis (e.g. top-quartile hazard ratio for SD-SBP: 1.38 [1.07-1.78], $p<0.05$ and for CV-SBP: 1.50 [1.17-1.93], $p<0.01$). Subanalysis including only patients who did not receive antihypertensive drugs showed the similar results.
Conclusions: Within-individual day-by-day SBP variability during the subacute stage predicts not only short-term functional outcome but also long-term outcome in acute ischemic stroke patients, independently of SBP levels. In-hospital BP measurements and their variability can provide valuable prognostic information in acute ischemic stroke patients.

P3519 | BEDSIDE
Carotid ultrasound accurately detects arterial calcification quantified by cone beam computed tomography

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Background and aim: Arterial calcification is often detected on ultrasound examination, the diagnostic accuracy of which is not well validated. The aim of this study was to determine the accuracy of carotid ultrasound B mode findings in detecting atherosclerotic calcification as compared with cone beam CT (CBCT).
Methods: We analyzed 98 carotid arteries, from 92 patients who underwent pre-endarterectomy ultrasound examination. Plaques with high echogeneic nodules and posterior shadowing were considered calcified. After surgery, the removed plaques were examined using CBCT, from which the calcification volume (mm^3) was calculated. Carotid artery calcification by the two imaging techniques was compared using conventional correlations.
Results: Carotid ultrasound was highly accurate in detecting the presence of calcification, with a specificity of 100% and sensitivity of 91.7%, p=0.007, having an area under the ROC curve (AUC) of 85% (95% CI=0.75-0.95), $p<0.001$. Using ROC analysis, a cut-off value of $14mm^3$ was determined. Carotid ultrasound sensitivity in detecting a calcification volume of ≥ 14 mm^3 was 96.1% and specificity was 100%. Of the 21 plaques with a 1-$14mm^3$ calcification, only 13 were detected by ultrasound, resulting in a sensitivity of 61.9%, with p=0.219.
Conclusion: Carotid ultrasound is highly accurate in detecting the presence of calcified atherosclerotic lesions of volume more than 14 mm^3. However it was less accurate in detecting small volume calcified plaques, with a relatively high false negativity.

P3520 | BEDSIDE
Proton pump inhibitors are associated with higher mortality in stroke patients receiving clopidogrel treatment - a nationwide propensity score-matched study

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Purpose: Proton pump inhibitors (PPIs) have been associated with diminished effect of clopidogrel in patients with cardiovascular disease. We examined the effect of PPIs on adverse cardiovascular events in clopidogrel treated patients treated with clopidogrel after first time stroke.
Methods: Retrospective nationwide propensity score matched study based on administrative data from all hospitals including all clopidogrel-treated patients surviving 30 days after first time stroke from 2000 to 2011, with follow-up for one year. The risk of the combined end point of cardiovascular death, myocardial infarction, or stroke and for secondary endpoints (see below) associated with use of PPIs was analyzed using Kaplan-Meier analysis, Cox proportional hazard models, and propensity score-matched Cox proportional hazard models.
Results: A total of 1281 patients receiving clopidogrel after first time stroke were included, matched by propensity score according to PPI treatment at baseline. During follow up 936 deaths were recorded, 402 (43%) and 534 (57%) in patients without and with PPI treatment, corresponding to incidence rates of 29 and 38 per 1000 patient-years respectively. Cox regression analyses showed hazard ratios (HRs) for patients receiving PPIs of 1.55 (95% CI 1.31-1.84; $P<0.001$) for the composite end point (Figure), 1.55 (1.31-1.84; $P<0.001$) for cardiovascular death only, 1.48 (1.30-1.68; $P<0.001$) for all-cause death, respectively.

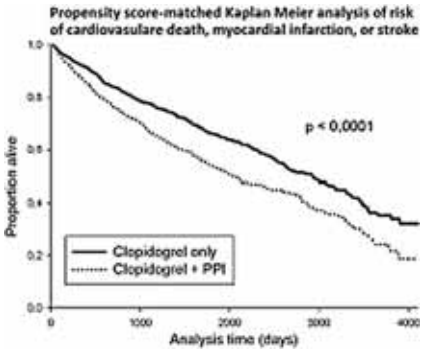

Figure 1. Propensity score-matched KM.

Conclusion: In clopidogrel-treated patients after first time stroke, treatment with PPIs was associated with higher cardiovascular and all-cause mortality.

P3521 | BEDSIDE
Time elapsed after ischemic stroke and risks of adverse cardiovascular events and mortality following elective non-cardiac surgery - a nationwide cohort study

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Purpose: To investigate the association of time elapsed between stroke and surgery and risk of perioperative outcomes.
Methods: All patients with a history of ischemic stroke within 5 years undergoing elective non-cardiac surgery in Denmark 2005-2011 were identified through

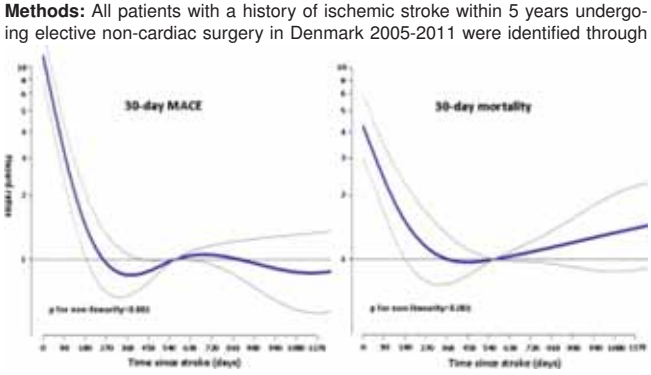

Figure 1

nationwide databases. The association of time elapsed between ischemic stroke and surgery, and risk of 30-day perioperative MACE (ischemic stroke, acute myocardial infarction and cardiovascular death) and mortality was assessed using Cox regression analyses and cubic regression splines adjusted for gender, age and surgery subtype.
Results: We identified 8,322 patients. Crude incidence rates (95% confidence interval) of MACE and mortality were 74.7 (68.9-80.6) and 41.1 (36.8-45.4) per 1000 patients. Splines revealed a nadir of MACE and mortality after 6-9 months; Figure 1.
Conclusion and relevance: A history of stroke seem to carry a time-dependent risk of MACE and mortality in surgery. Our data suggest that patients with recent stroke should preferably be postponed for surgery until 6-9 months. The time-dependency of risks may warrant attention in future guidelines.

P3522 | BEDSIDE
Medical treatment versus carotid endarterectomy in patients with severe asymptomatic carotid atherosclerosis: randomized clinical trial

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Background: The role of modern medical therapy (statins, antihypertensive treatment, and aspirin) in the treatment of patients with severe asymptomatic carotid atherosclerosis is undefined.
Aims and objectives: The aim of this randomized trial was to compare the efficacy of carotid endarterectomy and optimal medical therapy (CEA group) versus optimal medical therapy (OMT group) alone in patients with asymptomatic (70–79%) extracranial carotid stenosis.
Methods: The AMTEC study is a prospective, randomized, parallel, two-arm, multicenter trial. Patients were randomly assigned to CEA group or OMT group; all participants received aggressive lipid-lowering therapy (atorvastatin from 10 to 80 mg per day with a target level of LDL-cholesterol $<$100 mg/dl), aspirin and antihypertensive therapy (losartan and amlodipin). Primary endpoints were analyzed using standard time-to-event statistical modeling with adjustment for major baseline covariates. The primary analysis was on an intent-to-treat basis. The primary outcome are nonfatal stroke, nonfatal myocardial infarction, carotid/coronary revascularization and death during follow-up of up to five-years.
Results: There were 2 primary events in the CEA group and 12 events in the OMT group. The 3.0-year cumulative primary-event rates were 6.5% in the CEA group and 48.0% in the OMT group (hazard ratio for the OMT group, 3.75; 95% confidence interval [CI], 1.31 to 10.75; P=0.014). There were no significant differences between the CEA group and the OMT group in the composite of death, myocardial infarction, and stroke (6.5% vs. 32.0%; hazard ratio, 2.82; 95% CI, 0.89 to 10.43; P=0.12).
Conclusions: As an initial management strategy in patients with severe asymptomatic carotid atherosclerosis, CEA reduce the risk of death, stroke, myocardial infarction, carotid and coronary revascularization events when added to optimal medical therapy.

PERIPHERAL INTERVENTION I

P3524 | BEDSIDE
Comparison of vascular response to paclitaxel-eluting nitinol stent versus bare-metal nitinol stent in the superficial femoral artery lesion: a 3-dimentional intravascular ultrasound study

K. Miki, K. Fujii, M. Fukunaga, M. Nishimura, T. Horimatsu, T. Saita, H. Tamaru, T. Imanaka, T. Masuyama. *Hyogo College of Medicine, Nishinomiya, Japan*

Purpose: Although previous intravascular ultrasound (IVUS) studies reported that the drug-eluting stent (DES) dramatically inhibited neointimal hyperplasia (NIH) in the coronary artery lesion, no IVUS data after DES implantation in the superficial femoral artery (SFA) have been published. Therefore, we investigated the vascular response to self-expanding-paclitaxel-eluting stent (PES) versus self-expanding-bare-metal stent (BMS) in the SFA by IVUS.
Methods: We analyzed 51 SFA lesions that underwent endovascular therapy (EVT) with BMS (34 lesions) or PES (17 lesions). IVUS was performed immediately after stenting and at 6-month follow-up. Stent, lumen, and neointimal volumes were calculated using Simpson's rule in quantitative IVUS analysis. Mean stent, lumen and neointimal areas were computed as the volume divided by the stent length. Mean late lumen area loss was defined as mean lumen area immediately after initial deployment - mean lumen area at follow-up. Edge dissection, tissue protrusion, and luminal thrombus were assessed in qualitative IVUS analysis. The primary end point was mean late lumen loss during follow-up.
Results: Binary angiographic in-stent restenosis (ISR) rate was similar between 2 groups. Time course changes in volumetric IVUS parameters were shown in Figure. Mean neointimal area was smaller in the PES group compared to the BMS group ($3.3\pm1.0mm^2$ vs. $10.2\pm4.1mm^2$, $p<0.001$). Similarly, mean late lumen loss was lower in the PES group ($-2.3\pm3.7mm^2$ vs. $2.1\pm4.7mm^2$, $p<0.05$). There were no differences in qualitative IVUS findings between 2 groups.
Conclusions: Serial volumetric IVUS analysis confirmed significantly less NIH after PES compared with BMS implantation without abnormal morphological findings. EVT with DES for the SFA lesions might decrease NIH that associated with ISR.

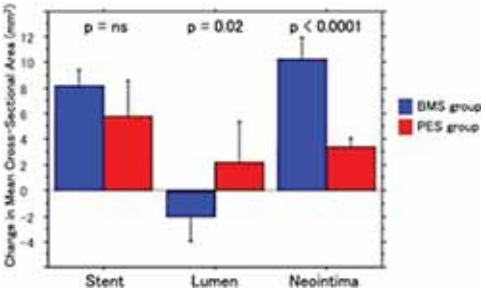

Figure 1

P3525 | BEDSIDE
Vascular flow reserve immediately after infrapopliteal intervention as a predictor of wound healing within 3-months in patients with foot tissue loss

M. Fukunaga, K. Fujii, K. Miki, M. Nishimura, T. Saita, T. Horimatsu, H. Tamaru, T. Imanaka, T. Masuyama. *Hyogo College of Medicine, Nishinomiya, Japan*

Purpose: The impaired coronary blood flow reserve after coronary intervention has been related to microvascular damage leading to increased morbidity and mortality. However, it is not clear whether it applied to patients with critical limb ischemia (CLI) undergoing endovascular treatment (EVT) for isolated infrapopliteal lesions.
Methods: A consecutive series of 28 limbs of CLI patients presenting with ischemic tissue loss undergoing EVT for isolated infrapopliteal lesions were enrolled. All lesions were treated by conventional balloon angioplasty alone. After the procedure, a pressure/temperature sensor-tipped guidewire was positioned in the proximal popliteal artery. By using thermodilution technique, mean transit time (Tmn) of a thermodilution-curve was obtained after bolus injections of 3 mL saline at baseline and at intra-arterial papaverine induced maximum hyperemia (30mg). Vascular flow reserve (VFR) was calculated as resting Tmn divided by hyperemic Tmn. Wound healing success was defined when complete healing of initial wound was obtained within 3 months after EVT and it was treated by plastic surgeon.
Results: VFR was successfully measured immediately after EVT in all patients without any complication. Wound healing success was achieved in 16 limbs after EVT (healing group) and not achieved in 12 (non-healing group). No significant differences existed in baseline lesion characteristics between two groups. Although there was no significant difference in pre-EVT VFR value between the non-healing and healing groups (3.7 ± 1.7 versus 3.6 ± 1.6), post-EVT VFR was significantly lower in the non-healing than in the healing groups (2.8 ± 1.1 versus 4.2 ± 2.0, $p<0.05$). A Receiver operating characteristic analysis identified post-EVT VFR >3.6 (sensitivity 68.8% and specificity 83.3%) as the best threshold value for wound healing success after EVT.
Conclusions: Post-procedural VFR is restricted in patients with poor wound healing due to the increase of resting blood flow. Post-EVT VFR >3.6 reliably identifies wound healing for CLI patients. This easily assessable VFR is useful in clinical risk stratification for patients with CLI immediately after EVT in the catheterization laboratory.

P3526 | BEDSIDE
Development and validation of a risk score to predict access site hematomas after peripheral vascular interventions

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Purpose: Access site hematomas (ASH) complicating peripheral vascular interventions (PVI) are associated with prolonged hospitalization and increased mortality. The aim of this study was to create a clinical scoring tool to stratify patients according to their risk of developing post-PVI ASH.
Methods: The Society for Vascular Surgery Vascular Quality Initiative database yielded 27,997 patients who had undergone PVI from July 2007 to January 2014 at 151 North American centers. Clinically and statistically significant ($p<0.05$) preprocedural risk factors associated with in-hospital post-PVI ASH were included in a multivariate logistic regression model with ASH as the outcome variable. A predictive model was developed with a random sample of 70% of the dataset and validated against the remaining 30%. Risk factors were assigned weighted integers based on their beta coefficients, and the sum constituted the risk score.
Results: Access site hematoma occurred in 939 (3.4%) patients. Predictors included in the model were: female gender, age >70, white race, bedridden ambulatory status, insulin-dependent diabetes mellitus, prior minor amputation, procedural indication of claudication and nonfemoral arterial access site (model c-statistic = 0.637). The discriminatory power of the risk model was confirmed by the vali-

dation dataset (Brier score = 0.033). Higher risk scores correlated with increased frequency of ASH: 1.9% for low risk (score 0 - 15), 3.4% for moderate risk (16 – 27) and 5.0% for high risk (28 - 34).
Conclusions: The proposed clinical risk score based on 8 preprocedural characteristics is a simple tool to stratify patients at risk for post-PVI ASH. The risk score may assist physicians in therapeutic decision-making, including selection of the appropriate bleeding avoidance strategy, to improve outcomes in patients undergoing PVI.

P3527 | BEDSIDE
Role of thrombin injection in management of postcatheterisation pseudoaneurysm in relation to the clinical predictors; primary PCI is a new risk factor

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Introduction: Iatrogenic femoral artery pseudoaneurysms occur between 0.2–0.5% of diagnostic coronary angiography studies and up to 8% of coronary interventions. The use of duplex-guided thrombin injection has allowed successful repair of pseudoaneurysm.
Aim of the study: To assess the success rate of percutaneous ultrasonographically guided thrombin injection in the treatment of post catheterisation pseudoaneurysms and to detect the clinical predictors of such complication.
Methods: 117 patients treated for pseudoaneurysms through thrombin injection as the initial therapy were retrospectively enrolled. Duplex was performed in patients with predictable vascular complications based on the presence of pain, Hematoma, audible bruit or post-procedural bleeding at the puncture site.
Results: Thrombin injection was successful in 100% of the patients with pseudoaneurysms. A single time thrombin injection was successful in 52.6% of the patients. Mean dose of thrombin injected was 117.7 IU $\pm$106. A strong positive correlation was found between the injected dose and the size of pseudoaneurysm ($r=0.81$; $p<0.0001$). Primary PCI was performed in 73 patients in our cohort presenting 62.9% among all patients. We didn't record any complications related to thrombin injection in our study.

Figure 1. Post-catherisation thrombin injection.

Conclusion and recommendations: Ultrasound-guided percutaneous injection of thrombin for the management of pseudoaneurysms is an effective, completely safe and time-saving procedure. In our study, primary PCI proved to be a key factor in developing post-catherisation pseudoaneurysm. Every patient with slight suspicion of pseudoaneurysm after primary PCI should receive arterial duplex scanning.

P3528 | BEDSIDE
Efficacy of the preoperative assessment with a ultrasonography vascular elastography in endovascular therapy

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Background: The success rate of endovascular therapy (EVT) for long chronic total occlusion (CTO) of femoropopliteal arteries has improved because of devices development and the introduction of the echo or IVUS guided EVT. In the diagnosis of peripheral artery disease, duplex ultrasonography is noninvasive, simple and usefulness, but it was impossible to assess the lesion morphology. Elastography is an ultrasonographic method that has been examined as a diagnostic tool for breast lesions. We applied this method to hardness measurement of CTO lesions by our original method. Our aim was to investigate the usefulness of the ultrasonography (US) "vascular elastography (VE)" in EVT for long CTO lesions of SFA.
Method: In 1274 consecutive cases which underwent EVT between April 2010 and May 2013, we focused on 57 cases of EVT for long CTO of femoropopliteal arteries, which CTO length was more than 150mm. We assessed the CTO lesions by duplex US and "VE" about lesion hardness with our original methods before procedure. US was performed with 8 MHz linear transducer, and off-line analysis of "VE" was performed with elasto-Q. We originally categorized into five types by original VE score. The ratio of hard appearance portion (VE score 0-1) to CTO (H/T ratio) was evaluated. Comparing investigation about procedure results was performed between hard group (H group: hard portion$>$20%) and non-hard group (NH group: hard portion$<$20%). In EVT, guide wire was penetrated with US guided from body surface without fluoroscopy.
Result: We could assess elastogram of target CTO lesions in all cases (H group: 27 cases, S group: 30 cases). No significant difference was detected in CTO lesion length (H: 28.9$\pm$6.8mm, S: 26.6$\pm$4.7mm). Hard portions were detected in CTO lesions (H: 10.2$\pm$6.9mm, H/T ratio 32.5$\pm$15.8% vs. S: 1.8$\pm$1.8mm, H/T ratio 7.3$\pm$6.6%; $p<0.001$). Operation time in H group was longer than S group (H: 248.0$\pm$115.1min vs. S: 142.9$\pm$42.1min; $p=0.01$). Success rate was H: 92.6% vs. S: 100%. No significant difference was detected in case of retrograde approach from popliteal artery (H: 29.6%, S: 10.0%). Retrograde approach was needed in only 17 cases which distal site of CTO was VE score 0 to 2 (VE score 0-2: 29.8% vs. 3-4: 0%; $p<0.01$). Cases in S group could be penetrated with hydrocoat soft guidewire (12.1% vs. 65.2%; $p<0.001$).
Conclusion: "Vascular Elastography" might be able to predict the difficulty of EVT, useful when we decide strategies and selections of device because we could assess the vascular morphology noninvasively before procedure.

P3529 | BEDSIDE
In vivo and protease-activated receptor-1-mediated platelet activation but not response to antiplatelet therapy predict two-year outcomes after peripheral angioplasty with stent implantation

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Background: Data linking the response to antiplatelet therapy with clinical outcomes after angioplasty and stenting for lower extremity artery disease (LEAD) are scarce. Moreover, associations of in vivo and thrombin-inducible platelet activation with the occurrence of adverse events have not been investigated in these patients, so far.
Methods: We assessed clinical outcomes and on-treatment platelet reactivity by four test systems in 108 patients receiving dual antiplatelet therapy after infrainguinal angioplasty and stenting for LEAD. Further, in vivo and thrombin receptor-activating peptide (TRAP)-6-inducible glycoprotein (GP) IIb/IIIa activation and P-selectin expression were measured as sensitive parameters of platelet activation. The primary endpoint was defined as the composite of atherothrombotic events and target vessel restenosis or reocclusion.
Results: Residual platelet reactivity to adenosine diphosphate and arachidonic acid was similar between patients without and with adverse outcomes within two-year follow-up (all $p>0.05$). Further, the occurrence of clinical endpoints did not differ significantly between patients without and with high on-treatment residual platelet reactivity by all test systems (all $p>0.05$). In contrast, in vivo and TRAP-6-inducible platelet activation were significantly more pronounced in patients with subsequent adverse events (all $p<0.05$), and high levels of platelet activation were independent predictors of the primary endpoint (adjusted hazard ratios: 3.5 for high in vivo activated GPIIb/IIIa, 2.9 for high TRAP-6-inducible activated GPIIb/IIIa, 2.3 for high in vivo P-selectin, and 3 for high TRAP-6-inducible P-selectin; all $p<0.05$).
Conclusions: In vivo and protease-activated receptor-1-mediated platelet activation predict two-year clinical outcomes in stable patients undergoing angioplasty and stenting for LEAD.

P3530 | BEDSIDE
Mid-term outcomes after endovascular therapy for femoropopliteal arteries in patients of end stage renal dysfunction on dialysis

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Back ground: Peripheral artery disease (PAD) patients have also increased with the increase in dialysis patients. Short to mid-term clinical outcomes after femoropopliteal (FP) endovascular therapy (EVT) with balloon angioplasty and nitinol stents is slowly becoming clear. However, the evidences of dialysis patients is a little from the world, the data accumulation is needed in the future. This study is to investigate the current status and mid-term outcomes of EVT for FP arteries in patients of end stage renal dysfunction on dialysis.
Methods: This study was a multicenter retrospective study. From January 2010 to March 2013, 455 consecutive patients (mean age 72.7 years; 62% male, dialysis group: n=125 non-dialysis group: n=330) who underwent successful EVT for de novo lesions were retrospectively analyzed. Outcome measures were basement patients and lesions characteristics, and primary patency, free from target lesion revascularization (TLR) and amputation free survival (AFS) rate. All patients had a minimum follow-up of 6 months. Restenosis was defined as $>$2.5 of peak systolic velocity ratio by duplex or $>$50% stenosis by angiogram. Primary patency was defined as treated vessels without restenosis and repeat revascularization. Outcomes were compared between the groups by the student t test, Kaplan-Meier and log-rank methods.
Results: There were a several significant difference in patients and lesions characteristics. The age ($p<0.0001$) and chronic total occlusion rate ($p<0.0001$) were higher in non-dialysis group. Critical limb ischemia ($p<0.0001$), poor below the knee arteries run off ($p=0.0081$), severe calcification ($p<0.0001$), and need to bailout stenting rate ($p=0.047$) were higher in dialysis group. There was no sig-

nificant difference in lesion length (non-dialysis 145±93mm, vs dialysis 132±89 p=0.148). Average follow-up period was 521 days. Primary patency of dialysis group was 55%, 43% at 1 and 2 years, respectively. Freedom from TLR and AFS was 76%, 64% and 80%, 71 at 1, 2 years. Compared to non-dialysis group, freedom from TLR (p=0.0433) and AFS (p=0.0002) were inferior with a significant difference. There was no significant difference in terms of patency between both groups.
Conclusion: The patient and lesion characteristics of dialysis patients were unique and clinical efficacy of EVT for FP disease was unsatisfactory compare to non-dialysis patients.

P3531 | BEDSIDE
Stenting of chronic total occlusion of iliac artery through transradial approach

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Purpose: The aim of the study is to show the safety and efficacy of transradial approach (TRA) for treatening complex iliac lesions.
Methods: TRA for treatment of aortoiliac occlusive disease (AIOD) nowdays is more common approach in order to achieve less post-procedural bleeding complications and low mortality. For a period of one year 13 patients (10 male and 3 female with mean age 58,7) with severe iliac disease were treated. Four patients had critical limb ischemia and nine patients had limiting claudications. Present risk factors were: hypertension, hyperlipidemia, smoking and diabetes. Ankle brachial index (ABI) before treatment in all patients was less than 0.5. Eleven patients were in Rutherford Class 3, and two in Rutherford Class 4. According TASC II classification 1 patient was with type D lesion, 4 with type C and 8 with type B.
Results: The interventions were performed using short 6F hydrophilic introducers. Diagnostic peripheral angiogram was done with Pig-tail or Multipurpose 125cm catheters. Guiding catheter 6F MB 125cm was inserted as close as possible to the origin of treated common iliac artery. For crossing the occlusion, coronary CTO wires were used. In two cases we used 0,035" stiff glide wire. After pre-dilatation wires were exchanged with stiff 0,035" 260cm wire. We deployed 15 balloon-expandable and 3 self-expandable stents. In all cases after stent deployment, balloon post-dilatation was done. Procedures were ended with control angiograms. Despite some difficult lesions (TASC II C/D) the overall primary procedural, technical success and acute patency rate was 100%. The secondary patency rate after 3 months follow-up was also 100%. The ankle brachial index (ABI) significantly improved from a mean of 0.46 to 0.90 and 0,94 on three months follow-up. Minor or major complications (hematoma, distal embolization, dissection, rupture, death) were not documented.
Conclusion: TRA is safe and efficient for treating complex proximal iliac lesions with low major and minor complications if performed by experienced radial operator. This technique is still limited by the lack of adequate equipment.

P3532 | BEDSIDE
Usefulness of duplex sonography guidance and bilateral approach for the endovascular interventions in the superficial femoral artery total occlusions and mid-term result

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Purpose: The crossing of chronic total occlusion (CTO) is sometimes difficult especially in case of long lesions. The duplex sonography guidance and bilateral approach for the superficial femoral artery (SFA) CTO endovascular intervention (EVT) may be helpful to pass the guidewire in the true lumen of CTO lesions, resulting improvement of prognosis and target vessel patency.
Methods: From January 2010 to July 2012, 54 patients (34 males, mean age 73±9) who were suffering from SFA CTO were treated with EVT in our institution. We collected patient characteristics, procedural characteristics, target vessel failure at 1year and mid-term composite endpoint of mortality, target vessel revascularization and failure of limb salvage rates.
Results: In 54 patients, we performed 62 EVT in 61 limbs. The second procedure 12 days after the first failure was successful in one patient, meaning that all 61 limbs were successfully revascularized. The classification of TASC II in 61 limbs were A (3%), B (21%), C (11%) and D (64%), respectively. Duplex sonography guided intervention 50 (81%) and bilateral approach 40 (65%) were used to revascularize SFA CTO. TASC II D limbs were significantly associated with the use of duplex sonography ($p<0.001$) or bilateral approach ($p<0.001$).
At 1 year follow-up, 3 (6%) patients died and 2 patients were lost to follow-up. The mean follow-up period was 537 days. The Kaplan-Meier estimates revealed the composite endpoint at 1 year in our cohort was 20% and there was no significant difference between TASC II A-C and TASC II D limbs (9% vs 29%, p=0.214, log-rank test). The target vessel patency was achieved in 34 limbs at 1 year. The risk factors for death or failure of vessel patency were female gender (odds ratio; OR 4.815, confidence interval; CI 1.569-14.777, p=0.006), TASC II D lesion (OR 5.294, CI1.499-18.698, p=0.010) and the value of HbA1C (OR 1.596, CI 1.027-2.480, p=0.038) in univariate analysis. Multiple logistic regression analysis revealed that the TASC II D lesion (OR 6.221, CI 1.030-37.575, p=0.046) and haemodialysis (OR 14.636, CI 1.102-194.431) were significantly associated with the death or failure of vessel patency at 1year.
Conclusions: Our procedural success rate was 98% and all limbs were successfully revascularized with the combined application of duplex sonography and bilateral approach. Although prognosis after SFA CTO EVT was relatively good, the TASC II D lesion was associated with the target vessel failure and still seemed to be challenging.

P3533 | BEDSIDE
Vascular stenting with a self-expanding stent graft for vascular complications after percutaneous TAVR

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Background: The vascular complications (VC) after percutaneous TAVR are independent predictors of post-operative mortality and are associated with sheath size, vessel diameter and female gender. For the acute treatment of VC different interventional approaches have been reported including the implantation self-expanding stent grafts into the "no stent zone" AFC.
Methods: Retrospective analysis of patients undergoing TAVR between 2010 and 2013 in which a covered Fluency ® plus stent graft (Bard Peripheral Vascular Inc., USA) was placed due to vascular access site complications. Patients were evaluated for in-stent restenosis and vascular graft complications (restenosis, obstruction) by doppler-sonography after 3, 6, 9 and 12 months.
Results: We identified 58 patients in whom a self-expanding Fluency ® stent graft was implanted (by a cross-over technique via contralateral approach). Of these, 39 (67%) had a routine angiological follow up (median 91 days). Of these, 36 patients (92%) had undergone transfemoral TAVR, whereas three patients were treated by transsubclavian access (8%) Stent graft placement was necessary due to minor vascular complications (failure of access site closure/paravasation) in 90% and major vascular complications (iliac artery dissection) in 10%. Technical success of the procedure was achieved in 100% leading to primary angiographic hemostasis. Angiologic follow-up revealed only one case of in-stent restenosis in a subclavian stent and no incidence of stent fracture. 1 year mortality was 5.1% (2/39).
Conclusion: In this observational study, the routine implantation of a self-expanding stent graft for vascular complications proved safe and feasible. Incidence of ISR, relevant vascular complications and mortality after mid-term follow in patients, who have received such a stent, is low.

P3534 | BEDSIDE
Angiographical lesion characteristics associated with clinical outcome after femoropopliteal intervension

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Purpose: This study investigated the angiographical lesion characteristics associated with the clinical outcome after femoropopliteal (FP) intervension.
Methods: Retrospective analysis of a prospectively maintained database for femoropopliteal intervension in our center was performed. Lesion characteristics were chronic total occlusion (CTO), calcification, lesion length (LL)>150mm, vessel diameter (VD)>5mm. This study endpoint were primary patency (PP), secondary patency (SP) and assisted primary patency (APP)
Results: A total of 1098 consecutive patients (1405 limbs) were performed with femoropopliteal intervension (male 68.8%, 73.3±9.0 years old, mean follow up period 2.8±2.2 years, diabetes mellitus 59.0%, hemodialysis 27.2%, CTO 41.8%, calcification 67.1%, LL>150mm 22.5%, VD>5mm 38.7%). Primary patency was significantly higher in non-calcification group (79.0%, 67.1% and 51.2% at 1, 2 and 5 years) than that in the calcification group (75.5%, 64.3% and 37.9% at 1, 2 and 5 years; P=0.0073). Other outcomes were not significantly different. By Cox proportional hazards analysis, only calcification in all angiographical lesion characteristics significantly affected primary patency (hazard ratio 1.26; 95% confidence interval, 1.05-1.53; P=0.0133).

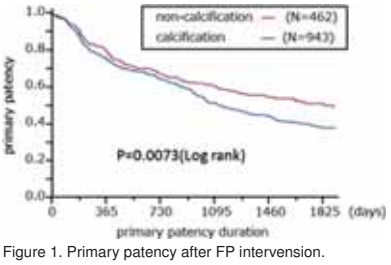

Figure 1. Primary patency after FP intervension.

Conclusions: Angiographical calcification is an independent predictor of decreased long-term primary patency after FP intervension.

P3535 | BEDSIDE
1-year results of paclitaxel-coating nitinol stent placement for chronic total occlusion in the femoropopliteal artey

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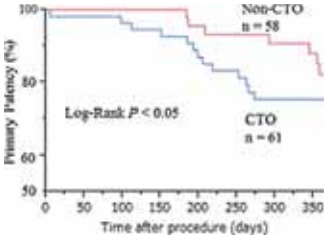
Purpose: To assess the 1-year outcomes of paclitaxel-coating nitinol stent (Zilver PTx®) placement for chronic total occlusion (CTO) and non-CTO in the femoropopliteal artery.
Methods: Zilver PTx® is a self-expanding nitinol stent with a polymer-free paclitaxel-coating. All patients enrolled in this prospective, single center study underwent Zilver PTx® placement for de novo or restenotic CTO and non-CTO in the superficial femoral and/or popliteal artery. Baseline and follow-up Rutherford classification and Ankle-brachial index (ABI) measurements were obtained. Follow-up was completed at 3, 6, 12 months.
Results: There were 61 of CTO and 58 of non-CTO treated. Mean age was 74±8 years and male was 82% in overall. Patients characteristics were not different significantly between two groups. However, CTO group had a longer mean lesion length than non-CTO group. Procedural success in both treatments was over 98%. The primary patency of CTO group was significantly lower than non-CTO group in Kaplan-Meier estimate curves at 12 months (75% vs 82%, Log-rank $P<0.05$). There were no significant differences in event-free survival or freedom from target lesion revascularization in Kaplan-Meier estimate curves at 12 months (68% vs 70%; Log-rank P=0.82, 63% vs 65%; Log-rank P=0.47, respectively). Both groups experienced a significant improvement in Rutherford classification and ABI after treatment, and these improvements were sustained to 12-months follow-up. Based on multivariate analysis, CTO was the negative predictor for primary patency at 12 months (HR 2.37, 95% CI 1.02 to 5.9, adjusted $P<0.05$).



Conclusions: CTO influences negatively the primary patency of drug-coating nitinol stent placed in the femoropopliteal artery.

PERIPHERAL INTERVENTION II

P3537 | BEDSIDE
Impact of perioperative complications after endovascular therapy in patients with peripheral artery disease due to femoropopliteal lesions

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Objectives: Incidence of 30-day perioperative complications (POC) following endovascular therapy (EVT) for femoropopliteal (FP) lesions and their impact on clinical outcomes remain unclear. We investigated factors associated with 30-day POC after EVT for FP lesions and compared prognostic outcomes between patients with and without POC.
Methods: We used a multicenter database of 2145 consecutive patients who successfully underwent EVT for FP lesions to investigate independent predictors of POC (logistic regression analysis) and impact of POC on prognostic outcomes (Cox proportional regression model adjusted for baseline clinical characteristics). We followed up 2110 out of 2145 patients for over 30 days (mean: 2.3±1.8 years).
Results: POC was observed in 209 (10%) patients. Body mass index (BMI) <18.5, critical limb ischemia (CLI), and TASC II class D were independently associated with POC (adjusted odds ratios and 95% confidence intervals (CI): 2.0 (1.3-2.9), 2.5 (1.9-3.3), and 1.6 (1.2-2.1), respectively). POC was positively and independently associated with major adverse cardiac limb events, major adverse limb events and restenosis (hazard ratio and 95% CI: 2.0 [1.6-2.4], 1.9 [1.5, 2.4] and 1.8 [1.4-2.3], respectively, $P<0.01$).
Conclusions: BMI<18.5, CLI and TASC D lesions were positively associated with POC. POC adversely impacted on patient, lower limb and vessel prognosis.

P3538

ABSTRACT WITHDRAWN

P3539 | BEDSIDE
Deficiency of circulating endothelial progenitor cells predicts aggressive venous intimal hyperplasia after balloon angioplasty

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Purpose: Venous intimal hyperplasia is a significant clinical problem in patients with hemodialysis arteriovenous fistulas and patients with bypass vein grafts. Circulating endothelial progenitor cells (EPCs) play a key role in vascular repair but are deficient in hemodialysis patients. Their role in the development of venous intimal hyperplasia after balloon angioplasty remained unknown. The purpose of our study is to investigate the relation between baseline EPCs and the subsequent development of venous intimal hyperplasia in hemodialysis patients.
Methods: We prospectively enrolled 144 hemodialysis patients with dysfunctional hemodialysis vascular access due to stenosis at venous limb of arteriovenous fistulas. After excluding 14 patients due to arterial stenosis, central vein stenosis, and failed angioplasty, 130 patients undergoing angioplasty for dysfunctional vascular access were prospectively enrolled. Flow cytometry with quantification of EPC markers (defined as CD34+, CD34+KDR+, CD34+KDR+CD133+) in peripheral blood immediately before angioplasty procedures was used to assess circulating EPC numbers. Patients were followed clinically for up to one year after angioplasty.
Results: During the one-year follow-up, 95 patients (73%) received interventions for recurrent access dysfunction. Patients in the lower tertile of CD34+KDR+ cell count had the highest restenosis rates (46%) at three month (early restenosis), compared with patients in the medium and upper tertiles of CD34+KDR+ cell count (27% and 12% respectively, p=0.002). Patients in the lower tertile of CD34+KDR+ cell count received more re-interventions during one year. Patients with early restenosis had impaired EPC adhesive function and increased senescence and apoptosis. In multivariate analysis, the CD34+KDR+ and CD34+KDR+CD133+ cell counts were independent predictors of target-lesion early restenosis.

Conclusions: Our results suggest that the deficiency of circulating EPCs is associated with early and frequent restenosis after angioplasty of hemodialysis vascular access.

P3540 | BEDSIDE
A novel MRI technique to examine renal blood flow: could it be used to evaluate the effects of renal artery interventions?

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Purpose: The neutral results of two key renal artery intervention trials of 2014: CORAL (stenting) and the formally unpublished SYMPLICITY HTN3 (ablation) has raised debate. A key limitation of these studies is the absence of mechanistic data regarding the physiological effect of the intervention on renal blood flow. To overcome this deficit our department has developed a novel MRI technique that can enable assessment of renal blood flow. We report our findings and explore how this technique could be used in future trials.
Methods: An interleaved spiral phase velocity sequence was developed on a 3T scanner using 1-1 water excitation and allowing full k-space coverage in 8 spiral interleaves of 12 ms duration (high temporal resolution). Data were acquired in a breath-hold. Cross-sectional proximal left and right renal artery phase velocity maps were acquired in two separate sessions from 10 healthy volunteers. For each vessel, the following data were extracted from the flow curves: peak systolic velocity (PSV, mm/s), end-diastolic velocity (EDV, mm/s), mean velocity (MV, mm/s), flow (L/min), resistive index (RI, [PSV-EDV]/PSV) and pulsatility index (PI, [PSV-EDV]/MV). The inter-scan reproducibility of these were determined as the mean ± standard deviation of the differences between scans and the intraclass correlation coefficient (ICC).
Results: See table 1.

Table 1. Renal haemodynamic data for initial and repeat scan. Standard deviation in brackets

(n=20)	1st Scan	2nd Scan	Mean difference	ICC	p-value for ICC
Flow (L/min)	0.45 (0.14)	0.48 (0.14)	–0.024 (0.059)	0.945	<0.001
Peak systolic velocity (mm/s)	469 (138)	447 (96)	21.276 (83.927)	0.860	<0.001
End diastolic velocity (mm/s)	128 (39)	124 (32)	4.699 (28.304)	0.821	<0.001
Mean velocity (mm/s)	225 (63)	219 (47)	5.497 (36.319)	0.885	<0.001
Pulsatility index	1.52 (0.32)	1.52 (0.46)	0.006 (0.211)	0.92	<0.001
Resistive index	0.72 (0.06)	0.72 (0.07)	0.003 (0.046)	0.858	<0.001

Conclusion: The described novel MRI technique can accurately and reproducibly determine markers of renal blood flow. In a randomised trial, to detect a clinically meaningful 10% change in renal blood flow (L/min) it would require 37 patients in each arm (80% power, α=0.05). Such mechanistic data will allow assessment of the effect of stenting and novel ablation techniques on renal artery blood flow.

P3541 | BEDSIDE
Impact of haemodialysis on clinical outcome after revascularization in patients with infra-inguinal arterial disease

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Background: Although revascularization with both surgical bypass procedure and endovascular therapy has become widely performed for peripheral artery disease (PAD) even in haemodialysis (HD) patients, clinical outcome in this population remains poor. In addition, clinical outcomes after revascularization for infra-inguinal artery lesion have not been fully evaluated in HD patients. We investigated the impact of HD on long-term clinical outcome after revascularization to infra-inguinal artery lesion.
Methods: A total of 1165 patients undergoing successfully revascularization with surgical bypass procedure and/or endovascular therapy for infra-inguinal artery were enrolled from multi-center registry. We compare 391 HD patients with 472 limbs and 774 non-HD (NHD) patients with 974 limbs in seven-year clinical outcomes. Primary endpoint was defined as major adverse cardiovascular events (MACE) including all-cause death, non-fatal myocardial infarction (MI) and stroke. Second endpoint was major adverse limb events (MALE) including target lesion revascularization (TLR) and major amputation. To reduce the differences of clinical characteristics between the two groups, propensity score adjusting with all baseline variables was performed.
Results: Prevalence of diabetes, coronary artery disease, congestive heart failure, left ventricular ejection fraction <0.5 and critical limb ischemia (≥Rutherford grade IV) were higher in HD group compared to NHD group. Seven-year event-free survival rate was significantly lower in HD group compared to NHD group for MACE (25.7% vs. 63.9%, p<0.0001) and for MALE (36.9% vs. 65.0%, p<0.0001), respectively. Propensity score-adjusted hazard ratio (HR) was higher in HD group compared to NHD group for MACE [2.42, 95% confidence interval (CI) 1.86-3.14, p<0.0001] and for MALE (1.52, 95%CI 1.18-1.97, p=0.0015), respectively. Similar results were also obtained for mortality, MI, stroke and TLR. However, although limb salvage rate was crudely lower in HD group compared to NHD group (88.2% vs. 95.9%, HR 2.63, 95%CI 1.54-4.50, p=0.0004), it was comparable between the two groups after propensity score-adjusting (94.6% vs. 95.3%, HR 1.01, 95%CI 0.53-1.91, p=0.98).
Conclusion: Even after adjusting for clinical differences, HD was identified as an independent predictor of adverse events such as all-cause death, MI and stroke after revascularization to infra-inguinal artery lesion. However, only limb salvage rate was even between HD and NHD after adjusting. These results suggest that detection at the early stage of PAD may potentially improve the poor outcomes in this population.

P3542 | BEDSIDE
Impact of renal artery stent implantation on hypertension in patients with hemodialysis

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Purpose: Benefit from renal artery stent implantation (RA-stenting) to treat atherosclerotic renal artery stenosis (ARAS) is not well understood in hemodialysis patients (HDs). We sought to evaluate effects of RA-stenting on hypertension of HDs, in comparison with non-HDs.
Methods and results: RA-stenting was successfully performed on 39 hypertensive patients (73.2±7.9 years, mean±sd, men 30) with ARAS. The patients were divided into 8 HDs and 31 non-HDs. Systolic blood pressure (BPs) was decreased from before to 6 months after RA-stenting in both HDs (163±30 mmHg to 121±22 mmHg, p=0.0015) and non-HDs (147±21 mmHg to 127±12 mmHg, p<0.0001). Percent decrease in BPs from before to 6 months after RA-stenting (100*((BPs-before - BPs-after)/BPs-before)) was greater in the HDs than the non-HDs (24.8±10.4% vs 12.1±12.2%, p=0.0102). Rate of renal flow (vessel length /frames /15), which was measured from renal angiogram before and just after RA-stenting by using both frame counts for contrast to reach to distal landmark of parenchyma from ostium and vessel length from ostium to distal landmark, was slower in the HDs than the non-HDs before RA-stentings (111.4±38.7 mm/sec vs 175.9±70.9 mm/sec, p=0.0186), while there were no differences in just after RA-stenting (153.3±60.5 mm/sec vs 180.3±75.2 mm/sec, p=0.3543).
Conclusions: RA-stenting for ARAS had more beneficial effects on hypertension in the HDs than in the non-HDs. The slower rate of renal flow before RA-stenting may be related with greater decrease of BPs in the HDs.

P3543 | BEDSIDE
Percutaneous cerebrovascular interventions vs. intravenous thrombolytic therapy for acute ischaemic stroke: a systematic review and meta-analysis

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Purpose: Percutaneous cerebrovascular intervention (intra-arterial recanalisation therapy) offers a new approach to the treatment of acute ischaemic stroke. The purpose of our systematic review and meta-analysis was to examine whether this intervention is more effective and safer than intravenous thrombolytic therapy.
Methods: We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials for randomised-controlled trials up to January 1st 2014 that compared percutaneous cerebrovascular interventions with intravenous thrombolytic treatment in patients with acute ischaemic stroke. Good functional outcome was defined as a modified Rankin Scale score of 0 to 2. We searched Clinicaltrials.gov, Current Controlled Trials, and Stroke Trials Registry for on-going trials. We contacted authors for additional unpublished data.
Results: We identified four trials with a total of 450 patients. Percutaneous cerebrovascular intervention was not associated with an improved proportion of patients with good functional outcome (relative risk (RR) 1.01, 95% confidence interval (CI) 0.82 to 1.25, P=0.92). At the end of follow-up there was a non-significant increase in the proportion of patients who died in the percutaneous vascular intervention group (RR 1.34, 95% CI 0.84 to 2.14, P=0.21).
Conclusions: Percutaneous cerebrovascular intervention was not superior to intravenous thrombolytic treatment for the treatment of acute ischaemic stroke. Endovascular devices for percutaneous cerebrovascular intervention are rapidly evolving, and new trials of the latest generation devices (stent-retrievers) are warranted.

P3544 | BEDSIDE
Neurological events of diabetic versus non-diabetic and symptomatic versus asymptomatic patients after carotid artery stenting - a 10 year follow up analysis from a single centre german registry

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Purpose: Since the CREST-study, carotid artery stenting is an established therapy alternative for carotid artery stenosis, but there are still very few long term

data about the neurological outcome after carotid artery stenting. In this analysis, we present data from a 10 year follow up of a single centre retrospective carotid artery stenting registry. The aim is to determine the difference in long term event free survival from ipsilateral minor and major stroke for diabetic versus non-diabetic and symptomatic versus asymptomatic patients over 10 years.
Methods: Data from a single centre registry from a German hospital including n=856 patients were analysed. Interventional and follow up data was assed by a rigorous independent neurological pre- and postprocedural examination with NIHSS documentation. After 30days mortality in the registry was 1,5% (n=13), any stroke occurred in 3,9% (n=34) and death or any stroke in 5,4% (n=47). Kaplan-Meier-Curves were plotted and time of neurological event free survival, cardiovascular death and neurological death was compared for each group using Log Rank Test. Chi-Square Test was used for assessment of the reintervention rate. Subgroups were divided into symptomatic stenosis (29,2%; n=250) versus asymptomatic stenosis (70,8%; n=606) and diabetics (33,1%; n=283) versus non-diabetics (66,9%; n=573).
Results: After 10 years. ipsilateral minor and major stroke occurred in 4,8% (n=41) of all, in 7,1% (n=20) of diabetic (p=0,02) and in 7,2% (n=18) of symptomatic patients (p=0,04). 1,8% (n=15) of all patients, 1,4% (n=4) of diabetics (p=0,36) and 2,8% (n=7) of symptomatic patients (p=0,65) died from neurological cause. Cardiovascular death occurred in 15,9% (n=38) of diabetic patients (p=0,01) and 10,8% (n=27) of symptomatic patients (p=0,81). Total reintervention rate for restenosis was 1,1% (n=9), 1,8% (n=5) for diabetics (p=0,14) and 0,8% (n=2) for symptomatic patients (p=0,64).
Conclusion: Patients with diabetes have significantly more ipsilaterlal minor and major strokes after carotid artery stenting than non-diabetic patients on the basis of data form a 10 year follow up single centre retrospective registry. The same findings could be made for symptomatic versus asymptomatic patients. There is no difference in death from neurological cause for both groups. Diabetic patients died significantly more often from cardiovascular cause. Reintervention rate was very low and did not differ within the various groups.

P3545 | BEDSIDE
Outcome of renal artery stenting in bilateral or one functional kidney renal artery stenosis in comparison to one-sided interventions

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There is much controversy whether renal artery stenting (RS) is associated with renal function (RF), systolic (SBP) and diastolic (DBP) blood pressure improvement or cardiovascular events (CVE) reduction. However it's commonly assumed that intervention in patients with bilateral renal artery stenosis (RAS) or with RAS of the one functioning kidney is rather beneficial. To test this hypothesis we compared the influence of RS on SBP, DBP, RF and CVE rate in subjects with bilateral intervention for RAS, RS of RAS in one functioning kidney and one-sided RS for unilateral RAS.
Methods: Study group comprised 180 patients with the mean RAS degree 70.5±13.2% referred to RS in accordance with current guidelines recommendations. Group I comprised 25 (8M) subjects in mean age 64.6±12.7y. who underwent bilateral RS, Group II – 20 (11M) aged 63±9.3y. with RS of the one functioning kidney, and Group III – 135 (79M) patients, aged 64.6±11.7y. who underwent RS for one-sided RAS. Creatinine level, number of antihypertensive agents, as well as mean SBP and DBP values on 24-hour ABPM were assessed before PTA and then at 12 months. The incidences of CVE: death (CVD), myocardial infarction (MI), ischemic stroke (IS) were recorded during follow–up (FU) of 57±37 months.
Results: The greatest SBP and DBP reduction was observed in Group II (mean SBP reduction of –27mmHg and DBP of -10mmHg), then in Group I (SBP:-12 and DBP:-7 mmHg), as compared to Group III (SBP:-7 and DBP:-2 mmHg), $p<0.05$ for all SBP and DBP values in comparison to Group III. Similarly, the number of blood pressure regiments decreased from 4.4±1.5 before PTA to 3.6±1.7 in Group II, from 3.5±1.1 to 2.9±1.3 in Group I, and from 3.2±1.2 to 3.0±1.2 in Group I (p=0.014, p=0.003, p=0.019, respectively). Similarly creatinine level decreased most prominently in Group II: from mean 180±72 to 131±59 umol/L ($p<0.001$), from 130±78 to 126±97 umol/L (p=0.586) in Group I, and from 125±49 to 114±44 umol/L (p=0.087) in Group III. During FU, CVD occurred in 2 (8%) patients in Group I, in 4 (21%) in Group II and in 13 (8.8%) in Group III (p=0.29, ANOVA). Composite CVE rate (CVD/MI/IS) was 7 (28%) in Group I, 6 (31.6%) in Group II and 33 (24.4%) in Group III (p=0.831, ANOVA).
Conclusions: The greatest improvement in respect of BP and RF was observed in patients with renal artery stenosis of the one functioning kidney, nevertheless also the prevalence of CVD but not CVE seems to be higher in this group of patients. Bilateral intervention seems more beneficial with regard BP reduction but not RF.

P3546 | BEDSIDE
Drug-eluting stents for the prevention of restenosis in patients with renal-artery disease: safety and efficacy in a large cohort at a single center institution

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Background: Atherosclerotic renal artery stenosis is a common clinical problem especially in the elderly population. Despite the ongoing controversy regarding the benefit of renal artery revascularization, endovascular therapy using bare metal stenting (BMS) is frequently used. Previously published trials, which failed to demonstrate a benefit of stenting over medical therapy, have mainly focused on clinical outcome regardless of the development of restenosis. However, since hemodynamic relevant in-stent restenosis occurs in up to 40% following BMS, this may be of clinical importance. Drug-eluting stents (DES) are well established in coronary interventions because they have proven to reduce in-stent restenosis and therefore are routinely used for implantation within the renal artery at our institution. This study aimed to assess the safety and outcome of DES for the endovascular therapy of renal artery stenosis.
Patients and methods: We retrospectively analyzed all endovascular procedures of de-novo renal artery stenosis using paclitaxel eluting stents at both sites of our institution between July 2004 and October 2013.
Results: During the observation period 142 endovascular procedures were performed in 125 patients. The overall technical success rate was 100% and all lesions were treated using at least one DES with a mean stent-diameter and length of 5.2±0,8mm and 27±11mm, respectively. The periprocedural complication rate was very low and included a renal artery dissection and an access site complication rate of 0.7% and 1.4%, respectively. Follow-up was completed after a mean of 18 month [range: 1-84month]. After this time period there was a non-significant decrease of mean systolic and diastolic blood pressure from 152±26mmHg to 147±24mmHg and 81±13mmHg to 79±12mmHg ($p>0.3$), respectively. Moreover, the mean number of antihypertensive drugs (3.2±1,2 vs. 3.2±1,2; p=0,95) as well as the renal function, as assessed by the index creatinin-level (1.1±0,5 vs. 1.2±0,7; p=0,4), were relatively stable over time. The overall rate of in-stent restenosis (>50%) was 7.3%.
Conclusion: Endovascular therapy of atherosclerotic renal artery disease using DES can be performed safely and successfully with an in-stent restenosis rate which is lower than reported for BMS in the literature.

P3547 | BEDSIDE
Pressure-wire-guided percutaneous transluminal pulmonary angioplasty: A breakthrough in the catheter-interventional therapy for chronic thromboembolic pulmonary hypertension

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Aims: Percutaneous transluminal pulmonary angioplasty (PTPA) has been demonstrated to be effective for treatment of chronic thromboembolic pulmonary hypertension (CTEPH). However, a major and occasionally-fatal complication after PTPA is reperfusion pulmonary edema (RPE). To avoid it, pulmonary edema predictive scoring index (PEPSI) was invented by us. The pressure wire has been used to detect insufficiency of flow in the vessel. The objective of this study was to prove safety and effectiveness of PEPSI and pressure-wire technique in PTPA.
Methods and results: We included 350 consecutive PTPA sessions in 103 patients with CTEPH from January the first in 2009 to December 31st in 2013. During this period, 140 PTPA sessions were performed without any guidance, 65 with guidance of PEPSI alone, and 145 with guidance of pressure wire and PEPSI. Each PTPA session has been finished after fulfilling both the PEPSI scores of less than 35.4 and the distal mean pulmonary arterial pressure less than 35 mmHg in each target lesion. The occurrence of clinically critical RPE and vessel injuries were the lowest in the group with guidance of pressure wire and PEPSI (0% and 6.9%, respectively). Furthermore, the group with guidance of pressure wire and PEPSI accomplished the same hemodynamic improvements in fewer number of the target lesions treated and sessions performed.
Conclusions: Combined approach using pressure wire and PEPSI produced more efficient clinical results and greatly reduced RPE and vessel complications, and will make PTPA a standardized, safe and promising therapeutic strategy for CTEPH.

P3548 | BEDSIDE
Long-term follow up results of balloon angioplasty for focal renal artery stenosis in young female patients with renovascular hypertension

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Introduction: Fibromuscular dysplasia (FMD) is a nonatherosclerotic arterial disease that most commonly involves the renal and carotid arteries. Angiographic

classification of arterial stenosis includes multiple stenoses with the 'string-of-beads' appearance, tubular, and focal types. In atherosclerotic lesions, we perform percutaneous transluminal renal angioplasty (PTRA) with stent. On the other hand, we have no consensus whether or not to use stent in nonatherosclerotic lesions.
Methods: We investigated the long-term results of balloon angioplasty for focal renal artery stenosis in young female patients. Six female patients (mean age 25, 17-37) with renovascular hypertension (RVH) underwent PTRA for focal right renal artery stenosis. All patients had a focal stenosis in the right renal artery (mean reference vessel diameter 4.0mm, mean lesion length 7.5mm). PTRA with balloon/artery ratio of 1.03 was performed and all lesions were successfully dilated (pre and post diameter stenosis 81%, 23%, respectively). Intravascular ultrasound imaging was used in 2 patients and optical coherence tomography imaging was used in one patient. During mean clinical follow up of 6.4 years (1 to 13 years), We monitored blood pressure, measured plasma renin activity (PRA) and Aldsterone, and performed doppler ultrasonography if suspected recurrence of hypertension.
Results: We could perform PTRA safely in all patients. By PTRA, we obtained enough drop of the blood pressure (Systolic blood pressure (SBP): 35±19, Diastolic blood pressure (DBP): 26±22) in acute phase. And in chronic phase, blood pressure transitioned stable (SBP: 125±9, DBP: 77±8). Furthermore, 5 patients didn't need to take antihypertensive medications during follow up. One patient showed a recurrence of RVH and a repeat PTRA was successfully performed. All other patients were uneventful during the follow up period.
Conclusion: Initial and long-term results of balloon angioplasty were excellent for focal renal artery stenosis in young female patients.

INFLAMMATION AND IMMUNITY

P3550 | BEDSIDE
In vivo evidence for local interaction between osteopontin (OPN) and pentraxin 3 (PTX3) in advanced coronary atherosclerosis: coronary rotational atherectomy study

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Background: Osteopontin (OPN) contributes to smooth muscle cell proliferation as well as vascular calcification. Pentraxin 3 (PTX3) is produced by the major cell types in atherosclerotic lesions in response to inflammatory stimuli. Rotational atherectomy (RA) ablates coronary atheroma into circulation, and therefore, molecules existing in the vessel wall would be released into blood stream after procedure. To explore in vivo evidence for the potential interaction between OPN and PTX3 in coronary atherosclerosis, we measured peripheral levels of OPN and PTX3 before and after RA.
Methods and results: We enrolled consecutive 81 patients (mean age: 69 years, M/F=46/35) treated successfully with RA. OPN levels (mean±SD, ng/ml) significantly ($p<0.0001$) increased immediately after RA (from 743±451 to 886±483), further increased to the peak of 1277±721 three hours later, and returned to 889±563 at the time of 24 hours after procedure. Similarly PTX3 levels (ng/ml) significantly ($p<0.0001$) increased immediately after RA (4.7±3.7 to 5.6±4.2), further increased to the peak of 8.2±5.3 three hours later, and decreased to 7.2±6.5 24 hours after. Preprocedural levels of OPN showed significant and positive association with those of In (PTX3) (r=0.416, p=0.0001). Furthermore, after RA, increases of OPN showed significant and positive association with those of In (PTX3) (r=0.464, $p<0.0001$), which suggested the strong functional link between these 2 molecules.
Conclusions: Our study demonstrated in vivo evidence for the functional link between OPN and PTX3 in advanced coronary atherosclerosis.

P3551 | BENCH
Coronary NET burden and DNase activity in ST-elevation acute coronary syndrome are predictors of infarct size

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Background: Mechanisms of coronary occlusion in ST-elevation acute coronary syndrome (STE-ACS) are poorly understood. We have previously reported accumulation of neutrophils (polymorphonuclear cells [PMNs]) in culprit lesion site thrombi. The goal of the present study was to quantify PMNs, their formation of neutrophil extracellular traps (NETs), and to examine the relationships of extracellular DNA, DNase and clinical outcomes.
Methods and results: We analyzed coronary thrombectomy aspirates from 112 patients undergoing primary percutaneous coronary intervention. Compared to systemic PMNs, coronary thrombus PMNs were characterized by high expression of activation markers and by the formation of aggregates with platelets. Nucleosomes, neutrophil elastase, myeloperoxidase and myeloid-related protein 8/14 were increased in coronary plasma, and NETs significantly contributed to the scaffolds of particulate coronary thrombi. Thrombus NET burden was directly correlated with infarct size, while culprit site DNase activity showed a reverse correlation with infarct size. Recombinant DNase accelerated lysis of coronary thrombi ex vivo.
Conclusion: PMNs are highly activated in STE-ACS and undergo NETosis at the culprit lesion site. Coronary NET burden and DNase activity are predictors of myocardial infarct size.

P3552 | BEDSIDE
Diagnostic and prognostic value of autoantibodies anti-apolipoprotein a-1 and phosphorylcholine in suspected acute myocardial infarction

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Purpose: Autoantibodies have been shown to play a critical role in predicting major adverse cardiovascular events in atherosclerotic patients. We aimed to assess the diagnostic accuracy of autoantibodies to apolipoprotein A-1 (anti-apoA-1 IgG), and to phosphorylchlorine (anti-PC IgM) for non-ST segment elevation acute myocardial infarction (NSTEMI) and to explore their potential prognostic value.
Methods: This prospective multicenter study included 1072 patients presenting to the emergency department (ED) for suspected NSTEMI. The final diagnosis was adjudicated by two independent cardiologists. For both antibodies alone or expressed as a ratio (anti-apoA-1 IgG/anti-PC IgM) we determined their i) diagnostic accuracy for NSTEMI, and ii) prognostic accuracy for major adverse cardiovascular events (MACE) during 1-year follow-up.
Results: A total of 154 patients (14%) had a final diagnosis of NSTEMI. Diagnostic accuracy or the diagnosis of NSTEMI as quantified by the area under the receiver-operating characteristics curve (AUC) was very low for both autoantibodies alone or expressed as a ratio: AUC anti-apoA-1 IgG 0.50 (95%CI, 0.47-0.53, p=0.99), AUC anti-PC IgM 0.53 (95%CI, 0.50-0.56, p=0.30), and AUC of the ratio 0.52 (95%CI, 0.49-0.55, p=0.47). In contrast, hs-cTnT levels had very high diagnostic accuracy with an AUC of 0.93 (95%CI, 0.91-0.94). Adding the anti-apoA-1 IgG/Anti-PC IgM ratio to hs-cTnT did not provide incremental diagnostic value over hs-cTnT alone (Fig. 1A). MACE occurred in 221 patients (21%) during follow-up. The autoantibodies, alone or expressed as ratio, also had very low accuracy to predict MACE (p=ns) (Fig. 1B).

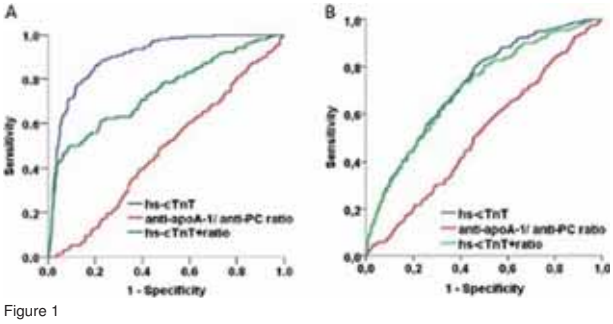

Figure 1

Conclusions: Anti-apoA-1 IgG, and anti-PC IgM autoantibodies do not seem to have diagnostic or prognostic value in patients with suspected NSTEMI.

P3553 | BEDSIDE
Does neutrophil to lymphocyte ratio have any prognostic impact in patients with acute coronary syndrome?

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Background: Several studies have demonstrated the importance of inflammatory biomarkers such as leukocytes and neutrophils in the pathogenesis and prognosis of acute coronary syndromes (ACS).
Aim: To determine the prognostic value of neutrophil to lymphocyte (N/L) ratio in ACS patients.
Methods: We retrospectively analysed 2315 patients who were admitted to our coronary care unit with ACS. Patients were grouped into tertiles according to the values of N/L ratio achieved: tertile 1 [N/L <2.90; n=772]; tertile 2 [$2.91 \geq$ N/L ≤ 5.56; n=774]; tertile 3 [N/L >5.56; n=769]. Clinical and laboratory features, treatment and adverse events were compared in each group of patients. The primary endpoint was the occurrence of death at 6 months.
Results: Patients in the 3rd tertile were older (61±12 vs 64±14 vs 67±13 years; $p<0.001$), more frequently women (22 vs 27.6 vs 28.1%; $p<0.001$) and had a higher prevalence of hypertension (60.1 vs 63.6 vs 65.5%; $p<0.001$) and dyslipidaemia (56 vs 46.6 vs 47.7%; $p<0.001$). On admission, they more frequently presented with ST-segment elevation myocardial infarction (36,5 vs 46.8 vs 61.3%; $p<0.001$), Killip class >1 (13.9 vs 18,8 vs 32,9%; $p<0.001$), anaemia (14.9 vs 21.3 vs 26.8%; $p<0.001$), estimated glomerular filtration rate (GFR) <60 ml/min (13.5 vs 20.3 vs 26.8%; $p<0.001$), left ventricular ejection fraction ≤40% (20.7 vs 22.5 vs 38.3%; $p<0.001$), and higher values of C-reactive protein ($p<0.001$), Pro-

BNP (p=0.01) and total leukocyte count (p<0.001). Individuals in the last tertile required more often aminergic support (4.4 vs 4.9 vs 9.9%; p<0.001), intra-aortic balloon pump (0.6 vs 0.9 vs 1.8%; p<0.05), and they were more often revascularized (80.6 vs 74.2 vs 88.2%; p=0.02). During hospitalization they had higher incidence of malignant arrhythmias (1.7 vs 3.9 vs 4.8%; p=0.007) and ischemic stroke (0.6 vs 1.2 vs 2.2%; p=0.024). Higher N/L ratio was associated with increased in-hospital (2.1 vs 3.5 vs 8.3%, p<0.001) and 6-month mortality (5.4 vs 8.6 vs 16.3%, p<0.001), and it was associated with an increased incidence of major adverse cardiovascular events at follow-up (stroke, ACS, death) (23.2 vs 28.7 vs 36.8%; p<0.001). Compared with first tertile, the 3rd tertile had 3.33 times higher 6-month mortality [OR 3.33; 95% CI (1.11 - 2.47)]; p<0.001]. In multivariate analysis, adjusting for the different baseline characteristics, the N/L ratio remained as an independent predictor of overall 6-month mortality [tertile 3 vs tertile 1, OR adjusted 1.91; 95% CI (1.227 - 2.961); p=0.004].
Conclusion: The N/L ratio is an independent predictor of in-hospital and 6-month mortality.

P3554 | BEDSIDE
Local matrix metalloproteinase 9 levels are associated with clinical manifestation in patients with myocardial infarction

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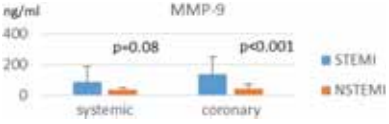
Aim: Expression of matrix metalloproteinase 9 (MMP-9) in coronary plaque plays important roles in the mechanism of atherosclerosis and plaque vulnerability. However, few studies addressed direct relationship between local MMP-9 and clinical manifestations. The aim of this study was to investigate the relationship between local MMP-9 level in coronary plaque and clinical manifestation in patients with acute myocardial infarction.
Method: We enrolled 45 patients with acute myocardial infarction (STEMI group: n=32, NSTEMI group: n=13) performed primary PCI. Systemic samples were obtained before PCI from femoral artery, and plaque-delivered coronary samples were collected from the distal of culprit site using aspiration catheter just after PCI balloon inflation. MMP-9 level was measured at once by ELISA. Serum high sensitive CRP (hs-CRP), reflecting whole body inflammation levels were also measured on admission.
Result: There were no significant differences in baseline characteristics between groups. Plaque-delivered MMP-9 levels were significantly higher than systemic levels (systemic 69.7±90ng/ml vs. plaque-delivered 107.7±105.5ng/ml, p<0.01). While no significant difference was observed in systemic levels of MMP-9 (STEMI 84.3±103.3ng/ml vs. NSTEMI 33.7±17.2ng/ml, p=0.08), plaque-delivered MMP-9 levels were significantly elevated in the STEMI group (STEMI 133.9±114.3ng/ml vs. NSTEMI 43.2±26.5ng/ml, p<0.001). There was no difference in serum hs-CRP (STEMI 0.30±0.40mg/dl vs. NSTEMI 0.40±0.53 mg/dl, p=0.48), and no correlation was observed between hs-CRP and MMP-9 levels.



Plasma MMP-9 levels.

Conclusion: Our results suggest that local over expression of MMP-9 is associated with clinical manifestation independent of systemic inflammation. Local MMP-9 would be a therapeutic target for acute coronary syndrome.

P3555 | BEDSIDE
The association between serum levels of Galectin-3 and left ventricular dysfunction after anterior ST-elevated myocardial infarction. Preliminary data from GALAMI, a prospective single-centre study

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Background: Remodeling caused by scar formation and fibrosis is a deleterious adaptive response after myocardial infarction leading left ventricular (LV) dysfunction and heart failure (HF). Galectin-3 (G-3) is a new biomarker involved in inflammation, tissue repair and fibrogenesis. Whether G-3 is related to LV remodeling and systolic disfunction and HF after acute myocardial infarction is unknown.
Aim: To evaluate the value of G-3 in predicting development of LV remodeling and systolic dysfunction after acute anterior ST-elevated myocardial infarction (STEMI) we designed a prospective single-center study (GALAMI). Consecutive patients admitted with anterior STEMI treated with primary percutaneous coronary intervention for left anterior descending artery occlusion were enrolled since May 2013. Serum G-3 and NT-proBNP (VIDAS, bioMérieux), echocardiography and clinical events were evaluated at discharge, 30 days and at 6 months after anterior STEMI.
Results: We report preliminary data of the first 38 patients enrolled (aged 67.6±13.1 years; 65.8% men) with a complete follow-up at 30 days. G-3 was elevated (>17,7 ng/mL) in 11/38 pts (28,9%) at baseline and in 11/36 (30.5%) at 30 days. G-3 was higher among patients with LV ejection fraction (LVEF) ≤45% both at baseline (17.9±7.7 vs 13.4±3.5 ng/mL, p=0.041) and at 30 days (17.9±6 vs 12.2±3.2 ng/mL, p=0.002). G-3 at baseline correlated with NT-proBNP (r=0.429, p=0.009), age (r=0.498, p=0.002), LVEF (r=-0.372, p=0.028) and serum creatinine (r=0.581, p=0.002). G-3 at 30 days correlated with age (r=0.473, p=0.005) and LVEF (0.469, p=0.006). Multivariate analysis shows that only G-3 levels at 30 days independently correlated with LVEF. Patients with clinical signs of HF had higher levels of G-3 at discharge (13.7±3.5 vs 19.4±8.5 ng/mL, p=0.009), which persisted higher at 1 month (13.1±3.8 vs 19.5±6.3 ng/mL, p=0.001). Among patients with LVEF>45% G-3 decreased over time (13.7±3.6 at baseline vs 12.6±3.2 ng/mL at 30 days, p=0.03) whereas it remained high among patients with LVEF ≤45% (17.2±7.3 vs 17.9±6, p=n.s.). Patients with clinical signs of HF had higher G-3 at discharge (13.7±3.5 vs 19.4±8.5 ng/mL, p=0.009), which persisted higher after 1 month (13.1±3.8 vs 19.5±6.3 ng/mL, p=0.001).
Conclusion: Our preliminary results show that G-3 levels are persistently high among patients with clinical signs of HF and with reduced LVEF after anterior STEMI. We observed an independent correlation between G-3 and LVEF at 1 month after myocardial infarction. These findings suggest a potential role of G-3 in predicting LV remodeling and HF.

P3556 | BEDSIDE
The impact of high adiponectin levels on all-cause mortality and target vessel revascularization in patients treated with primary percutaneous coronary intervention for ST-Segment Elevation Myocardial

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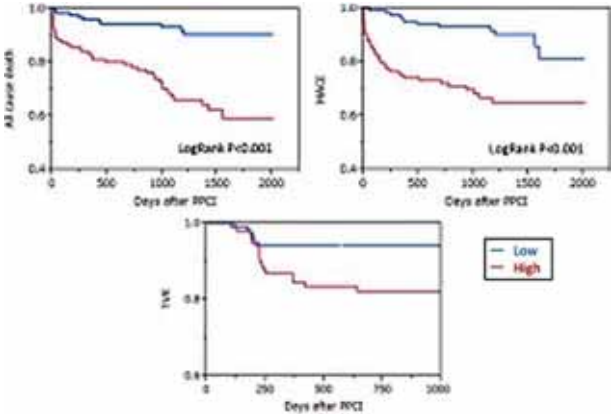
Aims: Cumulative evidence indicates that adiponectin (APN) protects against atherosclerosis and cardiovascular disease. This study aimed to investigate the prognostic impact of APN on clinical and angiographic outcomes in patients with ST-segment elevation myocardial infarction (STEMI).
Methods: In total, 252 consecutive patients with STEMI treated with primary percutaneous coronary intervention were included in this study. The plasma APN level was measured at admission. Patients were divided into two groups based on the median APN value (7.7 ng/ml). The primary outcome measures were all-cause death and major adverse cardiac events (MACE), defined as cardiac death, recurrence of acute coronary syndrome, and readmission for heart failure and target vessel revascularization (TVR).
Results: The median follow-up time was 1050 days. Patients with high APN value (≥7.7 ng/ml) had increased all-cause mortality (31.5% vs. 8.0%, p<0.001), MACE (31.5% vs. 9.6%, p<0.001), and TVR (13.4% vs. 5.6%, p=0.033) compared with patients with low APN value (<7.7 ng/ml). Multivariable Cox regression adjusted for APN and known risk factors indicated that high APN value positively correlated with all-cause mortality (hazard ratio: 5.44; 95% confidence interval: 1.68–24.66; p=0.003) and TVR (hazard ratio: 3.51; 95% confidence interval: 1.18–11.21; p=0.024).



Conclusion: In patients with STEMI, high plasma APN level independently predicts all-cause mortality, MACE, and TVR.

P3557 | BEDSIDE
Repeated intramyocardial cell injection again improves perfusion, anginal complaints and quality of life in previously responding cell therapy patients

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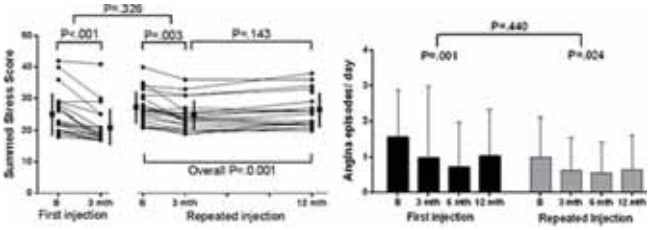
Purpose: We previously demonstrated that intramyocardial bone marrow cell (BMC) injection improves myocardial perfusion and anginal symptoms in patients with refractory angina pectoris. As some of these patients experienced recurrent anginal complaints, we evaluated the efficacy of a repeated intramyocardial BMC injection.

Methods: Patients with refractory angina pectoris who previously improved after intramyocardial BMC injection but experienced recurrent anginal complaints with documented stress-inducible ischemia were enrolled. Using the NOGA-system, $100x10^6$ autologous BMC were injected intramyocardially. Single-photon emission computed tomography was performed at baseline, and 3 and 12 months follow up to assess myocardial perfusion. Anginal symptoms and quality of life (QoL) were evaluated at baseline, and 3, 6 and 12 months follow-up.
Results: In total, 23 patients (17 male, 69±9 years) were injected 4.6±2.5 years after their first BMC injection. After repeated intramyocardial injection, summed stress score significantly improved up to 12 months (P=.001). Improvement after 3 months was similar to the effect of the first injection (1st vs. 2nd; P=.326). Patients reported a decrease of anginal episodes (P=.024), equal to the first injection. (1st vs. 2nd; P=.440). Qol improved from 56% at baseline to 63% at 3, 63% at 6 and 61% at 12 months (P=.025), similar to improvement after the first injection (1st vs. 2nd; P=.121)



Summed stress score and Angina episodes

Conclusion: Repeated intramyocardial BMC injection again improves myocardial perfusion and anginal symptoms in previously responding patients with recurrent anginal complaints and documented stress-inducible myocardial ischemia.

P3558 | BEDSIDE
Increased serum level of CTRP1 is associated with low coronary collateralization in stable angina patients with chronic total occlusion

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Objective: We aimed to determine whether serum levels of C1q TNF-related protein (CTRP) 1 and CTRP3 are associated with coronary collateralization in patients with coronary artery total occlusion, and whether CTRP affects angiogenesis of endothelial progenitor cells (EPCs).
Methods: In this cross-sectional study, we included 264 consecutive stable coronary artery disease (CAD) patients with angiographic total occlusion of at least one major coronary artery. The participants were categorized as low collateralization group (Rentrop score of 0 or 1, n=93) and high collateralization group (Rentrop score of 2 or 3, n=171). Serum levels of CTRP1, CTRP3 and high-sensitive C-reactive proteins (hsCRP) were measured. The impact of recombinant CTRP protein on angiogenesis of EPCs from patients with significant CAD was assessed.
Results: Serum levels of CTRP1 and hsCRP were significantly higher in patients with low collateralization than in those with high collateralization (both $P<0.05$), but CTRP3 levels were similar in the two groups. Serum CTRP1 levels correlated with the number of diseased coronary artery (Spearman's r=0.16, P=0.012). Multivariable regression analysis revealed that diabetes, dyslipidemia before statin medication, and CTRP1 were independently associated with low coronary collateralization. Addition of CTRP1 significantly improved C statistic ($P<0.01$). Recombinant human CTRP1 protein concentration-dependently inhibited in vitro angiogenesis in EPCs. Consistently, the expression of VEGFR2 was decreased by CTRP1 treatment in these EPCs.
Conclusions: This study has demonstrated an association between increased serum CTRP1 level and low coronary collateralization in patients with coronary artery total occlusion. CTRP1 inhibits in vitro angiogenesis of EPCs from CAD patients.

P3559 | BENCH
The association between monocyte subsets and coronary collateral development in diabetes mellitus

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Purpose: Monocyte heterogeneity in peripheral blood seems to be important in coronary collateral development in non-diabetic patients with stable coronary artery disease.
Our aim in this study was to find out any possible relationship between the levels of circulating monocyte subsets and coronary collateral development in type 2 diabetic patients.
Methods: Diabetic patients who had >95% stenosis of at least one major coronary artery in their first coronary angiogram were included consecutively in this study. Collateral development was graded as good or poor according to Cohen-Rentrop method. Blood samples underwent cytometric analysis for determination of monocyte subsets, CD14++CD16- and CD14+CD16+ monocytes.
Results: Out of 83 patients; 39 had good, 44 had poor coronary collateral development. The monocyte count was significantly higher in patients with good collateralization (512±161 vs. 381±105 per mm^3, $p<0.001$). After cytometric analysis, CD14++CD16- levels were found to be significantly higher in the good collateral group (407±151 vs. 277±93 per mm^3, $p<0.001$), but CD14+CD16+ cells did not differ between groups (89±26 vs. 86±26 per mm^3, p=0.59). When multivariate analysis was performed, increased CD14++CD16- levels were still significantly associated with good collateral development [OR: 1.013 (1.005-1.021), $p<0.001$] (Table 1).

Table 1

Predictors of coronary collateral development	OR (95% CI)	p value
CD14++CD16– monocytes (per mm^3)	1.013 (1.005–1.021)	<0.001
CD14++CD16– monocytes (per mm^3)*	8.46 (2.51–28.22)	<0.001
CD14+CD16+ monocytes (per mm^3)	0.99 (0.96–1.03)	0.54
Duration of ischemic symptoms (months)	1.06 (0.98–1.15)	0.16
Gensini score	1.04 (0.98–1.10)	0.10
HbA_{1C} (%)	0.67 (0.41–1.09)	0.09

*When the cut-off point for CD14++CD16– monocytes was taken as 350/mm^3. OR, Odd's ratio; CI, Confidence interval.

Conclusions: Herein, a significant association has been found between increased circulating CD14++CD16- monocyte levels and good coronary collateral development in diabetic patients. Further studies are needed to better understand the relationship between different subsets of monocytes and collateralization.

P3560 | BEDSIDE
A protective role of collateral blood flow in patients with ST-segment elevation myocardial infarction; Angiographic and cardiovascular magnetic resonance study

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Purpose: There has been conflict about whether the collateral blood flow to infarct-related artery (IRA) had an effective role in infarct size and myocardial salvage (MSI) in patients with ST-segment elevation myocardial infarction (STEMI). Aim of the study was to investigate the impact of collateral circulation on myocardial salvage in STEMI patients.
Methods: In 306 patients presenting with STEMI, collateral flow to IRA was assessed using coronary angiography and CMR was used to measure myocardial area at risk (AAR) and infarct size within 3 (IQR 3-5) days.
Results: Among 246 patients with pre-procedural TIMI flow 0, 54 (22%) had good collaterals (Rentrop grade ≥2, Coronary Collateral Score ≥2). Infarct burden and AAR were significantly smaller in patients with good collaterals than those with poor collaterals (Infarct size; 17.1±10.1%LV vs. 21.7±10.6%LV, p=0.005, AAR; 33.8±16.8 vs. 38.8±15.5, p=0.039). There was a significant difference of MSI between two groups (50.9±15.0% vs. 44.1±18.9%, p=0.016). In multiple regression analysis, the presence and extent of collateral flow were independent predictors for infarct size and MSI ($p<0.05$ for both).
Conclusion: As in patients with angina, the presence and extent of collateral blood flow to acutely occluded coronary artery reduced infarct burden and improved myocardial salvage in patients with STEMI. Our result supports that a high collateralization reduces mortality in acute MI patients.

P3561 | BEDSIDE
The effects of nicorandil on microvascular function in patients with STEMI undergoing primary PCI

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Purpose: Nicorandil, as selective potassium ATP-channel opener, has dual action including coronary and peripheral vasodilatation, as well as cardioprotective effect through ischemic preconditioning. Considering those characteristics, nicorandil was suggested to reduce the degree of microvascular dysfunction in patients with myocardial infarction. The aim of the study was to evaluate the effects of nicorandil on microvascular function evaluated by the index of microvascular resistance in patients with acute myocardial infarction with ST segment elevation (STEMI) undergoing primary percutaneous coronary intervention (pPCI).
Methods: We prospectively inlcuded 34 patients (mean age 55±10 years, male 27, female 7) with STEMI treated by pPCI. Immediately after PPCI, we measured index of microvascular resistance (IMR; thermodiluation method) during i.c. bolus of papaverine (left coronary artery 18mg, right coronary artery 13mg) before and after administration of nicorandil 12mg as i.c. bolus. TIMI flow was assessed before and after pPCI, and the value of creatin kinase (CK) was used routinely to estimate the amount of myocardial necrosis in pts with STEMI.
Results: pPCI was performed in 16, 4 and 14 pts with STEMI due to coronary occlusion of LAD, Cx, and RCA, respectively. Mean CK value was 1946±1585U/L. Before pPCI, in 33/34 (97%) pts TIMI flow was 0, whereas after successful pPCI

in all pts TIMI flow was 3 (100%). Nicorandil decreased IMR in 31/34 pts (91%). There was a significant decrease in IMR after i.c. administration of nicornadil from 15±5 to 11±5U ($p<0.001$), and a significant correlation between IMR and the amount of myocardial necrosis as estimated by CK (r=0.48, p=0.005).
Conclusion: Intracoronary nicorandil administration after primary PCI significantly decreases IMR, implicating that nicorandil improves the function of myocardial microcirculation in pts with STEMI.

INFLAMMATION AND OUTCOME IN ACUTE CORONARY SYNDROMES

P3563 | BEDSIDE
C-reactive protein in acute coronary syndromes: risk marker or risk factor?

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Purpose: C-reactive protein (CRP) is an inflammatory biomarker that is strongly associated with coronary heart disease and metabolic syndrome, playing an important role in the pathogenesis of acute atherothrombotic events. The importance of serum CRP has been discussed mainly in the acute coronary syndrome setting. We aimed to evaluate the long-term prognostic impact of elevated CRP after an acute myocardial infarction (MI).
Methods: We evaluated 2701 patients (age 68±13; 1805 males) discharged from an intensive care unit for acute MI, from May 2004 to August 2013. Patients were divided in four groups according to the quartiles of CRP at discharge: group 1 (<0.87 mg/dL, n=674), group 2 (0.87-2.19 mg/dL, n=674), group 3 (2.20-5.27 mg/dL, n=677) and group 4 (≥5.28 mg/dL, n=626).
Results: Patients with higher serum CRP values were significantly older, had higher glycaemia at admission, fasting glucose and oral glucose tolerance test, lower estimated glomerular filtration rate (eGFR), with no differences regarding prevalence of dyslipidemia, hypertension, smoking or obesity. Moreover, these patients had significantly higher prevalence of ST segment elevation (STEMI), higher levels of troponin, less non-significant stenosis at angiography, with higher prevalence of left anterior descending disease, and lower left ventricular ejection fraction (LVEF). The 1 and 2-year mortality was superior in patients with higher serum CRP at discharge. In a multivariate regression analysis, higher CRP levels were not an independent predictor of long-term mortality, unlike higher age, lower eGFR, higher troponin levels and lower LVEF.

Serum CRP and mortality rates

Serum CRP at discharge (mg/dL)	1-year mortality (%)	2-year mortality (%)
<0.87	3.3	4.5
0.87–2.19	4.9	6.3
2.20–5.27	5.7	7.0
≥5.28	8.2	9.7

Conclusions: Higher levels of CRP, as a marker of a pro-inflammatory state, were associated with worse cardiovascular risk profile. An independent association between CRP levels and outcome after an acute MI was not found, suggesting that the rise in CRP levels is just a marker of worse risk profile and not an incremental risk factor.

P3564 | BEDSIDE
ADMA levels and arterial wall stiffness in rheumatology patients

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Purpose: The aim of the present study was to compare the ADMA levels in patients with rheumatoid arthritis (RA), system lupus erythematous (SLE), systemic sclerosis (SSc), ankylosing spondylitis (AS) with healthy control and subjects with major cardiovascular risk factors and to determine the assocoation with arterial stiffness.
Patients and methods: We studied ADMA level in 67 patients with SSc, 31 patients with diffuse cutaneous SS and 27 patients with limited cutaneous disease and also 9 patients with overlap syndrome (median age was 53 (42-60), 42 patients with RA (median age was 55 (48-59), 41 patients with AS (median age was 37 (32-48), and 50 patients with SLE (median age was 36 (27-45), 50 subjects with major cardiovascular risk factors (median age was 51 (44-56). All rheumatology groups, were comparable according 10-years Framingham cardiovascular risk score. Ten healthy blood donors were used as a control group (median age was 25 (21-30). All patients were characterized with basic clinical, instrumental and laboratory tests. Vascular involvement was accessed by measurement of pulse wave velocity (PWV) and augmentation index (AI) with applanation tonometry employing the SphygmoCor system (AtCor Medical Pty Ltd., Sydney, Australia). ADMA level was assessed in serum samples by an ELISA (Immunodiagnostik, Germany), according manufacturer instructions.
Results: The highest levels of ADMA was detected in patients with SLE 0,77 (0,64-0,97) mcmol/L, SSc 0,66 (0,54-0,76) mcmol/L, RA 0,63 (0,56-0,74) mcmol/L. It was significantly lower in patients with AS 0,54 (0,46-0,57), subjects with major cardiovascular risk factors 0,54 (0,48-0,60) mcmol/L and in healthy controls 0,42 (0,13-0,47) mcmol/L ($p<0,001$). In SSc patients, ADMA correlated with main activity markers and with augmentation index (r=0,48, p=0,0007). In patients with RA a correlation of ADMA with PWV was documented (r=0,52, p=0,0007). In AS patients, ADMA level correlated significantly with traditional risk factors (age, glucose) and also with PWV (r=0,44, p=0,001). Besides, in group of subjects with cardiovascular risk factors, ADMA level correlated with traditional risk factors (age and smoking), but not with arterial stiffness. At the same time PWV was comparable between all groups.
Conclusions: In rheumatology diseases increased levels of ADMA as a marker of endothelial damage are observed, especially in diseases associated with autoantibodies production. At the same time ADMA appears to be associated with increases vascular stiffness in rheumatic diseases but not in patients with classic atherosclerosis

P3565 | BEDSIDE
Function of N-terminal pro-brain natriuretic peptide in Takayasu arteritis disease monitoring

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Purpose: The increased levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) are associated with cardiovascular morbidity and mortality. Inflammation may also affect NT-proBNP levels. As an inflammatory disorder, Takayasu arteritis (TA) is a chronic inflammatory condition primarily affecting the aorta and its main branches. This study was designed to investigate the relationship of NT-proBNP with inflammation, disease activity, severity, and progression of TA.
Methods: The plasma levels of NT-proBNP were determined in 68 patients with TA and in 90 age-, sex-, and body mass index (BMI)-matched healthy controls. Disease activity and severity in patients with TA were defined in accordance with the National Institutes of Health and Ishikawa's criteria, respectively.
Results: proBNP levels were higher in patients with active disease (915.0±328.0 pmol/l) and patients in remission (618.2±243.4 pmol/l) than those in the control subjects (427.2±81.4 pmol/l, $p<0.001$). Patients with severe TA showed significantly higher NT-proBNP levels than those with mild-moderate TA (924.0±332.4 pmol/l vs. 653.8±269.1 pmol/l, p=0.001). In patients with available longitudinal data, NT-proBNP levels at the active phase were significantly higher than those at the stable phase (944.1±216.7 pmol/l vs. 552.1±178.2 pmol/l, p=0.001). NT-proBNP showed significantly positive correlations with log (high sensitivity C-reactive protein; r=0.392, p=0.001), log (erythrocyte sedimentation rate; r=0.333, p=0.006), and white blood cell count (r=0.243, p=0.046) in patients with TA. After these parameters were adjusted for age, sex, BMI, disease duration, serum creatinine, left ventricular end-diastolic diameter, left ventricular ejection fraction, and prednisone use, the association between NT-proBNP and these inflammatory markers remained significant (R2 adjusted = 0.307, p=0.001).
Conclusions: proBNP levels were significantly increased in patients with active TA exhibiting severe complications. Furthermore, NT-proBNP levels were independently associated with inflammation. These results indicated that NT-proBNP may be a useful marker to assess the status, severity, and progression of TA.

P3566 | BEDSIDE
Associations between interleukin 6 and high sensitivity C-reactive protein (IL-6, hsCRP) and coronary heart disease (CHD) risk factors in elderly people (PolSenior Study)

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Background: Many studies supports the role of inflammation in the development of chronic diseases, such as CHD. Two common markers of systemic inflammation are IL-6 and hsCRP. Many cytokines are elevated in patients with CHD but few studies investigated them in the elderly, where a chronic low-grade proinflammatory state is associated with aging. The aim of this study is to investigate associations between hsCRP and IL-6 and CHD risk profile.
Material and methods: The research sample included 4976 respondents aged 65-104. IL-6 measurements were available in 3895 participants, while hsCRP in 4093. The study consisted of three visits performed by nurses and included a questionnaire survey, geriatric assessment and blood sampling. Serum IL-6 and hsCRP were measured using high-sensitivity ELISA tests.
Results: Mean both IL-6 and hsCRP concentration values were distinctly increasing with age and significantly higher in men (3,48 vs 3,31 for IL-6), in patients with elevated triglicerydes and decreased HDL-cholesterol, among current smokers, in patients with chronic kidney disease and in statin non-use group (Tab.1). Mean IL-6 values were significantly higher in patients with elevated LDL-cholesterol (3,74 vs 3,07) and depression (3,66 vs 3,01) while mean hsCRP concentrations were significantly higher in obese patients (4,98 vs 4,31) and lower socioeconomic status determined by income (4,51 vs 3,91).

Table 1

Variable		Mean values (pg/l)	
		IL-6	hs CRP
Age	65–74 vs 85–104	2.67 vs 4,34	4.15 vs 5,80
Triglicerydes	Normal vs elevated	3.06 vs 3,50	4.52 vs 4,95
HDL-cholesterol	Normal vs decreased	3.16 vs 4,18	4.38 vs 6,37
Smoking	Never vs current	3.37 vs 3,73	4.80 vs 5,72
CKD	No vs yes	2.98 vs 3,90	4.16 vs 5,64
Statin use		3.48 vs 3,15	5.15 vs 3,84

Conclusions: This analysis supports the hypothesis of the role of IL-6 and hsCRP in the prognosis of CHD, especially in the elderly. Several potentially modifiable, conventional and new risk factors were associated with a higher-risk inflammatory profile. Our results indicate the potential of inflammatory pathways as targets for cardiovascular disease prevention in the elderly (statin use for example).

P3567 | BEDSIDE
Association of plasma pentraxin-3 levels with coronary risk factors and the lipid profile

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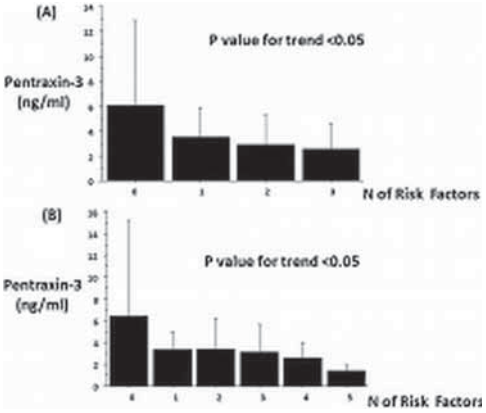
Purpose: Pentraxin-3, one of the superfamily of pentraxins which includes C-reactive protein (CRP), is produced in vascular endothelial cells in response to atherosclerotic change. The aim of this study was to evaluate the relationship between traditional risk factors, lipid profile and pentraxin-3.
Methods: One hundred and sixty-three patients with ischemic heart disease were enrolled in this study. The plasma levels of pentraxin-3 and the serum levels of LDL-C, HDL-C and high sensitivity-CRP were measured. These serological data were examined in the relationships with the traditional risk factors, hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM) and additional risk factors, obesity (body mass index: BMI >25) and high age (>75).
Results: Pentraxin-3 levels decreased with increasing the numbers of risk factor, classified according to the numbers of 3 traditional risk factors (HT, DL and DM) (Figure A.) and the numbers of 5 additional risk factors (HT, DL, DM, obesity and high age) (Figure B.) (both p value for trend <0.05). In contrast, high sensitivity-CRP tended to increase with increasing the numbers of risk factors. The pentraxin-3 level showed a positive association with HDL-C (r=0.229; P=0.050), whereas inverse association between the pentraxin-3 level and LDL-C was observed (r = -0.224; P=0.045). In multiple linear regression analysis, the number of 5 additional risk factors was a significant predictor of PTX3 values. (β=-0.404, 95% confidence interval; -2.120 to –0.537).



Conclusions: Although PTX3 and CRP were enhanced depending on the number of risk factors, their distribution precisely differed, suggesting that they play distinct biological roles in atherosclerosis.

P3568 | BENCH
T-cells phenotypes in patients with coronary artery disease

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Purpose: We have assessed the prognostic value of the composition of peripheral-blood Tcell subpopulations in patients with coronary artery disease (CAD).
Methods: We analyzed T-cell differentiation and activation status of in patients with STEMI, NSTE-ACS, chronic CAD and in control groups. Live mononuclear cells were stained with a cocktail of labeled monoclonal antibodies defining naïve (TNAIVE), central (TCM), effector (TEM) and regulatory (TREG) Tcells; activation was evaluated by the expression of HLA-DR and CD38.
Results: We found a correlation between T-lymphocyte differentiation and CAD progression. CD4 TCM frequency was higher in CAD than in control (STEMI 58.9%, NSTE-ACS 67.6%, chronic CAD 52% and control 44.9%; p<0.05). Similarly, CD8 TCM frequency was higher in STEMI and NSTE-ACS groups than in control (17.4%; 18.1% and 8.61%, respectively; p<0.05). Conversely, CD8NAIVE was higher in control group than in patients (control 22.3%, STEMI 10.03%, NSTE-ACS 10.2% and chronic CAD 4.9%, p<0.05). CD4 T cell activation was higher in STEMI, NSTE-ACS and chronic CAD than in control group (10.15%, 9.81%, 9.78% vs 6.51% respectively, p<0.05). CD8 Tcells were more activated in chronic and NSTE-ACS groups than in control (27.8%, 21.5% and 15.5% respectively, p<0.05). CD8 TEM fraction was higher in chronic CAD patients compared to STEMI and control (71.8%, 30.5% and 30.3% respectively, p<0.001); the fraction of TREG was significantly decreased in patients compared to controls (0.0412%, 0.0393%, 0.0233% and 0.255% in STEMI, NSTE-ACS, chronic CAD and controls respectively, p<0.005). Hyperlipidemia increased the fractions of CD8 and CD4 TCM as well the activation of CD4 and CD8 T cells while smoking decreased such activation. Hypertension decreased the fraction of CD4 and CD8 TNAIVE. Age correlated positively with the activation of CD4 and CD8 T cells and the abundance of CD4 TCM, CD8 TCM, CD8 TEM and negatively with the abundance of TREG and CD4 and CD8 TNAIVE cells.
Conclusion: Our finding that CAD is associated with different subtypes of T lymphocytes regardless of age is noteworthy. Our T lymphocytes phenotypic analysis revealed a correlation between the presence of activated T lymphocytes in the blood of patients with CAD and the progression of coronary heart disease, whereas, the prevalence of naive T cells in blood correlated with the absence of atherosclerosis. Moreover, activated T lymphocytes are positively associated with CAD risk factor such as hyperlipidemia. These findings support the active involvement of the immune system in the pathogenesis of atherosclerosis.

P3569 | BENCH
Soluble interleukin 6 receptor levels are highly heritable

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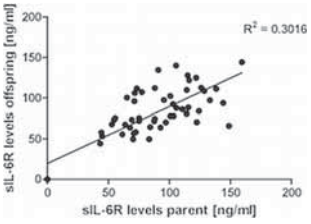
Introduction: Interleukin 6 receptor (IL-6R) signaling might have a causal role in the development of coronary heart disease and ischemic heart failure (IHF). However, the heritability of soluble IL-6R (sIL-6R) levels is unknown. The aim of this study was to assess the heritability of sIL-6R levels.
Methods: To assess the heritability of sIL-6R levels, we analyzed serum samples of patients IHF, healthy controls and their offspring, using sIL-6R enzyme-linked immunosorbent assay (ELISA).
Results: The median sIL-6R levels were 86.17 ng/ml (IQR 68.87 – 114.36 ng/ml) in IHF patients and 77.81 ng/ml (IQR 65.19 – 104.14 ng/ml) in their offspring, and 94.90 ng/ml (IQR 73.00 – 117.56 ng/ml) in controls and 84.00 ng/ml (IQR 69.58 – 112.11 ng/ml) in their offspring. We calculated the correlation between the sIL-6R levels in 30 IHF patients and their offspring (n=29), and the correlation between the sIL-6R levels in 22 healthy controls and their offspring (n=26). A significant correlation coefficient of 0.526 was found between IHF patients and their offspring (p=0.004). In addition, a similar correlation between controls and their offspring was observed with a correlation coefficient of 0.565 (p=0.005). In both groups, approximately 30% of the variance in sIL-6R levels of offspring can be explained by sIL-6R of one parent.



Parent versus Offspring sIL-6R levels.

Conclusion: sIL-6R levels are highly heritable and might explain part of the heritability of IHF.

P3570 | BEDSIDE
The relationship between platelet to lymphocyte ratio and the clinical outcomes in ST elevation myocardial infarction underwent primary coronary intervention

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Objectives: The platelet to lymphocyte ratio (PLR) has been investigated as a

new predictor for cardiovascular risk. The objective of our study was to investigate the role of admission PLR in predicting in-hospital and early mortality in patients presenting with ST segment elevation myocardial infarction (STEMI).
Methods: A total of 639 consecutive patients with STEMI who underwent primary PCI were included. The study population was divided into tertiles on the basis of admission PLR values. A high PLR (n=213) was defined as a value in the upper third tertile (PLR>174.9) and a low PLR (n=426) was defined as any value in the lower two tertiles (PLR ≤174.9). The patients were followed for clinical outcomes for up to 6 months after discharge.
Results: In Kaplan-Meier survival analysis, the rate of 6 months all-cause deaths was 7% in the high PLR group versus 3% in the low PLR group (P=0.03). In multivariate analyses, a significant association was noted between high PLR levels and the adjusted risk of 6 months all-cause deaths (odds ratio = 2.51, 95% confidence interval (CI)=1.058-5.95; p=0.03).
Conclusion: PLR is a readily available clinical laboratory value associated with 6 months all-cause death in patients with STEMI who undergo primary PCI.

Table 1. Significant predictors of in-hospital mortality

Variables	Univariate analysis		Multiple logistic regression analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Age	1.060 (1.033–1.088)	<0.001	1.045 (1.005–1.087)	0.027
Male gender	0.541 (0.296–0.990)	0.046	0.546 (0.217–1373)	0.198
Left ventricular EF	0.924 (0.895–0.954)	<0.001	0.980 (0.935–1.028)	0.414
PLR	1.014 (1.009–1.019)	<0.001	1.012 (1.005–1.019)	<0.001
STEMI as the cause of ACS	3.370 (1.547–7.339)	0.002	0.446 (0.128–1.549)	0.203
Multi vessel disease	3.924 (1.802–8.542)	<0.001	1.959 (0.717–5.349)	0.190
Diabetes mellitus	2.020 (1.097–3.721)	0.024	1.099 (0.436–2.775)	0.841
Previous MI history	2.530 (1.275–5.019)	0.008	0.395 (0.122–1.285)	0.123
Creatinin	2.859 (1.550–5.273)	0.001	3.541 (1.558–8.047)	0.003
LDL	0.987 (0.975–0.998)	0.019	0.993 (0.978–1.009)	0.382
HDL	0.934 (0.895–0.974)	0.002	0.963 (0.923–1.004)	0.080

P3571 | BEDSIDE
Effects of rituximab therapy on elastic properties of vascular wall and endothelial function in patients with progressive systemic sclerosis

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Purpose: Since effective interventions with anti-B cell agent rituximab have been reported in PSS, the aim of this study was to investigate the influence of combined treatment with rituximab and cyclophosphamide on vascular stiffness and endothelial function (ED) in patients with refractory progressive systemic sclerosis (PSS).
Methods: 10 patients with diffuse cutaneous PSS classified according to LeRoy classification were included. Diagnosis of PSS was confirmed according to ACR (ARA) criteria 1980. Median age was 39 (33-52) years and median disease duration was 3,5 (1,5-6,0) years. Median Rhodnan skin score value was 20 (10-30) points. All patients were refractory to standard treatment with cyclophosphamide in combination with low-dose steroids, showing progression of interstitial pulmonary fibrosis and skin involvement persistent over the past 6 months despite ongoing therapy. All patients with SSc were characterized with basic clinical, instrumental and laboratory tests. Vascular involvement was accessed by measurement of pulse wave velocity (PWV) and augmentation index (AI) with applanation tonometry employing the SphygmoCor system (AtCor Medical Pty Ltd., Sydney, Australia). ED without any vasoactive medication was assessed by EndoPat 2000 system (Itamar, Israel). Treatment regimen consisted of 2 infusions of rituximab in a dose of 1000 mg at day 1 and day 14 after standard premedication with histamine blocker, glucocorticosteroid and paracetamol. At day 1 and day 14 all patients received 500 mg of cyclophosphamide. Follow-up evaluation was performed 6 months after anti-B-cell therapy.
Results: After 6 months of follow-up, a partial improvement of symptoms or stabilization of organ involvement was seen in 7 out of 10 patients. PWV decreased significantly from 6,6 (5,9-7,8) m/sec to 6,2 (5,8-7,8) m/sec (p=0.05). ED as a reactive hyperemia index (RHI) also improved, but it was not significant.
Conclusions: This is the first demonstration of possible improvement of arterial wall structure and function in patients with PSS after initiation of a combination anti-B cell therapy with rituximab and cyclophosphamide. This may indicate involvement of B cells into pathogenesis of vascular damage in PSS.

P3572 | BEDSIDE
Platelet to lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome

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Purpose: Platelets and inflammatory cells are vital elements of acute coronary syndromes (ACS). Recent studies have shown that the platelet to lymphocyte ratio (PLR) is associated with several malignancies however there is no enough data in cardiovascular diseases. Therefore, the aim of this study was to explore the association between PLR and in-hospital mortality in patients with ACS.
Methods: We retrospectively collected patients with ACS undergoing coronary angiography. Total and differential leukocyte counts were measured by an automated hematology analyzer.
Results: In total 587 patients with a mean age of 61.8±13.1 years (68.4% male) were enrolled in the study. Patients were divided into 3 tertiles based on PLR levels. In-hospital mortality was significantly higher among patients in the upper PLR tertile when compared with middle and lower PLR tertile groups (29 (14.8%) vs. 17 (8.7%) and 2 (1.0%); p<0.001). On multiple logistic regression analysis, a high level of PLR was independent predictor of in-hospital mortality together with age, total leukocyte count and creatinine. Using a cut point of 142, the PLR predicted in-hospital mortality with a sensitivity of 69% and specificity of 63%.
Conclusions: Different from other inflammatory markers and assays, PLR is an inexpensive and readily available biomarker that may be useful for cardiac risk stratification in patients with ACS.

P3573 | BENCH
Monocyte heterogeneity in myocardial infarction with and without ST elevation and its association with angiographic findings

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Purpose: To investigate monocyte heterogeneity in acute STEMI and non-STEMI separately and find out any possible relationships between monocyte heterogeneity and coronary angiographic characteristics.
Methods: Thirty STEMI, 30 non-STEMI and 25 SAP patients were enrolled. Blood samples were taken immediately at admission, and on days 2,3,4,5 and 7 after STEMI or non-STEMI to undergo cytometric analysis to determine monocyte heterogeneity.
Results: Peak levels of CD14++CD16- monocytes were higher and reached later in the STEMI group (Table 1). Gensini score was found to be correlated with peak CD14+CD16+ monocyte levels in the non-STEMI and SAP groups. Patients with total occlusion of the culprit artery had significantly higher levels of CD14++CD16- monocytes (642.3±113.2 vs. 532.5±98.2 per mm^3, p<0.001). Peak levels of both CD14++CD16- and CD14+CD16+monocytes were higher in patients with no reflow when compared with the patients with TIMI 3 flow after PCI of the culprit lesion (688.1±104.6 vs. 565.1±111.0, p=0.002, 82.3±12.1 vs. 71.2±10.6, p=0.02 respectively).

Table 1. Monocyte subsets in 3 groups

	STEMI (n=30)	Non-STEMI (n=30)	SAP (n=25)	p value*
Peak monocyte level (/mm^3)	692.7±129.6	602.3±112.8	320.0±106.3	<0.001 (0.011)
Peak CD14++CD16– level (/mm^3)	631.6±116.7	539.6±103.0	291.5±94.6	<0.001 (0.003)
Peak CD14+CD16+ level (/mm^3)	74.8±12.2	71.2±10.8	58.8±11.7	<0.001 (0.47)
Day peak levels were reached:				
Total monocytes	2.78±0.71	2.35±0.69	NA	0.016
CD14++CD16– monocytes	2.73±0.64	2.27±0.74	NA	0.011
CD14+CD16+ monocytes	4.97±1.19	4.43±1.01	NA	0.066

Data are expressed as mean ± SD or n (%). *p values were obtained after comparison between 3 groups with one-way ANOVA. The variables which were found to be significantly different between 3 groups underwent post-hoc Tukey's test. In parenthesis, comparisons between STEMI and non-STEMI patients after post-hoc test are shown. Where the data were not available for SAP patients, independent samples t-test was used to compare 2 groups.

Conclusions: Monocyte heterogeneity differs in STEMI and non-STEMI. Peak levels of CD14++CD16- monocytes are higher and reached later in the STEMI group when compared to non-STEMI group. More importantly, worse angiographic characteristics related with prognosis are associated with monocyte heterogeneity in both STEMI and non-STEMI patients.

P3574 | BEDSIDE
Neutrophil to lymphocyte ratio correlates with contrast-induced nephropathy in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention

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Purpose: The development of contrast-induced nephropathy (CIN) after primary percutaneous coronary intervention (pPCI) is associated with increased mortality and morbidity. An increased inflammatory status has been suggested to contribute to the development of CIN. The aim of this study was to investigate the association between the neutrophil to lymphocyte ratio (NLR), an aspecific inflammatory marker, and the development of CIN.
Methods: We prospectively enrolled all consecutive ST-segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (pPCI) in our Department in 2006-2012 (n=1271). After exclusion of patients with incomplete creatinine and leucocyte values (7.1%) we analyzed

1180 patients. CIN was defined as an increase in creatinine values >0.5 mg/dl in the first 72 hours. We divided our population in four quartiles based on NLR distribution, comparing the 4th quartile with the other three. The NLR was obtained by blood samples collected at admittance (T0) and the following day (T1). Independent predictors of CIN were evaluated with a logistic regression model.
Results: The high risk patients for NLR (4th quartile) were significantly older ($p<0.001$), had higher creatinine value (p=0.001), higher CK-peak ($p<0.001$), lower left ventricular ejection fraction (LVEF) ($p<0.001$), higher Killip class ($p<0.001$) and lower TIMI final flow (p=0.01). They presented more often cardiogenic shock (p=0.006), anterior STEMI (p=0.03), lower incidence of ST-resolution (p=0.003), had higher in-hospital mortality (1.6% vs 5.4%, p=0.01) and long-term (3 years) mortality (7.3% vs 14.1% p=0.02). CIN occurred in 2.7%, 3.3%, 5.4% and 9.0% (p=0.002) of patients in the 1st, 2nd, 3rd and 4th quartile, respectively. Multivariable analysis demonstrated that NLR T1 was significantly associated with CIN (Odds ratio 1.08 95% confidence interval 1.03-1.13 p=0.002). The other independent predictors of CIN were age, anterior AMI, LVEF and a GFR <60 ml/min. Use of IABP, baseline haemoglobin, diabetes and prior AMI were not independent predictors of CIN.
Conclusions: In patients with STEMI undergoing primary PCI, the Neutrophil to Lymphocyte Ratio was independently associated with the incidence of contrast-induced nephropathy. This finding supports the potential role of the acute inflammatory response to acute MI in the development of contrast-induced nephropathy.

COLLATERALS AND MICROCIRCULATION

P3576 | BEDSIDE
Epicardial fat tissue thickness predicts altered duke treadmill score in syndrome X patients

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Purpose: Cardiac Syndrome X (CSX) is a challeging and heterogeneous clinical entity with different and poorly understood pathophysiological mechanisms. Endothelial dysfunction plays a crucial role in pathogenesis of CSX. As a metabolically active organ, epicardial fat tissue (EFT) is a rich source of inflammatory cytokines which might be associated with endothelial dysfunction. We aim to assess the relationship between EFT thickness measured by echocardiography and Duke Treadmill Score (DTS) in CSX patients.
Methods: In CSX patient group, prevalence of hypertension (43.4% vs 23.5%, p=0.032) were higher than control group. The other baseline characteristics and drug usage were similar. The study included 106 patients with angiographically normal coronary arteries. Based on the patients' symptoms and exercise ECG parameters, patients were divided into two groups as 55 CSX (male 42.0%, mean age 52.3) and 51 asymptomatic patients with normal coronary arteries (male 43.1%, mean age 49.9) as control group. EFT thickness was measured from parasternal long axis view at end systole in at least three consecutive beats.
Results: In patients with CSX, EFT thickness was significantly higher than the control group (7.68±1.5 mm vs 6.4±0.8 mm). Correlation analysis revealed a significant negative relationship between EFT thickness and DTS (β: -0.527, $p<0.001$). A cut-off value of 6.85 mm for EFT thickness has 75.5% sensitivity and 72.5% specificity for prediction of CSX (AUC: 0.754, $p<0.001$).

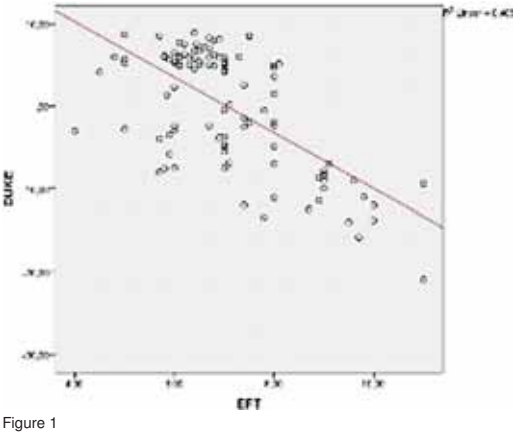

Figure 1

Conclusion: We demonstrated that in CSX patients, EFT thickness increased and had a relationship with a prognostic indicator as DTS. This noninvasive, simple measurement may guide us at risk stratification of patients with angiographically normal coronary arteries.

P3577 | BEDSIDE
Effects of rosuvastatin vs. atorvastatin at high doses acutely after STEMI: endothelial dysfunction and inflammatory biomarkers evaluation

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Purpose: Recent guidelines recommend high dose statins acutely after ST-elevation myocardial infarction (STEMI). Nevertheless, no studies to date have compared the two most powerful statins (Atorvastatin and Rosuvastatin) in this setting. The aim of the present study was to evaluate the efficacy on endothelial function and inflammatory biomarkers of high and moderate doses of these statins administered acutely after STEMI treated with primary percutaneous coronary intervention (PCI).
Methods: We randomized 42 patients within 48 hours from a STEMI treated with primary PCI to Atorvastatin 80 mg (n=13) or 20 mg (n=13), or to Rosuvastatin 40 mg (n=8) or 10 mg (n=8). Every patient underwent endothelial function evaluation by reactive hyperemia–peripheral arterial tonometry index (RH-PAT index) at 1st day and after 1 and 4 months. Moreover we measured levels of high-sensitivity C-reactive protein (hs-CRP) at 1st day and after 1 month.
Results: hs-CRP significantly decreased in all groups ($p<0.05$ for all). RH-PAT index, instead, remained stable in Atorvastatin groups at both follow-ups, while significantly worsened at 1st month in Rosuvastatin groups and then improved at 4th month without reaching statistical significancy (Table 1).

RH-PAT index values in the four groups

Variable	A80	A20	R40	R10	p
RH-PAT index T0	1,81±0,75	1,96±0,35	2,24±0,51	2,01±0,45	0,801
RH-PAT index T1	1,59±0,20	2,05±0,24	1,67±0,08	1,32±0,46	0,050
RH-PAT index T2	–	–	2,16±0,40	1,59±0,21	0,801
p T0-T1	0,285	1,000	0,043	0,028	–
p T1-T2	–	–	0,109	1,000	–
p T0-T2	–	–	1,000	0,109	–

A80, Atorvastatin 80 mg; A20, Atorvastatin 20 mg; R40, Rosuvastatin 40 mg; R10, Rosuvastatin 10 mg; T0, 1st day; T1, 1st month; T2, 4th month.

Conclusions: Acutely after STEMI Atorvastatin seemed more quick and efficacious in restoring a good endothelial function than Rosuvastatin. We hypothesized that this phenomenon could be explained considering hydrophilicity, thanks to which Atorvastatin may act more directly on endothelial cells.

P3578 | BENCH
Relationship between level of oxidative stress and the no-reflow phenomenon in acute myocardial infarction

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Introduction: Despite successful recanalization after AMI, microcirculation perfusion is restored in only 35-70%. This phenomenon called No-reflow (NR) is a multifactorial process involving neutrophil activation, endothelial dysfunction and oxidative stress (OS). Myeloperoxidase (MPO) released by activated neutrophils appeared to be associated with NR. Nevertheless, the precise role of MPO and its links with OS remain unclear. The aim of the study was to assess locally and systemic circulation plasma MPO levels, hydroperoxides (HP) concentration, the Oxygen Radical Absorbance Capacity (ORAC) of the plasma in order to evaluate the impact of ROS as a predictor of NR.
Methods: Thirty-one consecutive patients admitted with STEMI within 12h after symptom onset who underwent coronary angiography for primary or rescue PCI were recruited. No-reflow was assessed using the coronary angiograms analysis, and defined as a TIMI<3 at the end of PCI. Plasma MPO concentrations, HP, total plasma ORAC were determined respectively by ELISA, free oxygen radical test, and the fluorimetry method.
Results: Patients with NR after PCI had higher MPO levels in peripheral vein (749.72 ng/mL±394.62 vs 465.32ng/mL±217.10, p=0.016) and at culprit lesion (798.34 (557.14-1327.73) vs 529.69 (414.35-768.25), p=0.033) than patients without NR. They had also a higher anti-oxidant activity at the culprit lesion (2.55 (0.94-0.30) vs 1.99 (0.57-0.13), p=0.05). Independently of NR, patients after MI had significantly lower levels of HP and ORAC values at the culprit lesion (p=0.014 and p=0.008) than in non-culprit artery.
Conclusion: After AMI there is, at the culprit lesion site, a collapse of anti-oxidant defenses. Thus, NR is associated with higher MPO plasma levels in both culprit lesion site and peripheral vein, but also with increased HP levels and anti-oxidant capacity at the culprit lesion site. We can hypothesize that despite increased local antioxidant defenses, they are overwhelmed by OS, which might leads to the development of NR phenomenon.

P3579 | BEDSIDE

Impact of hypertension and renal dysfunction on coronary collateralization in type 2 diabetic patients with stable angina and chronic total occlusion

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Objective: We investigated whether hypertension and renal dysfunction are related to coronary collateralization in type 2 diabetic patients with stable angina and chronic total occlusion.
Methods: Systolic and diastolic blood pressures were measured and glumerolar filtration rate (GFR) was estimated based on serum creatinine and cystatin C levels in 302 type 2 diabetic patients with stable angina and angiographic total occlusion of at least one major coronary artery. The degree of collaterals supplying the distal aspect of a total occlusion from the contra-lateral vessel was graded as poor (Rentrop score of 0 or 1) or good collateralization (Rentrop score of 2 or 3).
Results: Hypertension was less common and GFR was lower in patients with poor (n=125) than in those with good collateralization (n=177). Diastolic blood pressure and mean arterial pressure correlated positively with Rentrop score (Spearman's r-0.126, p=0.030; Spearman's r=0.125, p=0.029). The occurrence of poor collateralization was lower in hypertensive than in normotensive patients with (50.0% vs. 70.0%) or without (25.4% vs. 42.3%) renal dysfunction (both $P<0.05$), especially when GFR was estimated based on cystatin C levels. In multivariable analysis, female gender, age $\geq$65 years, smoke, dyslipidemia, non-hypertension, and GFR $<$90 mL/min/1.73m^2 were independent determinants for poor collateralization.
Conclusions: Hypertension is inversely, while renal dysfunction is positively, related to poor coronary collateral development in type 2 diabetic patients with stable angina and chronic total occlusion. Aggressive control of high blood pressure should be cautious in this unique cohort particularly with renal dysfunction as it may compromise collateral pressure and exacerbate myocardial ischemia.

P3580 | BEDSIDE

Collateral growth in patients with chronic total coronary occlusions: enhanced proliferative activity in the collateral circulation of diabetics

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Despite extensive preclinical evidence, there are few data demonstrating a functional role of growth factors (GF) in the development of collateral arteries in patients. Patients with diabetes mellitus (DM) have a reduced number of collaterals and reduced collateral function. Elevated levels of bFGF, PlGF and MCP-1 were shown in patients with chronic total coronary occlusions (CTO). In the present study we have investigated the endothelial proliferative activity of serum from the collateral circulation (CC) and compared this with the proliferative activity in the systemic circulation (SC) in patients with CTOs.
In 42 patients with CTO blood was collected distal to the occlusion (CC) and from the aortic root (SC) immediately prior to revascularization. The mitogenic activity of different sera was assessed using human umbilical vein endothelial cells in vitro and a [3H]thymidine incorporation-based proliferation assay.
In patients without DM the ability to stimulate endothelial proliferation was significantly lower in CC compared to SC ($p<0.02$, n=23). Such a difference could not be observed in serum from diabetic patients where proliferative capacity of serum from CC was higher, reaching the level of serum from SC (n.s., n=16). In patients without previous myocardial infarction (MI), the proliferative activity of serum from CC was significantly lower than from SC ($p<0.05$, n=26), a situation similar to the one in non-diabetic patients. Likewise, in patients with normal regional myocardial function, the proliferative activity of serum from CC was significantly lower than from SC ($p<0.02$, n=22), while in patients with reduced regional myocardial function, no such a difference could be observed. Serum from patients with the duration of occlusion between 1 and 3 months triggered significantly higher DNA synthesis ($p<0.05$) as compared to the samples from occlusions of either shorter or longer duration.
In conclusion, the serum from CC from patients with CTO and without DM has reduced proliferative activity on endothelial cells. In patients with DM and in patients with a previous MI or with impaired regional myocardial function, this gradient is eliminated and the proliferative activity is enhanced in serum from CC. Our data are consistent with the hypothesis that the arteriogenic stimulus is increased in patients with impaired collateral development. These data support a crucial role of GF in the development of collateral circulation and provide further insight into the dynamics of the process of collateral development and should help to develop interventional strategies for therapeutic arteriogenesis.

P3581 | BEDSIDE

The association between early and persistent microvascular obstruction by CMR and the index of microcirculatory resistance assessed invasively following STEMI

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Background: Microvascular obstruction (MVO) by CMR is a predictor of poor prognosis following STEMI. The index of microcirculatory resistance (IMR) is an invasive measurement of the microcirculation that has recently been shown to predict poor long-term outcomes with an IMR $>$40. The aim of the study was to determine the association between MVO by CMR, and the IMR measured at the time of PPCI in patients with STEMI.
Methods: 50 patients were prospectively recruited to the study. Patients were included if they presented with STEMI, TIMI flow I/0 in the infarct related artery, and proceeded with PPCI. IMR was performed at maximal hyperaemia using adenosine, and following stent insertion. CMR was performed day 2 following STEMI. We used IMR quartiles to investigate an association between MVO and IMR. Early MVO was measured on dynamic imaging following contrast, persistent MVO was measured 10 minutes following contrast. The difference between IMR quartiles was assessed using the Kruskal-Wallis test. The difference between MVO in patents with an IMR $\leq$/ $\geq$40 was assessed using the Mann-Witney test. All patients provided informed written consent, the study was approved by ethics committee.
Results: The median IMR was 38.5 (range 9 to 202). The median persistent MVO was 1.9% LV (range 0 to 21.0% LV). As IMR increased, both early and persistent MVO index (MVOI=MVO/infarct size) increased (Figure 1a +1b). This association was most marked with persistent MVOI (early MVOI p=0.02 vs. persistent MVOI p=0.002). The IMR cut-off of 40 significantly predicted the presence of persistent MVO on CMR (p=0.0003).

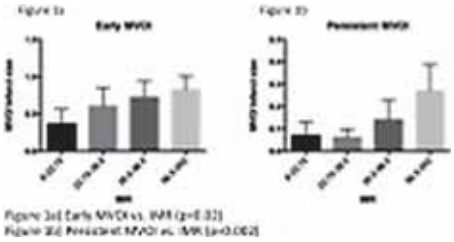

Figure 1

Conclusions: This study provides an invasive functional insight into MVO measured non-invasively by CMR. IMR at the time of PPCI can predict the presence and size of MVO day 2 following STEMI.

P3582 | BEDSIDE

Effect of insulin resistance on coronary collateral development in nondiabetic patients with total coronary artery occlusion

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Purpose: In this present study, we aimed to investigate the effect of insulin resistance on coronary collateral development in nondiabetic patients with total coronary artery occlusion.
Method: The study comprised 40 nondiabetic patients (mean age 61.65$\pm$8.99 years) whose coronary angiography, performed with prediagnosis of coronary artery disease, showed total occlusion in only one of the coronary arteries. Collateral development was classified in reference to the Rentrop classification. Insulin resistance levels were measured by Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) method. The patients with poor collateral [(group-1) (n=20, Rentrop grades 0 and 1)] and good collateral [(group-2) (n=20, Rentrop grades 2 and 3)] were compared in terms of insulin resistance.
Results: When the basic characteristics of both groups were evaluated, no difference was found between the groups in terms of age, gender, smoking, Body mass index (BMI) and presence of hypertension. Whereas there was no significant difference also in terms of biochemical parameters including TSH, LDL, HDL, triglyceride, hemoglobin and HbA1c, significant difference was found between the

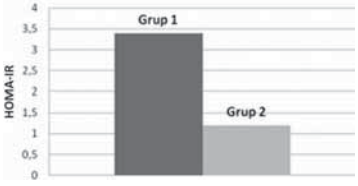

Figure 1

groups in terms HOMA-IR (3.40±3.45 vs. 1.20±1.35, p=0.001) (figure 1), fasting plasma glucose (93.75±13.5 vs 84.15±14.76 mg/dl, p=0.039) and fasting plasma insulin (14.2±13.2 vs 5.3±5.1 μIU/ml p=0.002) levels.
Conclusion: The results of this present study revealed that insulin resistance level was statistically significantly high in the nondiabetic patients with total coronary occlusion and with poor collateral development as compared to those with good collateral development.

P3583 | BEDSIDE
Histological and rheological evaluation at coronary artery lesions in patients with Kawasaki disease during early periods from onset

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Background: Some paper reported that intravascular ultrasound (IVUS)-virtual histology (VH) showed atherogenesis in the evolution of coronary artery lesions (CAL) in adolescents and young adults long after Kawasaki disease (KD). However, there is no report about those findings during early phase of KD.
Purpose: We perform coronary intimal histologic evaluation by IVUS-VH for KD patients with CAL within two years from onset. Furthermore, we calculate shear stress in the target site and examine whether rheological potential affects to vascular histological change after KD.
Subjects and methods: IVUS-VH was performed in 10 Japanese KD patients (median age, 5.0 years) during 2 years after onset of KD (median, 14.2 months) who had small aneurysm (s-AN) in 9 patients and regressed s-AN in 9 patients. All these patients had giant aneurysm in another branches, and 3 patients had CABG and 1 patient had POBA. We investigated 18 coronary branches including 9 sites of small aneurysm (s-AN), 9 sites of regressed s-AN, and 18 sites of normal segment. Each of the 4 plaque components was assigned a respective color and defined as follows: fibrous area (green); fibro-fatty area (yellow) which is densely packed collagen; necrotic core area (red) which is necrotic region consisting of cholesterol clefts, foam cell, and micro-calcification; and dense calcium area (white) which is calcium depositing without adjacent necrosis. Moreover, we measured average coronary peak flow velocity by Flow wire and calculated shear stress in the each sites.
Results: Nine sites of s-AN showed prominent endothelial hypertrophy with fibrous and/or fibro-fatty plaques. In 6 sites of these 9 sites, dense calcium and necrotic core localized which indicates early phase of atherosclerosis. Nine sites of regressed s-AN had circumferential endothelial hypertrophy occupying mainly fibrous and/or fibro-fatty plaques composition. In 6 sites of these regressed 9 sites, dense calcium and necrotic core locally existed. On the other hand, normal segment in 18 sites had no plaque in 17 sites and trivial plaque in 1 site. Moreover, shear stress in all evaluated VH sites were within normal limit, which shows rheological potential doesn't affect to vascular remodeling in such coronary artery lesions.
Conclusions: IVUS-VH study revealed that initial atherosclerotic findings locally existed not only at small aneurysm site but also at regressed site. Therefore, careful further investigation to vascular remodeling in KD patients with CAL including regressed s-AN will be need.

P3584 | BEDSIDE
Impact of percutaneous coronary intervention on 12-month chronic total occlusion outcomes in patients with limited coronary collateral flow

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Background: Limited coronary collateral flow is known to have an adverse effect on clinical outcomes of coronary artery diseases. The impact of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) in pts with limited collaterals is not clear. We compared the 12-month clinical outcomes of pts treated by PCI with optimal medical therapy (OMT) for CTO lesions in pts with limited collaterals.
Methods: A total of 166 consecutive CTO pts with coronary collateral flow grade <2 were divided into 2 groups; one group underwent PCI (PCI group; n=100) and the other group was treated with OMT (OMT group; n=66). Major clinical outcomes were compared between the two groups up to 12 months.
Results: At baseline, the OMT group had a lower LVEF% and a higher prevalence of elderly, left main disease, multivessel disease, multivessel CTO, and LCX-CTO, whereas the PCI group had a higher prevalence of prior MI and prior PTCA. Clinical outcomes at 12 months showed higher incidence of non Q-wave MI in the OMT group (Table). After baseline adjustment by multivariate analysis, however, there was no difference between the 2 groups.

Table. 12-month clinical outcomes

Variable,n	PCI (n=99)	Mx (n=52)	P Value (Unadjusted)	P Value (Adjusted)	OR (95%CI)
Mortality	5 (5)	7 (13.4)	0.069	0.465	0.47 (0.06-3.47)
Cardiac death	4 (4)	5 (9.6)	0.169	NS	-
Non cardiac death	1 (1)	2 (3.8)	0.235	NS	-
Myocardial infaction; MI	5 (5)	6 (11.5)	0.145	0.359	0.35 (0.04-3.20)
Q wave MI	0 (0)	3 (5.7)	0.851	NS	-
Non W wave MI	0 (0)	3 (5.7)	0.016	NS	-
Revascularization	13 (13.1)	9 (17.3)	0.489	0.807	0.81 (0.15-4.16)
TLR	12 (12.1)	3 (5.7)	0.215	NS	-
TVR	13 (13.1)	7 (13.4)	0.955	NS	-
Non TVR	1 (1)	2 (3.8)	0.235	NS	-
All MACE	16 (16.1)	8 (15.3)	0.901	0.791	0.83 (0.22-3.07)
TLR MACE	18 (18.1)	14 (26.9)	0.212	NS	-
TVR MACE	18 (18.1)	15 (28.8)	0.132	NS	-

Adjusted by gender, age, myocardial infarction, hypertension, diabetes, chronic kidney disease, current smoker, multivessel disease, collateral vessels(≤grade 2), and failed CTO procedure

Conclusions: In our study, mechanical revascularization by PCI for CTO lesions in pts with limited collaterals seems to have no definite benefit in reducing 12-month morbidity or mortality. Long-term follow up with larger study population will be necessary for further determination of the benefit and risks of interventional therapy in CTO pts.

P3585 | BEDSIDE
Circulating EPCs predicts the occurrence of major adverse cardiac events and early adverse remodeling in patients with STEMI

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Purpose: To assess the prognostic significance of circulating EPCs level and indices of endothelial damage/dysfunction in patients with STEMI.
Methods: In 85 consecutive patients with acute STEMI, the number and function of peripheral blood CD31+/CD34+ EPCs, as well as the indices of endothelial damage/dysfunction [Von- willebrand factor (vWF) and flow mediated dilatation (FMD)] were determined. The primary end point was a composite of all-cause mortality, recurrent non-fatal MI, or heart failure (MACEs) during follow-up period of 30 days, with the echocardiographically assessed 30 day-left ventricular (LV) remodeling as the secondary end point.
Results: 78 patients with acute STEMI were analyzed. The mean age was 53.8±10.6 years (62 males & 16 females). During the follow-up, MACE occurred in 17 (22%) patients. EPC level [87 (78-95) versus 75 (26-88) %, respectively; P=0.004], VEGFR2 gene expression (qPCR) [1.02±0.31 versus 0.80±0.36, respectively; P=0.02), vWF level [835±349 versus 623±343 pg/mL, respectively; P=0.03), FMD [3.5±1.4 versus 5.9±3.1%, respectively; P=0.006), anterior wall MI location [82.4% versus 47.5%, respectively; P=0.01), LVEDD [5.9±0.5 versus 5.2±0.7 cm, respectively; P<0.0001), LVESD [4.5±0.6 versus 3.7±0.8cm, respectively; P<0.0001), LVEDV [93±32 versus 78±26 mL, respectively; P=0.04), LVESV [60 (38-78) versus 33 (25-44) mL, respectively; P=0.001], LVEF [40±8 versus 53±12%, respectively; P<0.0001), LV WMSI [1.98±0.29 versus 1.66±0.36, respectively; P=0.001), LV MPI [0.79±0.16 versus 0.66±0.14, respectively; P=0.002), between patients who developed MACE and those who did not. Multivariate analysis showed that EPC level and LV ejection fraction were the most independent predictor of MACE. There was a significant correlation between the EPC level and function in the low EPC-group (level ≤82%) and not in the high EPC-group (level >82%). The areas under the receiver-operating characteristic curve (AUC) for EPC level, FMD, and the logistic model with both markers were 0.73, 0.75, and 0.82 respectively. There was a significant increase in LV end-diastolic volume baseline-to-follow-up in the high EPC-group and not in low EPC-group.
Conclusions: High level of circulating EPCs predicts the occurrence of MACE and early adverse remodeling in patients with STEMI. An EPC level of >82% and FMD ≤4.7% are a cutoff levels for the prediction of the 30-days MACE with a sensitivity of 76.5% & 93.3% and specificity of 63.9% & 63.9% respectively. FMD complements the EPC level to improve risk stratification after acute STEMI.

P3586 | BENCH
Fibrocytes accumulate at the coronary culprit lesion site in STE-ACS

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Introduction: ST-elevation acute coronary syndrome (STE-ACS) is a major cause of death. A Collagen-I+CD34+CD45+ progenitor cell population ("Fibrocytes") is increased in cardiac tissue in ischemia. In ACS patients, circulating fibrocytes were shown to be decreased compared with healthy controls. We hypothesized that fibrocytes are increased, more active and more susceptible to mitogenic signals within the coronary vessels, contributing to occlusion and consecutive reparative processes by production of Collagen-I.
Methods: Culprit site blood samples from STE-ACS patients (n=13, male=92%, mean age=65±9.6y) drawn at primary percutaneous coronary intervention were analyzed. Flow cytometry was employed to characterize fibrocytes by expression of Collagen-I, BMPRII, CD34, CD11b, CXCR4 and CD45.
Results: Fibrocyte count was increased at the culprit lesion site compared to femoral blood (1145±1172/106 CD45+ cells versus 508±630/106 CD45+ cells, p=0.035). Furthermore, culprit site fibrocytes displayed increased expression of CD11b (mean fluorescence intensity (MFI)=87447±47197 versus MFI=59679±20588, p=0.029) and Collagen-I (22634±12750 versus 15058±10659, p=0.049). No differences in expression of BMPRII, CXCR4, CD34 and CD45 were observed.
Conclusions: The two-fold increase of culprit site fibrocytes compared to femoral blood could indicate homing to the coronary vessels in STE-ACS. Increased coronary CD11b and increased Collagen-I expression might reflect enhanced migratory and reparative activity of fibrocytes within the coronary vessels. Further experiments will clarify the contribution of fibrocytes to STE-ACS.

STABLE CORONARY ARTERY DISEASE

P3588 | BEDSIDE
Divergent effects of C338A polymorphism of endothelin-1 converting enzyme gene, on endothelin-1 levels is healthy subjects and in subjects with coronary artery disease

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Purpose: Endothelin-1 (ET-1) is strongly implicated into the pathophysiology of atherosclerosis and of ischemic heart disease. Although a number of genetic polymorphisms have been identified in ET-1 gene, their effects on the expression of ET-1 and its circulating levels are unclear. We examined the effect of C338A polymorphism of endothelin-1 converting enzyme gene (ECE-1b C338A) on ET-1 levels in coronary artery disease (CAD) patients and control subjects.
Methods: The study population consisted of 151 (mean age 61±10 years) consecutive subjects with angiographically documented stable CAD and 190 (mean age 60±10 years) control subjects. Plasma levels of ET-1 were measured by ELISA, while the presence of (ECE-1b C338A) polymorphism was determined by PCR.
Results: Between CAD and control subjects there was no difference in age while the prevalence of male gender was higher among CAD subjects (78% vs. 58%, $p<0.001$). Subjects with CAD had also significantly elevated levels of ET-1 compared to control subjects (2.38±2.94fmol/ml vs. 1.24±1.25fmol/ml, $p<0.001$) even after adjustment for gender. However, there was no significant difference in the distribution of ECE-1b C338A polymorphism between CAD (CC: 88%, CA: 8%, AA: 5%) and control subjects (CC: 87%, CA: 7%, AA: 6%), (p=0.84). Interestingly, in CAD subjects the presence of A allele on ECE-1b C338A polymorphism was associated with significantly increased levels of ET-1 (5.43±1.96fmol/ml vs. 1.96±2.33fmol/ml, $p<0.001$) while in control subjects the presence of A allele on ECE-1b C338A polymorphism had no impact on ET-1 levels (1.40±1.13fmol/ml vs. 1.22±1.26fmol/ml, p=0.41).
Conclusions: The presence of A allele on ECE-1b C338A polymorphism is associated with significantly higher levels of ET-1 in CAD patients. These findings may partially explain the difference observed in ET-1 levels between control subjects and CAD patients and provide further insights into the pathophysiology of atherosclerosis and of ischemic heart disease.

P3589 | BEDSIDE
Abnormalities of mineral metabolism: prevalence in coronary artery disease and relationship with plasma biomarkers and lipid levels

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Background: Abnormalities of mineral metabolism have been related traditionally with renal disorders. However, in the recent years, it has been shown that low vitamin D plasma levels, as well as enhanced fibroblast growth factor-23 (FGF-23), parathyroid hormone (PTH) and phosphate levels are associated with an increase in the incidence of cardiovascular events. In spite of this, data on the prevalence of abnormalities in these components of mineral metabolism in patients with coronary artery disease (CAD) are sparse.
Methods: We assessed the prevalence of alterations of mineral metabolism [calcidiol (a vitamin D metabolite), FGF-23, PTH, and phosphate plasma levels] in 704 patients with stable CAD, as well as their relationship with several biomarkers.
Results: Age was 61.4±12.3 years and 75% of the patients were men. Estimated glomerular filtration rate was 77.7 (63.6, 89.9) ml/min/1.73 m^2; in 79.7% of patients this value was >60 ml/min/1.73 m^2.
Calcidiol levels showed severe deficiency (≤10.0 ng/ml) in 10.9% of cases, moderate deficiency (10.01-20.00 ng/ml) in 46.4%, were suboptimal (20.01-30.0 ng/ml) in 32.3%, and normal (>30 ng/ml) in 10.4%. FGF-23 levels [69.9 (54.5, 96.3) RU/ml] were elevated (>130 RU/ml) in 11.5% of cases. PTH levels [59.7 (45.5, 77.5) pg/ml] were increased in 30% of cases (>74 pg/ml). Phosphate levels [3.2 (2.8, 3.5) mg/dl] were high in only 0.9% of cases (>4.5 mg/dl).
Calcidiol levels showed a weak correlation with monocyte chemoattractant protein-1 (MCP-1) (r=-0.085, p=0.024) and pro-brain natriuretic peptide (proBNP) (r=-0.084, P=0.026), but not with age, glomerular filtration rate, high-sensitivity C reactive protein (hsCRP) or galectin-3. FGF-23 displayed a mild-moderate correlation with age (r=0.104, p=0.010), glomerular filtration rate (r=-0.286, $p<0.001$), MCP-1 (0.182, $p<0.001$), proBNP (r=0.439, $p<0.001$), hsCRP (0.127, p=0.002) and galectin-3 (r=0.203; $p<0.001$). PTH showed also a mild-moderate correlation with age (0.209, $p<0.001$), glomerular filtration rate (r=-0.374, $p<0.001$), MCP-1 (r=0.148, $p<0.001$), pro-BNP (r=0.355, $p<0.001$) and galectin-3 (r=0.171; $p<0.001$) but not with hsCRP. At multiple linear regression analysis, these variables along with lipid values did not explain calcidiol, FGF-23 and PTH levels (adjusted R2: 0.068, 0.218, and 0.203, respectively)
Conclusions: Patients with CAD show a high prevalence of alterations of calcidiol, FGF-23 and PTH plasma levels, which may be related to an adverse outcome. These changes are not explained by age, glomerular filtration rate, inflammatory biomarkers and lipids.

P3590 | BEDSIDE
Effectiveness of different clinical risk scores to predict different outcomes in patients with coronary artery disease

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Purpose: There are not accepted prognostic risk scores for patients with stable coronary artery disease (SCAD). We have assessed the usefulness of three previously published clinical risk scores to predict different outcomes in patients with SCAD.
Methods: We have evaluated these clinical risk scores in 603 patients with SCAD: 1) The D'Agostino score, based on the Framingham study, which takes into account age, sex, high density lipoprotein, diabetes, smoking and blood pressure; 2) The Marschner score, from the LIPID (Long-Term Intervention with Pravastatin in ischemic Disease) study, which uses 15 variables including age, sex, cardiovascular risk factors, and cardiovascular history, among others; and 3) The simplified VILCAD (Vienna and Ludwigshafen Coronary Artery Disease) score, calculated with age, ejection fraction, creatinine levels, heart rate and hemoglobin A1c. The secondary outcomes were the incidence of acute ischemic events (any acute coronary event, stroke or transient ischemic attack), and heart failure or death. The primary outcome was the combination of secondary outcomes. A Net Reclassification Index (NRI) was calculated to assess the improvement in risk prediction gained by adding every risk scale to models constructed with adjustment variables.
Results: Age was 61.2±12.3 years and 75.1% of patients were men. Follow-up was 2.08±0.97 years. Forty-two patients developed an acute ischemic event, 22 met the outcome of heart failure or death, and 60 developed the primary outcome. By Cox regression analysis, recurrence of acute ischemic events was predicted only by D'Agostino score [Hazard Ratio (HR) 1.046, confidence interval (CI) 1.012-1.082; p=0.029], with a NRI of 9.7% (9.6-9.8). The Marschner (HR 1.126, CI 1.041-1.217; p=0.005) and the VILCAD scores (HR 1.988, CI 1.480-2.670; $p<0.001$) predicted the development of heart failure or death with NRIs of 5.8% (5.7-5.9) and 18.6 (18.3-18.9), respectively. The development of the combined primary outcome was predicted by Marschner (HR 1.096, CI 1.031-1.165; p=0.005) and VILCAD scores (HR 1.387, CI 1.132-1.700; p=0.003), with NRIs of 3.4% (3.3-3.5) and 19.4% (19.3-19.6), respectively.
Conclusions: The accuracy of different risk scales in SCAD varies according to the outcome studied. While scores assessing cardiovascular risk factors predict the incidence of acute ischemic events, those including variables related to myocardial and renal function perform better in the prediction of heart failure and death. These findings must be taken into account when developing new prognostic scores.

P3591 | BEDSIDE
The predictive value of high-sensitive cardiac troponin I in stable coronary artery disease depends on age and other clinical variables

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Purpose: The prognostic usefulness of high-sensitive cardiac troponin I (hs-cTnI) plasma levels in patients with stable coronary artery disease (SCAD) has not been fully elucidated. We have assessed the ability of hs-cTnI to predict different outcomes in patients with SCAD.
Methods: We studied 706 patients with SCAD. At baseline clinical variables were recorded and hs-cTnI was determined. Secondary outcomes were the incidence of: 1) acute ischemic events (any acute coronary syndrome, stroke, or transient ischemic attack), and 2) heart failure or death. Primary outcome was the composite of secondary outcomes.
Results: Hs-cTnI was >0 ng/mL in 62,1% of cases, with median and maximal values of 0.008 (0.003-0.017) and 3.446 ng/mL respectively.
At univariate analysis, cases with hs-cTnI >0 were older [64.0 (55.0-74.0) vs 56.0 (50.0-65.0) years; $p<0.001$], had lower Glomerular Filtration Rate (GFR) [74.3 (59.1-86.7) vs 81.4 (71.3-93.8) mL/min/1.73 m^2], a more frequent history of hypertension 69.9 vs 57.3%; p=0.001), atrial fibrillation (7.1 vs 1.9%; p=0.002), ejection fraction <40% (16.7 vs 3.7%; $p<0.001$), therapy with angiotensin converting enzyme inhibitors (ACEI) (58.9 vs 49.1%; p=0.012), diuretics (23.5 vs 13.1%; p=0.001) and acenocumarol (8.7 vs 1.9%; $p<0.001$) than those with hs-cTnI =0.
Follow-up was 2.2±0.99 years. Fifty-three patients suffered an acute ischemic event, 33 died or suffered heart failure and 78 developed the primary outcome. By Cox regression analysis, hs-cTnI >0 was associated with higher risk of de-

veloping the primary outcome [2.360 (1.359-4.099); p=0.001], and heart failure or death [5.932 (1.806-19.482); p<0.001], but not with acute ischemic events. When controlling for age, the statistical signification was lost.
By logistic regression analysis, age [Odds ratio (OR) 1.026 (1.009-1.044); p=0.003)], ejection fraction <40% [OR 4.099 (2.043-8.224); p<0.001], anticoagulants [OR 2.785 (1.049-7.395); p=0.040)], ACEI [OR 1.471 (1.064-2.034); p=0.020], and GFR [OR 0.988 (0.977-0.999); p=0.027] were associated to hs-TnI >0.
Conclusions: In patients with SCAD, positive hs-cTnI is associated with incidence of heart failure or death, but not with acute ischemic events. Nevertheless, this association is explained by standard clinical variables, making unnecessary to determine hs-cTnI in this population.

P3592 | BEDSIDE
Deterioration of glucose tolerance over time may contribute to adverse prognostic effect of asymmetric dimethylarginine in stable coronary artery disease

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Purpose: Endothelial dysfunction, a well-recognized predictor of adverse cardiovascular outcome, was reportedly associated with incident type 2 diabetes. Our aim was to estimate whether changes of glucose tolerance over time might contribute to the adverse prognostic effect of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthesis, in stable coronary artery disease (CAD).
Methods: We studied 125 non-diabetic men (age 56±11 years) with stable angina, obstructive CAD and without heart failure who underwent a successful elective percutaneous coronary revascularization in our center and were receiving a standard medication according to practice guidelines. Plasma ADMA was measured prior to coronary angiography during index hospitalization. Adverse coronary events included death from CAD, non-fatal myocardial infarction, resuscitation after cardiac arrest, hospitalization for unstable angina and symptoms-driven coronary revascularization, whichever occurred first. Predictors of adverse coronary outcome were assessed by Cox regression with deteriorating glucose tolerance as a time-dependent confounder. A decline in glucose tolerance was defined as a diagnosis of new-onset type 2 diabetes or progression to pre-diabetes from a normal glucose tolerance after index hospitalization.
Results: Over a median follow-up of 5 years we recorded 51 adverse coronary events, 15 patients developed type 2 diabetes and 19 progressed to pre-diabetes from a normal glucose tolerance. The subjects with incident decline of glucose tolerance exhibited higher baseline plasma ADMA compared to the remainder (0.54±0.13 vs. 0.47±0.11 μmol/l, p=0.003). By a univariate Cox regression, ADMA was associated with the risk of adverse coronary events (mean hazard ratio [HR] per 1-SD increase in plasma ADMA: 1.38 [95% confidence interval, 1.11–1.72], p=0.004), which was maintained after controlling for baseline clinical, biochemical and angiographic characteristics (HR: 1.35 [1.09–1.68], p=0.007). However, the prognostic ADMA effect was attenuated (HR: 1.26 [1.02–1.58], p=0.04) upon further adjustment for incident decline of glucose tolerance.
Conclusion: An association between plasma ADMA levels and future deterioration of glucose tolerance may contribute to the adverse prognostic effect of ADMA in non-diabetic men with stable CAD.

P3593 | BEDSIDE
The evaluation of reactive oxygen metabolites during intracoronary acetylcholine spasm provocation test in patients with vasospastic angina

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Background: Nitric oxide (NO) plays an important role in the regulation of coronary blood flow, and is counterbalanced by the formation of reactive oxygen species (ROS). Thus, an imbalance in vascular NO and ROS production contributes to endothelial dysfunction, which is associated with coronary artery disease. Although the bioavailability of NO in the coronary circulation is commonly evaluated by acetylcholine (ACh)-induced vasodilation, a change in reactive oxygen metabolites after ACh administration is unknown in the coronary circulation.
Methods: We directly measured the serum diacron reactive oxygen metabolites (dROMs) in the coronary sinus vein by using the dROMs test in consecutive 26 patients with chest pain and normal coronary arteriograms who underwent an intracoronary ACh provocation test. We also assessed the metabolism of myocardial lactate during ACh administration in the patients by measurement of lactate in paired blood samples from the coronary artery and coronary sinus vein.
Results: ACh provocation test was positive in 18/26. Testing of paired samples of arterial and coronary sinus venous blood showed that lactate was produced after ACh administration in the provocation positive group. There was no difference in baseline dROMs levels between the provocation positive group and the negative group (234±50 vs. 228±52 CARR U). The provocation negative group had significantly lower dROMs levels after ACh administration (190±46 vs. 228±52 CARR U, P<0.01) than baseline. The dROMs levels after ACh administration in the provocation positive group were significantly higher than the negative group (220±49 vs. 190±46 CARR U, P<0.01), suggesting lower antioxidant activity of NO in the provocation positive group (the patients with vasospastic angina).
Conclusion: Direct measurement of dROMs levels in the coronary sinus vein by using the dROMs test in the ACh provocation test may be useful to evaluate the interaction of NO and ROS in the coronary circulation.

P3594 | BEDSIDE
Use of proton pump inhibitors predicts heart failure and death and is associated to increased plasma levels of galectin-3 and monocyte chemoattractant protein-1 in coronary artery disease

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Purpose: Proton pump inhibitors (PPIs) have been said to increase the incidence of cardiovascular events in patients (pts.) with coronary artery disease, mainly in those using clopidogrel. We have analyzed the impact of PPI use in the prognosis and biomarker plasma levels of pts. with stable coronary artery disease.
Methods: We followed 706 pts. with stable coronary artery disease who had an acute coronary syndrome (ACS) 6-12 months before. Secondary outcomes were: 1) acute ischemic events (ACS with/without ST-elevation, stroke, or transient ischemic attack) and 2) heart failure or death. The primary outcome was the combination of secondary outcomes.
Results: Pts. on PPIs were older [62.0 (53.0-73.0) vs 58.0 (50.0-70.0) years; p=0.003], had a more frequent history of stroke (4.9% vs 1.1%; p=0.004) and shorter time from last ACS (218±89 vs 233±94 days; p=0.027) than the no-PPI group. There were no differences in cardiovascular risk factors, existence of peripheral artery disease, ejection fraction, cardiovascular therapy (aspirin: 91.4% vs 92.7%; clopidogrel: 66.8% vs 69.1%), glomerular filtration rate, and number of diseased vessels, type of revascularization, and use of drug-eluting stents (44.5% vs 50.9%) at the previous ACS.
Follow-up was 2.2±0.99 years. Fifty-three pts. developed acute ischemic events, 33 heart failure/death, and 78 met the primary outcome. PPI use was an independent predictor of the primary outcome [Hazard Ratio (HR) 2.281 (1.244-4.183); p=0.008], along with hypertension, body-mass index, glomerular filtration rate, atrial fibrillation, and nitrate use. It was also an independent predictor of heart failure/death [HR 5.713 (1.628-20.043); p=0.007], but not of acute ischemic events (Cox regression).
Pts. on PPI had higher plasma levels of galectin-3 [8.12 (6.47-9.92) vs 7.51 (5.16-9.23) ng/ml; p<0.001] and MCP-1 (monocyte chemoattractant protein-1) [147.1±69.6 vs 136±55.9 pg/mL; p=0.027], which are related to fibrosis and inflammation, respectively. No differences in high-sensitivity C-reactive protein or NT-probrain natriuretic peptide plasma levels were seen.
Conclusions: In pts. with stable coronary artery disease, PPI use is an independent predictor of the development of heart failure or death. Pts. on PPIs had increased plasma levels of MCP-1 and galectin-3, that are related to inflammation and fibrosis. Further study is needed to clarify these findings.

P3595 | BENCH
Interaction between risk factors and fibrinogen genetic polymorphisms in patients admitted for stable angina pectoris: focus on underlying processes

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Purpose: It is well established that hypertension (HTN) and diabetes mellitus (DM) are strongly associated with coronary artery disease (CAD. In addition, inconsistent data exist regarding to the role of fibrinogen genetic variability in atherosclerosis. Therefore, we examined the effects of the rs180070 and rs2070011 fibrinogen polymorphisms on coagulation and inflammatory processes as well as the risk for CAD in patients with DM and HTN admitted with stable angina pectoris.
Methods: In 3 year period, 744 subjects were enrolled in our study. The two polymorphisms were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Fibrinogen, interleukin-6 (IL-6), high sensitivity C-reactive protein (hsCRP) CD40L, D-dimer and factors V, X activity were measured with appropriate methods.
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). 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 associa-

tions were observed in HTN and DM patients. 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)]. Finally, the AA homozygosity (rs180070) was associated with higher IL-6 an D-dimer, but not hsCRP levels in the general population.
Conclusions: Our findings suggest that the presence of AA genotype (rs180070) is associated with increased levels of inflammatory mediators and higher risk of CAD. However, elevated fibrinogen levels >443 mg/dl remained the most significant predictor of CAD.

P3596 | BEDSIDE
Higher levels of cardiac troponin t in patients with stable angina pectoris predict increased risk of myocardial infarction

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Purpose: Previous studies among patients with stable angina pectoris (SAP) have shown that cardiac troponin T (hs-cTnT) concentrations as determined by highly sensitive assays are significantly associated with risk of cardiovascular death, but the association with acute myocardial infarction (AMI) is less clear. We assessed the relationship between baseline hs-cTnT levels and risk of AMI in SAP patients.
Methods: 3882 patients who underwent elective coronary angiography 2000 – 2004 were followed to subsequent AMI or end of 2006. Univariate and multivariate survival analyses according to hs-cTnT groups (≤3 ng/L; n=1796, 4-9; n=1199, 10-19; n=689 and 20-30; n=198) were studied by Kaplan Meier plots and by Cox regression.
Results: The population consisted of 2773 (71.4%) males with a median age of 61.7 years, of which 286 (7.4%) experienced an AMI. Kaplan Meier plots revealed a strong, graded association between hs-cTnT categories and risk of AMI (Figure 1). In a Cox model adjusted for age, sex, body mass index, hypertension, diabetes mellitus, smoking, Apo A1, Apo B, Lp(a) and CRP, hazard ratios (HRs) (95% confidence intervals [CIs]) were 1.05 (0.75 – 1.46), 1.94 (1.38 – 2.73) and 3.25 (2.13 - 4.95) when comparing the 2nd, 3rd and 4th to the 1st Hs-cTnT group, respectively (P for trend <0.001). The linear association remained significant (P for trend <0.001) even after adjusting for the number of significantly stenosed coronary arteries (0-3), left ventricular ejection fraction (%), estimated glomerular filtration rate (mL/min/1.73m^2), medication and previous peripheral vascular disease, percutaneous intervention or coronary bypass surgery.

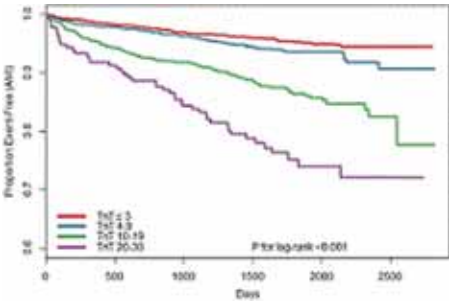

Figure 1

Conclusion: In patients with SAP, higher levels of hs-cTnT are associated with an increased risk of subsequent AMI.

P3597 | BEDSIDE
Predictors of death and myocardial infarction in patients with refractory angina

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Background: Patients with refractory angina (RA) usually have extensive coronary artery disease (CAD) leading to myocardial ischemia and disabling symptoms that cannot be controlled by a combination of medical therapy, angioplasty or surgery (CABG). It is estimated that about 10% of patients with symptomatic CAD have RA. Nevertheless, data about the natural history of RA and the predictors of events in this growing group of patients are very scarce.
Methods: 100 patients (70 men, mean age 62 years) were prospectively enrolled in this study. Optimal, maximally tolerated medical therapy was encouraged during a 3-month period. All patients underwent invasive coronary angiography, and cardiac magnetic resonance myocardial perfusion stress-testing; highly sensitive cardiac troponin T (hs-cTnT) levels were determined at baseline. The primary endpoint was the composite incidence of death and nonfatal myocardial infarction (MI). Kaplan-Meier curves were constructed for the event-free survival probability during a median follow-up period of 22.5 months (interquartile range, 11 to 37). Univariate analysis was performed using the log-rank test to identify variables associated with the primary endpoint, and the Cox proportional-hazards regression model for the multivariate analysis.
Results: Prior history of CABG or angioplasty was found in 79% and 57% of patients, respectively. Cardiovascular assessment revealed that 71% of patients had a previous MI, 74% had three-vessel disease, and 11% had moderate to severe left ventricular dysfunction. There were 15 events (6 deaths and 9 myocardial infarctions) giving an estimated 22.5-month cumulative event rate of 10%. Univariate predictors of death and MI were: hs-cTnT quartile (P<0.0001), median age (P=0.008), left ventricular dysfunction (P=0.019), and chronic kidney disease (P=0.008). After multivariate analysis, only hs-cTnT (P<0.0001) continued to be statistically significant.
Conclusion: This study demonstrated for the first time that plasma levels of hs-cTnT were the only independent predictors of death and MI in patients with refractory angina.

TOPICS IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION

P3599 | BEDSIDE
Prognostic impact of a primary PCI regional network implementation for the treatment of patients with ST-segment elevation myocardial infarction

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Background: Primary percutaneous coronary intervention (P-PCI) is superior to fibrinolysis in patients presenting with acute ST-elevation myocardial infarction (STEMI) when it can be expeditiously performed by an experienced team in a hospital with a 24h/7d P-PCI programme and PCI related time delay compared to fibrinolysis is no longer than 90-120min.
Aim: To determine if the availability of a 24h/7d regional P-PCI programme is associated with improved prognosis in STEMI patients.
Methods: We analysed 2327 patients admitted consecutively in our coronary care unit with a diagnosis of STEMI and included in a prospective registry, from Jan 2002 to Jun 2013. Patients were divided in three groups corresponding to different time periods: 2002-2004 (group 1, n=627, 26.9%) - without cath lab in our hospital (STEMI patients were treated with fibrinolysis and rescue/elective PCI); 2005-2009 (group 2, n=742, 31.9%) - with elective PCI available two to four periods of five hours a week; and 2010-2013 (group 3, n=958, 41.2%) - with a 24h/7d PCI programme. For each group we compared clinical and laboratory features, treatment and adverse events. Primary endpoint was the occurrence of death at 6 months; follow-up was completed in 98% of patients.
Results: Age difference between groups was not statistically significant. Patients in group 3 were more often men (77.8 vs 74.5 vs 80.4%; p=0.016), had higher body mass index (p=0.001), higher prevalence of dyslipidaemia (37.2 vs 45.3 vs 49.9%; p<0.001), smoking (30.3 vs 29 vs 36.7%; p=0.001), and history of CABG (0.3 vs 1.6 vs 4.6%; p<0.001). On admission, they presented more often with Killip 4 (2.1 vs 2.4 vs 4.1%; p=0.043), anaemia (14.1 vs 19.2 vs 21.8%; p=0.005) and renal insufficiency (eGFR <60 ml/min) (15.6 vs 17.5 vs 23.8%; p<0,001). Patients in group 1 were more frequently treated with fibrinolysis (51 vs 44.5 vs 3.3%; p<0.001) and less often treated with beta blockers (78.8 vs 87.6 vs 84.6%; p<0.001), statins (78.8 vs 97.7 vs 98.0%; p<0,001) and PCI (31.1 vs. 69 vs. 87.7%; p<0.001). In-hospital (10.1 vs 7.1 vs 5.8%; p=0.007) and 6-month mortality (15.2 vs 12.2 vs 10.3%; p=0.017) were lower in groups 2 and 3 compared with group 1. In multivariate analysis, group 3 remained associated with a 39% risk reduction of 6-month mortality compared to group 1 [adjusted OR 0.61, 95% CI (0.403 - 0.924); p=0.02].
Conclusion: Overall improvement of care and implementation of a 24h/7d P-PCI programme was associated with a progressive reduction of mortality in STEMI patients admitted to our coronary care unit over the past 12 years, despite an increasing risk profile.

P3600 | BEDSIDE
Endovascular myocardial reperfusion in patients with AMI and acute occlusion of the left main coronary artery

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Purpose: To study the feasibility, safety and effectiveness of emergency endovascular myocardial reperfusion in patients with AMI and acute occlusion of the left main coronary artery (LCA).
Background: The prognosis in acute occlusion of the LCA is very unfavorable. Most patients die within the first minutes and hours of the disease, before admission. However, few patients survive until the admission and can receive emergency treatment. Special hopes for improving the prognosis are put on urgent endovascular myocardial reperfusion. Meanwhile the experience in this field is quite small.

Material and methods: In 2000 – 2012, 5187 patients with AMI underwent endovascular treatment in our Center. 42 (0,8%) of them had acute occlusion of the LCA. All those patients had cardiogenic shock of various degree. Coronary angiography revealed complete occlusion of the LCA with collateral filling (Rentrop 2-3) of distal segments from the RCA. Average LV EF was 27,4±5,6%.
Results: 32 patients (76,9%) had endovascular recanalization and stenting of the LCA resulting in antegrade blood flow TIMI 2-3. In 26 cases PCI were preceded by intraaortic balloon pumping of at least 24 hours duration in all patients. 19 of 42 patients received intracoronary metabolic cytoprotectors following the original technique elaborated in our Center. Mechanical vacuum thrombextraction from the LCA was performed with positive results in 3 cases. 13 patients (30,7%) died in hospital from progressive LV failure, the remaining were discharged in satisfactory condition. Mid-term follow-up (11,7±3,1 months) was obtained in all 29 patients. One patient died in 10 months from acute coronary insufficiency (probably, stent thrombosis after stopping antiplatelet therapy). Another 10 patients with multivessel coronary disease underwent CABG. Another 16 patients had repeated endovascular procedure related to in-stent stenosis of BMS or stenting of another sites in coronary vessels. The remaining 2 patients were angina free, and CAG did not reveal any signs of progressing stenosis or in-stent changes. All 28 patients were in NYHA class 1-2. LV EF was 36,5±6,8% on the average.
Conclusions: Our first results of endovascular myocardial reperfusion in patients with AMI and complete occlusion of the LCA seem more favorable and encouraging in comparison with conservative therapy, particularly if these procedures are combined with intraaortic balloon pumping and other effective therapeutic procedures (thrombextraction, intracoronary metabolic cytoprotectors, etc.). However, additional experience is needed to make definite conclusions.

P3601 | BEDSIDE
Is fibrinolysis still a viable alternative for patients with ST elevation myocardial infarction: results from a mixed-reperfusion model of ST elevation myocardial infarction care

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Purpose: The preferred method of reperfusion for ST elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PCI) when performed in a timely manner. STEMI treatment has been regionalized to improve reperfusion times and in a large geographic region, a mixed-reperfusion model utilizing both PCI and fibrinolysis is necessary. We aimed to evaluate the outcomes of STEMI management in a mixed reperfusion model.
Methods: Retrospective analysis of consecutive patients with a STEMI presenting within a region of both rural and metropolitan hospitals between 03/2007 and 12/2011 was performed. Patients were treated with either PCI or fibrinolysis based on the presenting hospital. The primary outcomes of interest are in-hospital and 1-year mortality. The outcomes were compared for both treatment groups by infarct territory.
Results: By infarct territory, anterior and non-anterior STEMI were well matched for baseline characteristics, anatomy and treatment. Cardiogenic shock on presentation was more prevalent in anterior versus non-anterior STEMI (6.6% versus 3.3%, p=0.007). Median door-to-balloon time was 83 mins (IQR 55-118 mins) and median door-to-needle was 39 mins (IQR 22-65 mins). The table below shows outcomes by infarct territory and initial reperfusion therapy.

	Anterior STEMI (n=548)			Non-Anterior STEMI (n=676)		
	PCI (n=438)	Fibrinolysis (n=110)	p-value	PCI (n=515)	Fibrinolysis (n=161)	p-value
Symptom-to-reperfusion time <3 hours	53%	69.1%	0.009	50.4%	70.2%	<0.001
Intracranial hemorrhage	1.8%	0%	0.368	0.8%	0.6%	1
Bleeding requiring transfusion	8%	7.3%	0.802	2.5%	3.1%	0.779
Cardiogenic shock	14.4%	10%	0.229	8.2%	5%	0.178
Ejection fraction < 30%	13%	7.3%	0.042	1.9%	1.2%	0.201
In-hospital mortality	7.5%	2.7%	0.084	4.7%	1.2%	0.058
1-year mortality	9.8%	3.6%	0.037	7.2%	2.5%	0.036

Conclusions: A significantly higher proportion of patients had reperfusion <3 hours and lower 1-year mortality with no increase in intracranial hemorrhage or bleeding requiring transfusion with fibrinolysis compared to PCI. In situations with a long anticipated PCI-related delay, fibrinolysis is a viable alternative and offers improved outcomes.

P3602 | BEDSIDE
Fluoroscopy assisted scoring of myocardial hypoperfusion (FLASH) as a novel predictor of mortality after primary percutaneous coronary intervention in patients with ST elevation myocardial infarction

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Aim: Reperfusion can be assessed by TIMI flow grade (TFG), corrected TIMI Frame Count (CTFC) and Quantitative Blush Evaluator (QuBE), but all have important drawbacks. A more accurate angiographic assessment could yield better risk stratification in patients with ST elevated myocardial infarction (STEMI). The aim of this study was to investigate whether FLuoroscopy Assisted Scoring of myocardial Hypoperfusion (FLASH) could predict cardiac mortality after primary Percutaneous Coronary Intervention (pPCI) in STEMI patients.
Methods and results: Coronary blood flow (CBF) was measured in 453 STEMI patients treated by pPCI and 38 control patients by multiplying the contrast passage time by the vessel length and cross sectional area obtained by QCA. FLASH was then expressed as a relative difference of CBF in the culprit artery compared to that in the reference artery. FLASH was calculated in 453 STEMI and its relationship with mortality was investigated. Clinical, procedural, angiographic and survival data were collected. Cardiac mortality after 6 months was 5% (20/435). FLASH had a high accuracy of predicting cardiac mortality at 6 months with a significant higher area under the curve (AUC) (AUC: 0.75) as compared with CTFC (AUC: 0.57) and QuBe (AUC: 0.51) (p=0.036 and p=0.002, resp.) but not significantly higher than TFG (p=0.236). However, FLASH-measurement distinguished patients with different risk of cardiac mortality within TFG groups. The optimal cut off value was determined using receiver operating characteristic (-97%) yielding a sensitivity and specificity of respectively 85% and 69%. FLASH was an independent predictor of mortality at 6 months (HR=0.72 per 100-percent increase, p<0.001).
Conclusion: FLASH is a simple, non-invasive method to predict mortality after pPCI in STEMI patients with a higher accuracy compared to presently used angiographic scores. FLASH provides risk stratification and may also be used in clinical trials as a measure of reperfusion success.

P3603 | BEDSIDE
Impact of the mode of arrival at emergency medical service on treatment modalities and the short term outcome in patients with ST elevation myocardial infarction (STEMI)

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Purpose: Emergency Medical Services (EMSs) play a key role in the recognition and treatment of ST-segment elevation myocardial infarction (STEMI). This study evaluates reperfusion treatment and patients' outcomes according to their mode of arrival.
Methods: A total of 1988 STEMI patients that were entered in the Belgian STEMI database between 01/04/2012 and 30/09/2013 were retrospectively analysed and subdivised into two study groups: patients who were admitted by EMS (Group I) versus patients that did not use EMS system (group II). We compared baseline risk profile (expressed as TIMI risk score), reperfusion modalities and in hospital outcome between both study groups.
Results: Among 1988 patients, 68.8% arrived by EMS (Group I) and 31.2% (group II) by their own means. Patients in group I were significantly older (64y vs 61y, p=0,0005), presented more frequently with cardiac arrest, (13.8% vs 4.84%, p=0.0000) and had a higher TIMI risk score (4.3 vs 3.8, p=0.0000). More patients within group I received primary PCI (94.4% vs 90.9%, p=0.002). The time interval between the appearance of symptoms to the time of reperfusion therapy intervals were shorter in group I (257min vs 501 min, p=0,0011) and more patients in group I got primary PCI within 90 minutes (72,2% vs 61,2%, p=0,0000) respectively. 30 days mortality was significantly higher in group I (8.62% vs 2.74%, p=0,000). However, after correction for differences in baseline characteristics, mortality was not significantly different among both study groups
Conclusion: Two thirds of STEMI patients were admitted in hospitals via EMS in Belgium. The use of EMS was associated with shorter ischemic times and a higher use of primary PCI. These data favor the use of EMS as preferred transfer system for patients with chest pain suspect for STEMI.

P3604 | BEDSIDE
Early vessel healing after primary PCI for STEMI relation between incomplete stent apposition and thrombus

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Aim: This study was to confirm the relation between incomplete stent apposition and thrombus at early follow-up as assessed by optical coherence tomography (OCT) in stents implanted during primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).Incomplete stent apposition (ISA) and the absence of strut endothelialization might be linked to stent thrombosis. STEMI might have a higher risk of thrombosis.
Methods: An early OCT evaluation of stents that were deployed in culprit lesions for STEMI was performed at 9- 18days. The primary end-point was the percentage of incomplete stent apposition and that of struts covered with a thrombus. Secondary end-points were the percentage of neointima covered struts.
Results: 20 lesions in 20 patients (4,614 struts) were analyzed. Median follow-

up time was 12 (range 9 to 18) days. The frequency of incomplete stent apposition was 14%. The frequency of stent covered with thrombus was 11%. The percentage of incomplete stent apposition covered with thrombus and that of well apposition covered with thrombus were 73% and 27% (P=0.02).
Conclusions: Stents implanted for STEMI had a high frequency of incompletely apposed struts at early phase using OCT. These struts of incomplete stent apposition were obviously coated a thrombus compared with apposition struts at the early stage.

P3605 | BEDSIDE
Impact of right ventricular involvement on character of transient myocardial ischemia in patients with inferior ST segment elevation myocardial infarction

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Purpose: ECG Holter monitoring makes it possible to quantify not only symptomatic but silent ischemic episodes (IEs) during daily activities. The aim of the study was to evaluate the impact of right ventricular (RV) involvement on frequency of episodes of transient myocardial ischemia as well as on incidence of silent ischemic episodes in acute and late posthospital periods of inferior ST segment elevation myocardial infarction (STEMI).
Methods: The study involved a cohort of 524 consecutive patients (mean age 57 y.o., males 453) with primary acute inferior STEMI with (Group 1; n=210) and without (Group 2; n=314) RV involvement. PCI frequencies and other clinical variables did not differ significantly between groups. All patients underwent double 24-hour ECG Holter monitoring in the pre-discharge day and one year after their discharge to deduct any IE defined as ≥1 mm horizontal or down-sloping ST segment depression lasting at least one minute and separated from other episodes by at least one minute (1x1x1 rule). For both groups we calculated the total daily duration of IEs (TDD), total number of IEs per day/person (TNDP) as well as percentages of silent IE of total ones.
Results: For the pre-discharge day, we observed significantly higher mean of TDD and TNDP of IEs in Group 1 than in Group 2 (866±129 sec. vs. 559±47 sec., $p<0.001$ and 3.4 IEs/person vs. 2.0 IE/person, $p<0.05$ correspondingly). For the same period, cases with silent IEs were about 1.5 times frequent in Group 1 than in Group 2 (61.5% vs. 40.9%, $p<0.001$). One year after the discharge, however, we found no between-group differences of above parameters (369±53 sec. vs. 315±40 sec. for TDD; 1.3 IEs/person vs. 1.2 IEs/person for TNDP; and 37.1% vs. 36.7% for silent IEs, $p>0.05$ for all three cases). We also measured sizes of 1-year changes of above parameters and found that TDD, TNDP and frequencies of silent IEs were decreased in Group 1 in a significantly greater extent than in Group 2 (by 497 sec. vs. by 244 sec., $p<0.05$; by 2.1 IE/person vs. by 0.8 IE/person, $p<0.05$; and by 24.4% vs. by 4.2%, $p<0.001$ correspondingly).
Conclusion: In patients with inferior STEMI, RV involvement is associated with higher TDD and TNDP of transient myocardial IEs including silent once in pre-discharge period yet a greater extent of improvement of the same parameters after 1 year of STEMI.

P3606 | BEDSIDE
Coronary intraplaque hemorrhage is frequently observed in patients with ST elevation myocardial infarction

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Background: Coronary intraplaque hemorrhage (IPH) is associated with lipid-core expansion and plaque inflammation. Therefore, IPH contributes to conversion of stable asymptomatic plaque to an unstable plaque. Plaque rupture and subsequent thrombotic lumen occlusion at the site with previously non-stenotic lesion is associated with ST-elevation myocardial infarction (STEMI).
Methods: In 37 patients who underwent percutaneous coronary intervention (PCI) for STEMI (n=13), non-STEMI (n=9) and stable angina pectoris (SAP, n=15), atherothrombotic debris were collected from culprit plaque using filter-based distal protection guidewire device (Filtrap) during PCI. We immunohistochemically determined CD14 (proinflammatory macrophage marker) and CD163 (Hb scavenger receptor) -positive macrophages (IPH marker) in filtered debris. We also examined the culprit plaque volume and components by ultrasonic tissue characterization using VH-IVUS.
Results: Plaque area were not different among three groups, however, lumen area in STEMI (4.5±1.0mm^2) were larger than those in non-STEMI (3.6±0.4mm^2, P=0.02). Similarly, remodeling index in STEMI (1.15±0.07) were larger than those in non-STEMI (1.05±0.05, $P<0.01$). Necrotic core component of culprit plaque in STEMI (28.9±8.6%) were not different from those in non-STEMI (23.6±7.8%), but were larger than those in SAP (19.7±6.6, P=0.01). Dense calcium component of culprit plaque in non-STEMI (8.8±4.1%) were larger than those in STEMI (4.8±3.1, P=0.04). CD14-positive macrophage counts were higher in STEMI (16.5±9.1%) compared to those in non-STEMI (8.7±7.8%, p=0.04) and SAP (7.7±5.3%, $P<0.01$). CD163-positive macrophage counts were higher in STEMI (29.1±23.2%) compared to those in non-STEMI (10.2±8.5%, p=0.02) and SAP (7.6±11.6%, $P<0.01$).
Conclusions: Large necrotic core is associated with ACS. Large lumen with positively remodeled plaque is associated with STEMI. Plaque with intraplaque hemorrhage and inflammation is associated with STEMI.

P3607 | BEDSIDE
The first ST elevation myocardial infarction in diabetic patients: characteristics, delays and morbi-mortality within an established network for reperfusion therapy

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Purpose: Diabetes mellitus (DM) is a risk factor for higher mortality in acute coronary syndromes. The aim of this study is to evaluate whether, in known diabetic patients with a first ST elevation myocardial infarction (STEMI), there are differences with respect to patients without diabetes in clinical characteristics, in patients or health care systems delays, and in-hospital and 30 days mortality.
Methods: All first STEMI consecutive patients treated in an established STEMI network in the geographical area of Catalonia (7½ million people) were enrolled in 2010-11. Clinical characteristics, time delays, and in-hospital and 30 days mortality were analyzed in two established groups: known diabetic (D) and non–diabetic (ND). Baseline variables were compared between both groups using T-test and Chi-square for continuous and discrete variables respectively. Multivariable predictors of mortality were assessed using logistic regression modelling.
Results: Of 5097 patients with a first STEMI, 970 (19%) were diabetic. D were older (67.3±12 vs 61.2±13.8; $p<0.001$), most frequently women (31.3 vs 20.9%; $p<0.001$), fewer ST elevation in ECG (90.3 vs 92.9%; $p<0.05$) and most left bundle branch block (3.9 vs 2.0%; $p<0.05$). Patient related-delay and health care system delay were statistically larger in D: delay between symptom onset and first medical contact (FMC) (222.1±473 vs 165.2±346 minutes; $p<0.001$), between FMC-diagnosis (21.0±37.6 vs 17.7±35.2 minutes; $p<0.04$) and between symptom onset and reperfusion therapy (377.8±453 vs 319.8±371 minutes; $p<0.001$).There were no differences between D and non D in reperfusion rate but D had worse Killip class (Killip≥II in 21.7 vs 14.4%; $p<0.001$), higher in-hospital (4.4 vs 2.5%; $p<0.01$) and at 30 days mortality (6.2 vs 4.3%). Multivariate analysis identified age and Killip class but not diabetes as predictors of mortality.
Conclusion: In the STEMI setting, diabetes is associated with more delay and higher in-hospital and 30 days mortality. However, diabetes does not improve predictive ability over age and Killip class. There is room for improvement in educational strategies for diabetic patients and for the health care system too.

P3608 | BEDSIDE
Superior safety with similar efficacy of bivalirudin over glycoprotein IIb/IIIa inhibitors in primary percutaneous intervention

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Purpose: Bivalirudin is class I indication for primary Percutaneous Coronary Intervention (PCI). Although the safety is well established, there is inconsistent data in clinical studies about it's efficacy, when compared to heparin with glycoprotein (GP) IIb/IIIa inhibitors. We conducted a meta analysis comparing these two groups in primary PCI.
Methods: Four clinical studies involving 7985 patients were analyzed. The end points analyzed were - Primary Composite Outcome (Composite of Death, Re-infarction or non-CABG related bleeding at 30 days), Non-CABG related major bleeding, 30-day mortality and, Stent thrombosis at 30 days. Heterogeneity of the studies was analyzed by Cochran's Q statistics. The Mantel-Haenszel random effect model was used to calculate combined relative risks for outcomes.
Results: Bivalirudin significantly reduced the rate of primary composite outcome and major bleeding as shown in the table. Compared to heparin with GP IIb/IIIa group, bivalirudin caused significantly higher number of stent thrombosis at 30 days. However, bivalirudin had lesser number of deaths at 30 days, although statistically not significant.

Bivalirudin vs heparin + GP IIb/IIIa

Outcome	Studies	Participants	RR (95% CI)	P-value
Primary composite outcome	4	7985	0.73 (0.64–0.84)	P<0.001
Major bleeding (non-CABG related)	4	7985	0.51 (0.40–0.66)	P<0.00001
Stent thrombosis	4	7769	1.61 (1.11–2.33)	P=0.01
Death	4	7985	0.81 (0.64–1.03)	P=0.09
MACE	2	5538	1.03 (0.83–1.28)	P=0.80

Bivalirudin vs heparin + GP IIb/IIIa in primary percutaneous intervention.

Conclusion: Bivalirudin is safer, and has comparable efficacy compared to heparin with GP IIb/IIIa inhibitors in primary PCI. Caution should be exercised, however, given the significantly increased rate of stent thrombosis. Further randomized clinical trials are needed to this end.

STABLE ANGINA PECTORIS

P3610 | BEDSIDE
Wave intensity analysis to investigate the physiology of exercise induced ischaemia and its alleviation with nitroglycerine

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Purpose: The mechanisms governing exercise-induced angina and its alleviation by the most commonly used anti-anginal drug, nitroglycerine (GTN), are incompletely understood. In this study we measured central and coronary hemodynamics during incremental exercise to gain further understanding.
Methods: 21 Patients (67±6 years) with exertional angina and documented coronary artery disease underwent cardiac catheterisation via radial access and performed incremental exercise using a supine cycle ergometer during the procedure. As patients developed limiting angina or approached maximal effort, sublingual glyceryl trinitrate (GTN) was administered and exercise continued for two minutes at the same workload. Throughout exercise, distal coronary pressure and flow velocity were recorded in the culprit vessel using a dual sensor wire while central aortic pressure was recorded using a second wire.
Results: Patients exercised for a mean of 321±106 seconds to reach limiting symptoms or approaching maximal effort. Compared to rest, this was associated with significant ST-segment depression in the territories subtending the diseased arteries (0.164±0.026mV, P<0.0001 compared to rest) confirming ischaemia. This reduced significantly following GTN administration to 0.119±0.021mV (P=0.0028 compared to peak exercise) despite identical workload. This was accompanied by a 31% reduction in aortic pressure augmentation (P<0.01), and a reduction in tension time index (P<0.01), major determinants of left ventricular afterload. Despite reductions in aortic pressure and afterload, coronary pressure and flow were maintained (P=NS). This was accompanied by a reduction in coronary microvascular resistance (P=0.01) and a significant increase in both the energy of the diastolic microcirculatory backward expansion wave, thereby increasing microcirculatory conductance and relaxation, and the systolic backward compression wave (BCW), related to myocardial contractility (P<0.05).
Conclusions: This exercise protocol provides a new paradigm with which the physiology of ischaemia as well as the performance of novel and established anti-anginals can be studied. In patients with exercise-induced angina, administration of GTN causes harmonious changes in the systemic and coronary circulation that combine to maintain coronary perfusion while simultaneously reducing afterload. The increase in the BCW likely arises from increased myocardial contractility, consistent with observations in animal studies. This is the first time that a coronary derived index has shown potential to measure myocardial contractility.

P3611 | BEDSIDE
Impact of lesion-specific factors on the discrepancy between angiographic and functional assessment in patients with angina pectoris

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Background: Although coronary angiography still plays a pivotal role to evaluate lesion severity, we sometimes mislead lesion severity with only angiographic lesion assessment. Fractional flow reserve (FFR) has been recognized as the gold standard modality to evaluate functional lesion severity. There was not well discussed the association between lesion-specific factors and visual-functional discrepancies. Thus, the aim of this study was to evaluate lesion-specific factors of concordance and discordance pattern between angiographic and functional assessment by FFR.
Methods: A total of 276 consecutive stable angina patients with 385 isolated lesions were confirmed in this study. Lesions were measured FFR with intravenous adenosine triphosphate and assessed by quantitative coronary angiography. According to the results of diameter stenosis (DS) and FFR, the study subjects were classified into 4 groups, and compared with them on the association of various lesion-specific factors.

Comparison with Concordance and Discordance According to DS and FFR

	DS ≥50%			DS<50%		
	FFR >0.80 (Discordance)	FFR ≤0.80 (Concordance)	p value	FFR ≤0.80 (Discordance)	FFR >0.80 (Concordance)	p value
Number of lesions	92	134		68	99	
LAD location (%)	30	59	<0.01	88	34	<0.01
Proximal/middle/distal location (%)	22/ 68/ 15	45/ 41/ 14	0.02	35/ 55/ 10	24/ 53/ 23	0.07
Type B2/C (%)	41	63	<0.01	65	34	<0.01
Eccentric (%)	45	54	0.18	43	31	0.13
Calcification (%)	9	11	0.5	13	4	0.09
Bifurcation (%)	29	46	0.01	43	17	<0.01
Diffuse (%)	15	23	0.14	25	7	<0.01
Minimum lumen diameter (mm)	1.2±0.6	1.8±0.3	<0.01	1.5±0.3	1.8±0.5	<0.01
Lesion length (mm)	13.6±6.1	15.9±7.7	0.02	14.3±6.9	11.7±6.9	0.02

Results: In all lesions, reference diameter was 2.8±0.6 mm, DS was 52±13%, lesion length was 14.0±7.2 mm, and FFR was 0.80±0.12. There showed significant correlation with DS, lesion length and FFR (r = -0.354, p<0.001 and r = -0.220, p<0.001, respectively). In this subject, visual-functional discordance was observed in 152 (40%) lesions. The comparative data on lesion-specific factors were shown in the table.
Conclusion: The difference of lesion-specific factors related to discrepancy between angiographic and functional assessment. These results may help us to decision making of therapeutic strategy.

P3612 | BEDSIDE
Noninvasive fractional flow reserve derived from quantitative perfusion positron emission tomography

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Background: Quantitative myocardial perfusion imaging with positron emission tomography (PET) is increasingly utilized for the diagnosis of coronary artery disease (CAD). Recently, thresholds for hyperemic myocardial blood flow (MBF) and flow reserve were established, taking fractional flow reserve (FFR) as a reference standard. In contrast to FFR, perfusion PET is not lesion specific but a composite measurement of the entire coronary tree yielding potential physiological disconcordancy. Quantitative perfusion imaging additionally allows to noninvasively calculate FFR. This so called relative flow reserve (RFR) is defined as the ratio of hyperemic MBF in the stenotic area to hyperemic MBF in a contralateral normal perfused area. The aim of the present study was to validate RFR against FFR and to compare its diagnostic accuracy with hyperemic MBF.
Methods and results: From a cohort of 319 patients without previously documented CAD who underwent H215O cardiac PET and invasive coronary angiography, 92 patients with single (n=64) or two vessel (n=28) disease were included (n=120 arteries). Intermediate lesions (diameter stenosis 30 - 90%, n=98) were interrogated by FFR. Fifty-one (43%) vessels were deemed hemodynamically significant (>90% stenosis or FFR ≤0.80). Hyperemic MBF and RFR were lower for vessels with a hemodynamically significant lesion (1.99±0.81 vs. 2.88±1.22 mL·min-1·g-1, p<0.001, and 0.68±0.23 vs. 0.94±0.15, p<0.001, respectively). The correlation between RFR and FFR was moderate (r=0.54, p<0.01). ROC curve analysis showed a comparable area under the curve for hyperemic MBF and RFR (0.76 vs. 0.82, p=0.33) to diagnose CAD. The optimal cutoff value for RFR was 0.78 with a diagnostic accuracy of 79%, whereas hyperemic MBF showed a diagnostic accuracy of 74% (optimal cutoff value of 2.35 mL·min-1·g-1).
Conclusions: Noninvasive estimation of FFR with quantitative perfusion PET by calculating RFR is feasible, yet diagnostic accuracy is comparable to hyperemic MBF assessment alone.

P3613 | BEDSIDE
Assessing risk in stable coronary disease patients: when should we intensify cares and follow-up? Results from a meta-analysis of observational studies

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Purpose: Among the large numbers of clinical and laboratory markers predictors of adverse events for patients with stable angina, no data have been reported to appraise those more related to prognosis, to allow physicians a tailored follow up and management. We searched published literature to extract more powerful predictors of prgnosis in stable coronary disease patients.
Methods: Medline and PubMed were systematically searched for eligible studies published up to 2013, reporting multivariate predictors of cardiovascular events (death, acute myocardial infarction, stroke and need for revascularization) in patients with stable angina. Study features, patient characteristics, and prevalence and predictors of such events were abstracted and pooled with random-effect methods (95% CIs).
Results: 39 studies (101551 patients) were included. After a median follow-up of 57 months, cardiovascular events occurred in in 7.8% (95% CI 6.0% to 9.6%). Age, male sex (OR 1,28 95% CI 1,13 - 3,4), low EF (OR 8,53 95% CI 1,9 - 16,84), diabetes (OR 1,93 95% CI 1,1 - 11,2), prior myocardial infarction (OR 2,06 95% CI 1,4 - 5,64) and C-reactive protein (OR 1,67 95% CI 1,21 - 6,41) were the most powerful predictors of cardiovascular events.
Conclusions: This meta-analysis demonstrated that simple and low-cost clinical features may help clinicians in identifying the most appropriate diagnostic and therapeutic approaches within the broad range of outpatients presenting with stable coronary artery disease.

P3614 | BEDSIDE
Impaired cortical pain processing in patients with silent myocardial ischemia

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Purpose: In the present study, we investigated whether the function of brain areas specifically devoted to nociception presents any abnormalities in patients with silent myocardial ischemia (MI), as compared to those with symptomatic MI.
Methods: We studied 3 groups of individuals: 1) 11 asymptomatic, non-diabetic patients with documented obstructive coronary artery disease (CAD) (67±10 years, 6 men; group 1); 2) 10 patients with obstructive CAD and a clinical pattern of chronic stable angina (66.5±10 years, 6 men; group 2); 3) 14 apparently healthy subjects matched for age and gender to patients (63.2±9 years, 8 men; group 3). Patients with any chronic pain syndrome other than anginal chest pain were excluded. Cortical nociception function was assessed by cortical laser evoked potentials (LEPs) recording in response to chest skin stimulation by cutaneous CO2 laser pulses. Specifically, the N2/P2 wave of LEPs, which reflects cortical pain processing, was measured. Three sequences of painful stimuli (at the intensity of 2.5 times the individual sensory threshold) were applied, separated by 5-minute intervals.
Results: N2/P2 amplitude during the first sequence of chest skin stimuli was 9.3±4.0, 14.0±7.3 and 15.5±6.4 μV in group 1, group 2 and group 3, respectively (p=0.03). N2/P2 amplitude decreased across the three sequences of pain stimuli in group 2 (-37.5±14%) and group 3 (-23.0±15%), but not in group 1 (-0.14±37%) (comparison among groups, p=0.015).
Conclusion: CAD patients with silent MI show a reduced amplitude of N2/P2 LEP component and inadequate habituation to painful stimuli, compared to symptomatic angina CAD patients and healthy controls. This pattern is likely due to thalamic gate modulation of pain signals and can contribute to the lack of pain perception during MI in these patients.

P3615 | BEDSIDE
Impact of renal insufficiency on left main coronary artery disease and cardiovascular events in patients with stable angina pectoris

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Purpose: Left main coronary artery disease (LMCAD) has previously been shown to lead to the fatal prognosis in patients with coronary artery disease (CAD), however the risk factors associated with LMCAD remain unclear. Recently cardio-renal interaction has been shown to play a critical role in pathogenesis of CAD. We investigated an impact of renal dysfunction on LMCAD in patients with stable angina pectoris (SAP).
Methods: We performed coronary angiogram to 1601 consecutive patients between 2006 and 2009. A total of 626 consecutive SAP patients with significant stenosis and 20 subjects with absolutely normal angiogram as the control group were enrolled. Patients with SAP were divided into two groups; LMCAD (n=95) and non-LMCAD (n=531). Singnificant stenosis was defined as percent luminal reduction >50% in left main trunk and >75% in the other parts. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR)<60 ml/min/1.73 m^2 and/or proteinuria, based on the creatinine obtained prior to angiography. Patients were followed after optimal therapy including coronary revascularization and medication.
Results: LMCAD patients had significantly lower eGFR among three groups (p<0.001). However there were no significant differences in age, sex, prevalence of diabetes and hypertension, smoking, polyunsaturated free fatty acid, malondialdehyde modified low density lipoprotein and brain natriuretic peptide. In SAP patients, the presence of LMCAD in patients with CKD was significantly higher than that in patients without CKD (18.5% vs 12.2%, p=0.03). Multiple logistic regression analysis revealed that eGFR was independently associated with LMCAD (p<0.001), and the odds ratio of LMCAD for CKD was 1.733 (95% confidence interval [CI]; 1.055 to 2.849, p=0.03) even after adjustment of conventional risk factors. In patients with LMCAD, major adverse cardiovascular events (MACE) in subjects with CKD was higher than that in subjects without CKD (eGFR≥60) at two year (p<0.02 by Kaplan-Meier analysis). MACE was defined revascularization, admission due to heart failure, cardiogenic death and cerebrovascular event. The LMCAD patients with CKD had more events compared to the non-LMCAD patients without CKD (hazard ratio, 9.41; 95% CI, 2.15 to 41.1). The risk of MACE in patients with CKD was similarly high in spite of the presence of LMCAD, even after optimal therapy for SAP.
Conclusion: CKD was independently associated with the presence of LMCAD and clinical outcome with LMCAD in SAP patients. Renal insufficiency is a residual risk and prognostic factor in LMCAD patients.

P3616 | BENCH
Echo-guided extracorporeal shock wave therapy for refractory angina improves regional left ventricular function along with myocardial blood flow

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Purpose: Low-intensity shock wave (SW) therapy (SWT) has been shown to improve symptoms and exercise tolerance in patients (pts.) with coronary artery disease (CAD). Induction of neovascularization and improvement of myocardial perfusion are mechanisms hypothetized to be involved.
Methods: 47 pts. with advanced diffuse CAD (mean age 67±10 years) not suitable for catheter-based or surgical revascularization, suffering from severe stable angina pectoris (CCS class III or IV), underwent a series of 9 echocardiography-targeted SW applications (3 applications/week in week 1, 5, and 9). The anteroseptal wall (LAD territory) was targeted in 20, the lateral wall (RCX territory) in 20, and the inferior wall (RCA territory) in 7 pts. A series of 300-500 shocks was applied per session. Anti-anginal drugs therapy was kept unchanged. Regional myocardial blood flow (MBF) to the targeted region was measured by NH3-PET, and longitudinal regional strain was assessed by speckle tracking echocardiography at baseline and 4-6 weeks after completion of SWT.
Results: Complications of SWT were not observed. At follow-up, 34 pts. (72%) reported improvement of angina to a tolerable level. CCS angina class decreased from 3.1±0.6 to 2.5±0.6 (p<0.001). MBF in the LV region targeted by SWT improved from 117±41 mL/min/100g at baseline to 128±46 mL/min/100g at follow up (p=0.037), while there was no change in the opposite wall segment (135±51 vs. 136±51 ml/min/100g; p=0.9). The midventricular segment of the targeted region improved from -14±5 to -17±6%; p=0.04.
Conclusions: SWT improved symptoms in a sizeable number of pts. with chronic refractory angina. Regional improvement of MBF in the region targeted by SWT was documented by PET imaging, and functional improvement by speckle tracking echocardiography. Additional studies are warranted to clarify the role of SWT in the armamentarium for this challenging patient group.

P3617 | BENCH
One of six patients with non-ischemic heart diaease had provoked coronary spasm: non-ischemic heart disease had no ischemia?

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Background: The majority of cardiologists do not perform spasm provocation tests in patients with non-ischemic heart disease (non-IHD) and non-obstructive coronary artery disease (non-ob-CAD). We examined the frequency of provoked spasm in non-IHD and non-ob-CAD patients such as atypical chest pain (Aty), valvular heart disease (Val), hypertrophic cardiomyopathy (HCM), congestive heart failure (CHF), and others (Oth).
Methods: We performed acetylcholine (ACh) spasm provocation tests during 22 years (1991-2012) in 1440 patients consisting of 981 IHD and 459 non-IHDs. We excluded 43 patients with significant organic stenosis and the remaining 416 patients were non-IHD and non-ob-CAD. ACh was injected incremental doses of 20/50/80 mg into the RCA and 20/50/100/(200) mg into the LCA. Positive coronary spasm was defined as transient >99% luminal narrowing.
Results: Positive coronary spasm was obtained in 17.3% non-IHDs (72/416). Positive spasm was 11.4% (15/132), 19% (8/42), 16.7% (5/30), 23.9% (16/67), 19.3% (28/145), and in patients with Aty, Val, HCM, CHF, Oth, respectively. Positive provoked spasm was higher in men than women but not significant (20.6% (46/223) vs. 13.4% (26/193), ns), while positive spasm frequency in late period (2001-2012) was significantly higher than that in early period (1991-2000) (36.8% vs. 7.0%, p<0.001).
Conclusions: We should perform spasm provocation tests in patients with not only IHD but also non-IHD with non-ob-CAD, because one of six non-IHD patients had provoked coronary spasm.

P3618 | BEDSIDE
Cystatin C- versus creatinine- based definition of renal function for evaluating coronary collateralization in patients with stable angina and chronic total occlusion

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Purpose: Renal impairment with decreased estimated glomerular filtration rate (eGFR) represents an independent risk factor for poor coronary collateral development. We investigated whether eGFR determined with cystatin C-based equation (eGFRcys) is superior to that with creatinine-based formula (eGFRcr) for evaluating coronary collateralization in patients with stable angina and chronic total occlusion.
Methods: We determined eGFRs with cystatin C- and creatinine-based equations in 427 patients with stable angina and angiographic total occlusion of at least

one major coronary artery. The degree of collaterals supplying the distal aspect of a total occlusion from the contra-lateral vessel was graded as poor (Rentrop score of 0 or 1) or good collateralization (Rentrop score of 2 or 3).
Results: Both eGFRcr and eGFRcys were lower in patients with poor (n=157) than in those with good collateralization (n=270). However, eGFRcys correlated more closely with Rentrop score than eGFRcr (Spearmen's r=0.39 vs. Spearmen's r=0.28, P=0.048). The area under the curve of eGFRcys was larger compared with that of eGFRcr (0.75 vs. 0.67, P=0.001) for detecting poor collateralization (72.2% vs. 66.7%), along with a net reclassification improvement of 11.8% (P=0.044) and an integrated discrimination improvement of 8.8% (P<0.001). The result patterns did not change when subgroups were stratified by presence or absence of diabetes, hypertension, and dyslipidemia.
Conclusions: Cystatin C-based definition of renal dysfunction indicates a potential better clinical utility than creatinine-based equation for detecting poor coronary collaterals in patients with stable angina and chronic total occlusion.

P3619 | BEDSIDE
The effects of age on circulating vascular markers and cardiac prognostic markers, before and after 2 months home-based high-frequency exercise training in patients with stable coronary artery disease

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Purpose: Vascular endothelial growth factor (VEGF) and stromal derived factor (SDF-1) play an important role in angiogenesis. Relaxin-2 (Rlx-2) has both angiogenic and vasodilatory properties, while endothelin-1 (ET-1) is a potent vasocontrictor.VEGF, SDF-1 and Rlx-2-levels have shown to be positively modulated by exercise training, while the effect of exercise on (Rlx-2) is not known. Age is a known risk factor for morbidity and mortality in coronary artery disease (CAD). We wanted to investigate how age affects levels of these vascular factors and known prognostic cardiac markers before and after high frequency exercise training (HFE), in patients with CAD.
Methods: Patients with stable CAD (age 48-80 years) were randomized to HFE (aerobic exercise 70% of max, 30 minutes, 5 times/week and resistance exercise 3 times/week), performed at home for 8 weeks, or usual lifestyle (ctrl). Serum and plasma was collected from 21 controls and 24 HFE-patients and analyzed at baseline and after 8 weeks. VEGF, SDF-1, Rlx-2 and ET-1were analyzed with enzymelinked immunoadsorbent assay (ELISA). TnT and NT-pro-BNP were analyzed on Cobas e602 (Roche). Correlation was calculated using the statistical software Graph Pad Prism 6. Pearson's r was calculated to determine correlation between the factors prior to exercise, while Spearman's r was used for the analysis on the exercise induced effects of the HFE-group. The exercise-induced effect on cardiac biomarkers was determined by comparing % change (from baseline to 8 weeks) between HFE and Ctrl using Mann-Whitney U-test.
Results: At baseline, there was a significant positive correlation between age and TnT (r=0.38, p<0.05) and a non-significant positive correlation between age and NT-proBNP (r=0.36, p=0.06), while no correlation was found between age and levels of vascular markers (VEGF r=-0,14, SDF-1 r=-0,13, ET-1 r=0,08, Rlx-2 r=0,06, p=ns for all). As we have previously shown, home-based HFE decreased VEGF (2,6+29% (ctrl) and -3,9 +13% (HFE), p<0,05), but the other studied factors were not significantly affected. We found no correlation between age and changes in cardiac markers after exercise.
Conclusions: Elderly patients with stable CAD have higher levels of TnT and NT-proBNP, indicating a higher degree of underlying CAD. This may also reflect their higher mortality in CAD. HFE-training may lower VEGF in patients with stable CAD. Interestingly, there seems to be no difference in the response to exercise in cardiac biomarkers, between younger and older CAD patients.

CORONARY ARTERY DISEASE AND COMORBIDITIES

P3621 | BEDSIDE
Change of cardiovascular and respiratory parameters before and after ischemic preconditioning and imitation of preconditioning in COPD patients

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Ischemic preconditioning (IP) seems to be universal protective method for patients with cardiovascular diseases: in coronary angiography, acute coronary syndrome and myocardial infarction. We proposed that IP could have some effects in patients with chronic obstructive respiratory disease (COPD). Aim. To study IP effects on respiratory function test (RFT), arterial stiffness (AS), pulsoxymetry, pulse wave velocity (PWV) and heart rate variability (HRV) in COPD patients.
Methods: The randomized controlled crossover design study with active control in 26 patients with COPD (forced expiratory volume, FEV1 40-70%) was performed. The RFT, AS, PWV and HRV were estimated before and after IP (blood pressure +50 mm Hg, ΔIP+10) or IP imitation (+10 mm Hg, ΔIP+10) according to randomization. The next day the same patients were investigated before and after on the contrary from the from former test IP imitation/IP.
Results: IP did not change heart rate in both groups (table 1); did not change systolic and diastolic blood pressure (p>0,05); in IP+50 group was the tendency to increase FEV1, SpO2 and to decrease PWV (p>0,05). IP+50 in compare to IP+10 significally increased some HRV parameters (Triangular Index, SDANN, SDNN Index) and had the same tendency in the rest of them.

Change of cardiovascular and respiratory

Parameter	Δ (IP = +10 mm Hg) between tests	Δ (IP = +50 mm Hg) between tests
HR, beat/min	4.4	5
SpO_2 , %	0.96	–0.88
FEV_1 , %	2.56	–2.82
PWV, m/sec	0.41	0.52
RMSSD	6.75	–10.6
Triangular Index	0.75*	–2.08
SDNN Index	3.04*	–10.51
SDANN	2.61**	–7.96

P.s.: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV, forced expiratory volume; AP, aortic pressure; PWV, pulse wave velocity. *p<0,05; **p<0.01 between groups.

Conclusions: Thus IP showed positive effects on autonomic heart rate regulation and some cardiovascular and respiratory parameters that raises the question of its use in patients with COPD. The study was supported with President Foundation MD-2459.2014.7 grant.

P3622 | BEDSIDE
Impact of circulating cathepsin K on the coronary calcification and the clinical outcome in chronic kidney disease patients

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Purpose: Chronic kidney disease (CKD) is a cause of coronary artery calcification (CAC) and an independent predictor of major adverse cardiac and cerebrovascular events (MACCE). Cathepsin K (CatK) is a lysosomal cysteine protease which affects vascular calcification and glucose metabolism. We investigated the relationships among the CatK level, CAC, diabetes mellitus and MACCE.
Methods: Total of 113 consecutive CKD patients were enrolled in the study. Their CAC was evaluated by computed tomography. The patients were divided into two groups based on the CatK levels, and were followed-up for up to three years. A subanalysis was conducted to elucidate the impact of the impaired glucose tolerance.
Results: A Kaplan-Meier analysis demonstrated a significantly higher incidence of MACCE in the high CatK group (P=0.028). Cox's model revealed that a higher plasma CatK level and a higher BNP level were independent predictors of MACCE (P=0.043 and P<0.01, respectively). The subanalysis showed a significant correlation between the CatK level and the CAC score only in patients without DM. In non-diabetic CKD patients, the high CatK group had a significantly higher level of LDL-C and a higher LDL-C/HDL-C ratio (P<0.05 and P<0.001, respectively) than did the low CatK group. These lipid disorders were independent predictors of CatK elevation.

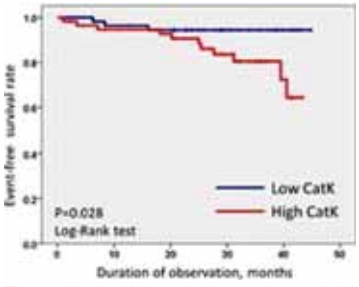

Figure 1. Kaplan-Meier analysis event-free survival from MACCE based on the CatK level.

Conclusions: Our results indicated that higher CatK level had an impact on the CAC and MACCE in CKD patients. CatK may participate in lipid metabolism and contribute to CAC, leading to a poorer prognosis in non-diabetic CKD patients.

P3623 | BEDSIDE
Prognostic implication of obstructive sleep apnea diagnosed by post-discharge sleep study in patients presenting with acute coronary syndrome

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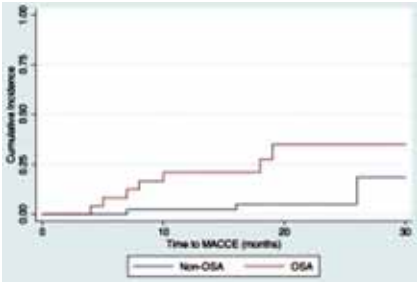
Purpose: Obstructive sleep apnea (OSA) diagnosed during the in-hospital phase of acute coronary syndrome (ACS) may be a false-positive finding. We sought to determine the prevalence and cardiovascular consequences of OSA diagnosed after hospital discharge in patients presenting with ACS.
Methods: Patients presenting with ACS and treated with percutaneous coronary intervention (PCI) were recruited prospectively for a home-based portable sleep study within 30 days after hospital discharge. Major adverse cardiac and cerebrovascular events (MACCEs; cardiac death, myocardial infarction, stroke, unplanned revascularization and hospitalization for heart failure) were compared between OSA and non-OSA groups.
Results: Of the 85 patients recruited, 68 successfully completed the study. OSA (Apnea-Hypopnea Index $\geq$15) was diagnosed in 24 patients (35.3%) and a drug-eluting stent was implanted into the target lesion in 45 patients (66.2%). The median follow-up duration was 20 months (range: 4-30), and it was similar in both OSA and non-OSA groups (17.5 months vs. 21 months). At 24-month follow-up, the MACCE incidence was 34.9% in the OSA group and 5.1% in the non-OSA group (p=0.008, log-rank test). After adjusting for age, gender, coronary intervention indications, hypertension, smoking and body mass index, OSA remained an independent predictor of MACCEs (adjusted hazard ratio: 6.95, 95% confidence interval: 1.17-41.4, p=0.033).



Kaplan Meier MACCE cumulative incidence.

Conclusions: Based on post-discharge home sleep studies, a high prevalence of OSA was present in patients presenting with ACS and OSA was independently associated with MACCEs at 24-month follow-up.

P3624 | BEDSIDE
Vitamin D metabolism and acute coronary syndromes

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Introduction: Vitamin D (vD) deficiency affects almost 50% of the population worldwide, constituting an independent risk factor for total mortality. Together with parathyroid hormone (PTH), this vitamin plays an important role in phospho-calcium metabolism. The main circulating metabolite, 25-hydroxy vitamin D (25[OH]D) is used to classify vD status: sufficient ($\geq$30 ng/mL), insufficient (20–30 ng/mL) and deficient ($<$20 ng/mL). Recently, hypovitaminosis D has been associated with several cardiovascular risk factors and to an adverse prognosis in ischemic cardiomyopathy.
Objective: To assess the prevalence of hypovitaminosis D and the influence of the factors involved in its metabolism during acute coronary syndromes (ACS).
Methods and results: We performed a prospective study including 152 consecutive patients (P; mean age 62 years, 82.2% male) admitted in a Coronary Unit for the period of 6 months, with a 6 month follow-up, from whom 25[OH]D was collected during the first 24 hours after admission. All patients included in this study presented vD deficiency (mean value of 7.52$\pm$3.04 ng/mL, with a maximum of 17.39 ng/mL). To facilitate analysis, we decided to subdivide P into two groups: mild ($>$10 ng/mL, 18.4%) and severe ($<$10ng/mL, 81.6%) vD deficiency. There were no statistically significant differences between the two groups in respect to demographics, risk factors and cardiovascular history. During hospitalization, P with severe hypovitaminosis D had lower creatinine clearance (85.5 vs. 101.6 mL/min/m^2, p=0.022). No other differences were found between the two groups. Considering prognosis, a trend towards higher overall mortality (in-hospital plus follow-up mortality) was seen in P with severe vD deficiency (9.6 vs. 0%), although without statistical significance. Regarding PTH, there was an association between high levels of this hormone ($>$72 pg/mL) and markers of severity, such as heart failure (p=0.001), renal failure (p$<$0.001), left ventricular dysfunction (p=0.002) and GRACE score (p$<$0.001). With respect to overall mortality, there was a trend towards higher mortality (11.5 vs. 5.6%) in these P, although without statistical significance.
Conclusion: Hypovitaminosis D was present in all patients hospitalized with ACS. Changes in the metabolism of this vitamin, including severe vD deficiency and PTH elevation, were associated with adverse events during hospital stay and a trend towards higher mortality, relation that did not reach statistical significance possibly due to the small sample size. In the future, the correction of vD deficit in these P might be a potential therapeutic target.

P3625 | BENCH
Activated prothrombin complex concentrate reverses dabigatran-induced bleeding in a lethal porcine polytrauma model

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Introduction: Dabigatran is a direct thrombin inhibitor that has shown efficacy and safety as compared to warfarin in patients with atrial fibrillation. A specific reversal agent in situations of life-threatening bleeding is currently not available and clinically used methods to reverse its effects have demonstrated conflicting results. This study assessed the ability of an activated prothrombin complex concentrate (aPCC) to reverse dabigatran anticoagulation and bleeding effects after polytrauma injuries.
Methods: The study was performed in 15 anesthetised male pigs after ethical approval. Dabigatran etexilate was given orally for 3 days (30 mg/kg bid) and then the active form was infused prior to injury on day 4. Trauma was induced by a blunt liver injury and bilateral femur fractures. Following hemorrhagic shock, blood loss (BL) was recorded 10 min post-trauma and animals were randomized (n=6/group) to a single injection of aPCC (25 or 50 IU/kg) or vehicle (control). BL and hemodynamic variables were monitored over 300 min or until time of death. Coagulation was assessed by thromboelastometry (TEM), coagulation parameters (ACT, PT, aPTT) and diluted thrombin time (dTT) for dabigatran plasma levels. Data were analysed by ANOVA ($\pm$ SD).
Results: Preliminary data show dabigatran plasma levels were between 438 (min) and 566 (max) ng/mL just prior to injury and remained elevated in all groups for the duration of the experiment. The degree of injury was similar among groups, BL at 10 min was 790$\pm$55 mL. In the group receiving dabigatran without aPCC BL was 3462$\pm$440 mL and mean survival time 135 min with 100% mortality (p$<$0.05 vs 50 IU/kg aPCC animals). Treatment with 25 IU/kg aPCC did not significantly reduce BL (3699$\pm$648 mL) or mean survival time (150 min, 100% mortality). Due to ongoing blood loss, coagulopathy in control and aPCC 25 IU/kg animals increased over time following trauma. In contrast, 50 IU/kg aPCC significantly reduced BL 1565$\pm$351 mL with 100% survival. Consistent with this, coagulation parameters improved substantially in aPCC 50 IU/kg treated animals. Anticoagulation as measured by the dTT and ACT were not affected by aPCC.
Conclusion: This lethal polytrauma model in pigs demonstrates that therapy with 50 IU/kg aPCC was effective and safe to reverse dabigatran anticoagulation under conditions of life-threatening bleeding resulting from severe trauma. The response of aPCC treatment on dabigatran-prolonged anticoagulation assays was inconsistent, assay dependent and was not predictive of cessation of bleeding.

P3626 | BEDSIDE
Cardiovascular mortality and risk assessement strategy in liver transplantation candidates

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Data regarding cardiovascular mortality (CVM) among patients undergoing liver transplantation (LT) is limited. The AIMS of this study were to assess 1) incidence of CVM, 2) its place among all causes of mortality (ACM) and 3) to identify potential predictive factors.

Patients characteristics

	Total LT patients (n=203)	Patients without cardiovascular mortality (n=198)	Patients with cardiovascular mortality at 30d (n=2)	Patients with cardiovascular mortality at 1y (n=5)
Age (years)	53	52	59.5	57.8
Hypertension	36%	36%	0%	40%
Dyslipidemia	26%	25.5%	50%	60%
Non-alcoholic steatohepatitis	16.5%	15.5%	50%	20%
Smokers	20%	19.5%	50%	40%
Diabetes mellitus	29%	29%	50%	40%
Known coronary artery disease	6.9%	6.5%	0%	20%
Pre-OLT arrhythmia	8.9%	7.5%	100%*	40%
Known cardiac disease (pre-op arrhythmia, CAD, QTc anomaly, structural anomaly)	16%	15%	100%*	60%*
Mean EF (%)	64	64	61	61
Mean QTc (ms)	446	446	469	448
Mean Creatinine (mmol/l)	98	97	102	101
Mean Platelet count (10^3mm^3	101	101	50	87
RIN	2.0	2.0	2.85	2.24

*p$<$0.05 compared with patients without CV mortality.

Methods: Baseline characteristics and data on pre-LT CV risk assessment from patients who underwent LT were collected. ACM and CVM (defined as death by either acute coronary syndrome (ACS), arrhythmia (AR) or heart failure (HF)) were assessed at 30d and 1y.
Results: All the patients (n=203) had an ECG and echocardiogram. 31% underwent a non-invasive test for ischemic disease (ordered because of a higher pre-test probability). ACM and CVM post LT were 5% (n=10) and 1% (n=2) at 30d and 12.3% (n=25) and 2.5% (n=5) at 1y respectively. CVM was the second cause of death after sepsis. No fatal ACS was observed. 2 patients died during LT from AR (1 asystole and 1 ventricular tachycardia) and both of them had a history of pre-LT arrhythmia. The 3 other patients died from HF and 2 of them had a preserved EF before LT.
Conclusions: Although a CV event is the second cause of mortality in patients undergoing LT, the CVM rate is low. Fatal ischemic events seem prevented by a non-invasive pre-LT cardiac risk assessment strategy.

P3627 | BEDSIDE
Prevalence of coronary artery disease evaluated by direct coronary angiography in liver transplantation candidates

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Purpose: Orthotopic liver transplantation (OLT) is the only effective treatment in patients with end-stage liver disease (ESLD). Evidences suggest that the prevalence of asymptomatic coronary artery disease (CAD) is significant in OLT candidates and is associated with an increased peri-operative 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. Moreover, predictive value of non invasive stress testing such as dobutamine stress ecocardiography in ESLD patients is still unclear. Aims of the present study were: a) to assess CAD prevalence in patients selected for OLT and b) to record cardiac events in 3 years follow-up after OLT.
Methods: From 2007 to 2013 all OLT candidates have been evaluated by physical examination, electrocardiography and ecocardiography. Coronary angiography (CGF) was directly performed a) in patients with CAD history and/or typical symptoms and b) in asymptomatic patients aged >50 years with two or more of the following risk factors: diabetes, active smoking, family history of CAD, peripheral vascular disease. A 3 years follow-up (1 visit/year) was scheduled only for post-OLT patients.
Results: 325 patients were considered for OLT (14 of them were excluded for pre-existent severe cardiac comorbidity), 262 (80.6%) underwent OLT. CGF was performed in 71 patients (21.8%, age 57±5.7 years, males n=64) according to the following indications: known CAD n=10 (3.1%); typical symptoms n=28 (11.6%); no symptoms and age >50 years with 2 or more risk factors n=51 (15.7%). In CGF group we found no coronary lesions in 66% (OLT vs no-OLT, p= ns), not significant coronary lesions in 25% (OLT vs no-OLT, p=ns). PTCA and coronary by-pass graft were performed, respectively, in 5% and 2% of patients: all of them underwent OLT. Fourteen patients (20%) referred to CGF were subsequently removed from liver transplant list for causes unrelated to coronary lesions. During the follow-up period (35±20 months) 13 patients died (18.3%). Only one patient died for congestive heart failure. No ischemic cardiac event was observed.
Conclusions: CAD detection remains a clinical challenge in ESLD patients candidates to OLT, but its prevalence does not seem higher than in general population. The evidence of a large number of normal coronary trees, even in presence of cardiovascular risk factors, demonstrates that direct angiographic approach in pre-OLT is not appropriate. The recommended method to detect CAD in asymptomatic ESLD patients is still debatable.

P3628 | BEDSIDE
Pulse wave velocity (PWV), augmentation index (AIx) or beta index as the surrogate marker for coronary disease or arterial ageing only?

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Arterial stiffness increases with ageing and with atherosclerotic process that involves coronary arteries too. Aortic stiffness affects the coronary blood flow.
PWV and AIx integrate the lasting influence of various cardiovascular risk factors on arterial wall that accelerate atherosclerotic processes and are considered as surrogate markers in coronary risk assessment.
β index is derived from a logarithmic transformation of the curvilinear relationship between pressure and diameter measured with ultrasonic probe over the common carotid artery and oscillometric arm cuff for arterial blood pressure and was evaluated as a marker for CAD severity in our study.
Observational study of 191 individuals was completed in 121 subjects, submitted to arterial stiffness investigation (PWV, AIx and β index) and coronary angiography (87 patients), because of angina (54 had coronary disease and 33 with no CAD on angiography) and 34 asymptomatic healthy volunteers. Patients without CAD on coronary angiography and healthy volunteers created the control group. Arterial stiffness parameters were determined by e-tracking method using ALOKA α 100 ultrasound, linear probe (10-12MHz).

Stiffness param.according to age and CAD

	β index mean±SD	PWV mean±SD	Aix mean±SD
Group A (age 15–30 y.)			
Controls, N=34	4.2853±1.23733	4.7265±0.90531	–3.667±5.313
Group B (age 31–59 y.)			
Control, N-13	4.9462±0.8282	5.1154±0.99737	19.22±7.07
Patients, N=24	9.5625±3.12171	7.1750±1.18917	21.39±13.53
p-value	0.001	0.682	0.434
Group C (age ≥ 60 y.)			
Control, N=20	6.1650±1.60239	5.6100±0.95084	23.83±10.556
Patients, N=30	9.9800±4.9174	6.9733±1.55717	24.31±12.42
p-value	0.003	0.022	0.399

Conclusions: Arterial stiffness measured as PWV, AIx and β-index was significantly higher in coronary patients compared to the control group as it could be expected; controls were significantly younger than patient group.
Control group subjects with risk factors for CAD had higher values of β index and PWV, but at significant levels only for β index (p=0.037 vs. p=0.418).
β-index values significantly better discriminate the patient coronary status in the same age cohort, compared to PWV. AIx values changes with ageing, but did not discriminate coronary from healthy in the same age group.
The presence of risk factors in healthy individuals does not significantly affect PWV values. β-index value in group without CAD was significantly high if risk factors were present compared to those with no risk. It might nested its potential as novel marker in coronary, atherosclerotic cardiovascular risk assessments.

P3629 | BEDSIDE
Serum levels of sRAGE in diabetic and non-diabetic patients admitted with acute myocardial infarction

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Purpose: Advanced Glycation Endproducts (AGEs) are emerging inflammatory biomarkers accused of mediating the atherosclerotic process, while serum receptor of AGE (sRAGE) may have protective functions. This study aimed at assessment of plasma levels of sRAGE in patients with acute myocardial infarction (MI), diabetic and non-diabetic, and its correlation with severity of coronary artery disease (CAD).
Methods: We have enrolled 112 consecutive patients presented with acute MI. Patients were categorized to either diabetic or non-diabetic and they had undergone: clinical evaluation, laboratory evaluation, sRAGE measurement, coronary angiography and assessment of coronary artery disease by Gensini score.
Results: We have evaluated 112 patients: 69 (61.6%) non-diabetic (mean age 59.9 years, 45 (65.2%) males, 41 (59.4%) smokers, 41 (59.4%) hypertension, 10 (14.5%) have Killip class more than 2, 26 (37.7%) with acute STEMI, mean sRAGE 769 pg/ml, and mean Gensini score 12.9). Diabetic patients were 43 (38.4%) (mean age 60.6 years 27 (62.8%) males, 24 (55.8%) smokers, 27 (62.8%) hypertension, 7 (16.2%) have Killip class more than 2, 17 (39.5%) with acute STEMI, mean sRAGE 584 pg/ml, and mean Gensini score 13.4). sRAGE was significantly lower in diabetic versus non diabetic patients with acute MI (584 vs. 769, p value<0.05). Univariate regression analysis revealed that low levels of sRAGE in all patients were associated with more severe evidence of CAD assessed by Gensini score. Likewise, multivariate regression analysis revealed that low levels of sRAGE were associated with high Gensini score.

Univariate logistic regression analysis for correlation of sRAGE plasma level quartiles and Gensini score in diabetic patients with acute MI

	Odds ratio	95% CI	P
Q1 vs Q4	4.521	3.542–8.132	<0.001
Q2 vs Q4	2.504	1.854–3.933	<0.001
Q3 vs Q4	2.116	1.483–3.208	<0.005

Q: quartile; MI: myocardial infarction; DM: diabetes mellitus; sRAGE: serum receptor for advanced glycation end product; CI: confidence interval.

Conclusions: sRAGE is lower in diabetic than non-diabetic patients with acute MI. Nevertheless, in both groups, low sRAGE is associated with severe CAD as assessed by Gensini score, even after controlling for other CAD risk factors. sRAGE could be an emerging biomarker that could predict CAD severity in diabetic and non-diabetic patients.

P3630 | SPOTLIGHT
Hemoglobin variation during hospitalization for acute coronary syndrome: a linear predictor of long term mortality?

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Introduction: Hemorrhagic complications during the management of acute coronary syndromes (ACS) worsen prognosis, prolong hospitalization and raise costs. The purpose of this study was to evaluate the prognostic impact on long term mortality of the variation of hemoglobin (Hb) levels during hospitalization for ACS.

Methods: Prospective observational study of 2640 patients admitted for ACS (38.6% ST elevation acute myocardial infarction [AMI], 58.2% non-ST elevation AMI, 3,2% new left bundle branch block) in a single coronary care unit from May 2004 until June 2013. All patients underwent standard clinical, laboratorial and echocardiographic evaluation, and were submitted to a coronary angiography and percutaneous coronary intervention if indicated. Four groups were created according to the quartiles of Hb variation during hospitalization (admission Hb minus lowest Hb value): group 1: ≥2.1 g/L; group 2: >1.1 and <2.1 g/L; group 3: >0.3 and ≥1.1 g/L; and group 4: ≤0.3 g/L. Follow-up was performed for all the patients. Primary endpoint was all-cause death at 1 year follow-up (secondary endpoint: all-cause death at 2 years).
Results: The mean age of the population studied was 68±13 years, and 66.4% were male. Admission Hb was 13.3±2 g/L, and was higher in group 1 (14.4 vs 13.6 vs 13 vs 12.3; p<0.001). There were no significant differences between groups regarding baseline characteristics. Patients in group 1 had a higher Grace score (145 vs 141 vs 137 vs 141, p≤0.001), were more frequently submitted to coronary angiography (82.3% vs 80.5% vs 74.5% vs 72.3%, p≤0.001), had more anterior descendent artery disease and were more revascularized (either PCI or CABG). Peak troponin I was also higher in group 1 (72.2 vs 40.1 vs 23.3 vs 22.4, p≤0.001). There were also stastistically higher levels in LDL and glycaemia at admission in group 1. In this group the glycoprotein inhibitors IIB/IIIA had higher use (34.9% vs 30.3% vs 23.3% vs 24.4%, p≤0.001). Left ventricular ejection fraction was lower in group 1 (49% vs 50% vs 53% vs 52%, p≤0.001). Regarding the primary endpoint, more patients in groups 1 and 4 died at 1 year (6.4% vs 3.7% vs 3.7% vs 6.8%, logrank=0.023). At 2 years of follow-up, the results were similar, with a higher mortality in group 4 (7.3% vs 4.3% vs 4.6% vs 9.2%; logrank p=0.003).
Conclusion: In our study, patients with both the highest and the lowest variation of Hb during hospitalization for ACS had the worst long term prognosis, which leads us to think that the admission hemoglobin may be an independent predictor of mortality.

P3631 | BEDSIDE
Intraventricular conductance disturbances in patients with suspected myocardial ischemia: incidence and prognostic value

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Purpose: The identification of intraventricular conduction disturbances often raises concern regarding myocardial ischemia as the underlying cause. The aim of our study was to investigate patient characteristics and diagnostic value of such electrocardiographic sings in patients presenting with suspected exercise-induced myocardial ischemia.
Methods: A total of 2367 consecutive patients scheduled to undergo myocardial perfusion single-photon emission computed tomography (SPECT) because of suspected exercise induced myocardial ischemia. Of these, 655 presented with any type of intraventricular conduction disturbance. We compared the incidence of different types of intraventricular conduction disturbances in patients with or without myocardial ischemia by Mann-Whitney-U-tests and their prognostic value by logistic regression. All pathologies which proved significant were then checked for independence against presence of CAD and known cardiac risk factors. The presence of myocardial ischemia was adjudicated based on perfusion SPECT combined with coronary angiography findings, if available.
Results: 655 patients (27.7%) showed any form of conduction disturbance. The incidence of the subtypes was: complete left bundle branch block (BBB) 127 (5.4%), incomplete left BBB 49 (2.1%), left anterior fascicular block 109 (4.6%), left posterior fascicular block 4 (0.2%), bifascicular block 41 (1.7%), incomplete trifascicular block 6 (0.3%), complete right BBB 104 (4.4%) and incomplete right BBB 215 (9.1%). Interestingly the left BBB had the same prevalence (5.6 vs 5.2% p=n.s.) in patients with or without exercise induced myocardial ischemia and showed no prognostic value in the logistic regression. In comparison, incomplete left BBB (3 vs 1.5%, p=0.014), incomplete right BBB (10.2 vs 7.3%, p=0.018) and left anterior fascicular block (6.3 vs 3.6%, p=0.002) were significantly more common in patients with myocardial ischemia. After multivariate logistic regression only the left anterior fascicular block proved to be an independent predictor of myocardial ischemia with an OR of 1.747 (p=0.007).
Conclusion: Different intraventricular conduction disturbances have very different likelihoods of myocardial ischemia. In contrast to other clinical situations left BBB showed no correlation to exercise-induced perfusion deficits. The left anterior fascicular block showed a strong association to myocardial ischemia, which should be investigated further.

P3632 | BEDSIDE
Is there association between coronary artery disease and severe asymmetric septal hypertrophy?

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The prevalence of asymmetric septal hypertrophy (ASH) is very high in patients with hypertrophic cardiomyopathy (HCM). In some cases coronary artery disease (CAD) may be associated with ASH without evidence of HCM. The incidence and clinical significance of severe ASH in CAD is open to discussion.
Purpose: The current study aimed to assess the relationship between severe ASH and clinical manifestations of CAD.
Methods: 6528 patients with stable CAD defined as ≥50% coronary stenosis of one or more epicardial vessels by angiography were registered into the database and analyzed.
Results: Patients were divided into two groups based on echocardiographic ventricular septum thickness to left ventricular (LV) posterior wall thickness ratio: ≥1.5 – group I (n=232) and <1.5 – group II (n=6296). Patients in group I were more likely to be male gender (93.5% vs 87.2%, p=0.004). The prevalence of prior myocardial infarction (MI) was higher in group I (69.3% vs 39.6%, p<0.001). ASH patients were in higher functional class of stable angina (65.9% vs 57%, p=0.012) and more of them had severe heart failure (NYHA class III/IV) (23% vs 16.3% p=0.008). The groups differed significantly in echocardiographic parameters: LV (53.5±6.8 mm vs 50.9±5.2 mm, p<0.001) and right ventricular (RV) end-diastolic dimensions (EDD) (26.1±3.1 mm vs 25.1±2.9 mm, p<0.001), LV ejection fraction (EF) (50.1±9.2% vs 55.4±8.5%, p<0.001), left atrial dimension (45.1±7.3 mm vs 42.1±5.7 mm, p<0.001), extent of LV wall motion abnormalities (23.9±16.2% vs 14.2±15.5%, p<0.001), frequency of moderate and severe mitral regurgitation (13.9% vs 9.3%, p<0.017), aortic stenosis (3.1% vs 0.5%, p<0.001) and LV myocardial mass (359.0±85.8 g vs 293.4±72.9 g, p<0.001). The frequency of stenosis and more severe (total occlusion) lesion of right coronary artery and left circumflex artery (LCA) were higher in patients with ASH. Multivariate logistic regression analyses revealed that RV EDD (OR (odds ratio) 1.95; CI (confidence interval) 1.00-1.10, p=0.031), LV EDD (OR 0.92;CI 0.88-0.95, p<0.001), aortic root diameter (OR 1.07; CI 1.03-1.11, p=0.001), aortic stenosis (OR 5.05; CI 2.26-11.28, p<0.001), impaired LV EF (OR 0.97; CI 0.94-0.979, p=0.001), previous MI (OR 3.23; CI 2.27-4.58, p<0.001) and severe lesion of LCA (OR 1.55; CI 1.15-2.10, p=0.004) were independently associated with ASH.
Conclusion: The existence of association between severe ASH and CAD can be explained by prior MI and stenosis of LCA. ASH is directly associated with more severe clinical manifestations of CAD and impaired LV and possibly RV function.

UPDATE ON CARDIOTOXICITY

P3634 | BEDSIDE
HER2 Ile655Val polymorphism and the trastuzumab-induced cardiotoxicity in women HER2 positive breast cancer

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Background: HER2 (ERB2, neu) is a proto-oncogene which encodes a trasmembrane protein with tyrosine kinase activity. Trastuzumab, a humanized monoclonal antibody which binds to the HER2 extracellular domain, is used for HER2 positive breast cancer's treatment. Although it is well tolerated, it has a significant adverse effect: cardiotoxicity.
Purpose: To evaluate the possible effect of ERB2 gene polymorphism at codon 655 (ATC/Isoleucine to GTC/Valine) (rs1136201) in cardiac disfunction related to trastuzumab in women diagnosed with HER2 positive breast cancer.
Materials and methods: 54 patients with HER2 positive breast cancer and treated with Trastuzumab in our hospital were evaluated prospectively from January to December 2012. Trastuzumab was administered as a loading dose of 8 mg/kg followed by 6 mg/kg every three weeks. For all patients, cardiac function (left ventricular ejection fraction, LVEF) was checked at baseline and every 3 months by echocardiogram or MUGA (multigated blood-pool imaging) scan. We considered cardiac toxicity when LVEF drops 10 percentage points from baseline and below 50%, as stated in the data sheet. For genotyping we used TaqMan probes and allelic discrimination technique. Statistical analysis was performed with Statcalc software packages and the level of significance was indicated by a p value of less than 0.05.
Results: The mean age of the patients was 51.11±12,16 years. The distribution for genotypes was 55.56% AA, 40.74% AG and 3.7% GG. Of all patients, 12 developed cardiotoxicity during the treatment with trastuzumab: 4 with genotype AA, 8 with AG and none with GG. Significant correlation wasn't found between genotypes AA (vs AA/GG) or GG (vs AA/AG) and cardiac disfunction. Instead, statistically significant differences were shown when comparing patients with genotype AG and AA/GG with cardiotoxicity (p=0.039, OR= 4.0 (1.03-15.60).
Conclusions: The results of our study show an association of ERB2 polymorphism Ile655Val with cardiac toxicity associated with trastuzumab. Patients with genotype AG have higher risk of developing cardiac disfunction related to trastuzumab than those with AA or GG. We need more studies on this polymorphism and with larger sample size to confirm these findings

P3635 | BENCH
Myofilament changes in doxorubicin-induced cardiotoxicity

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Several studies demonstrate that administration of doxorubicin, an anthracycline antibiotic used in cancer treatment, results in cardiac toxicity, and may lead to dilated cardiomyopathy. Alterations in titin have been reported in patients with this disease. The present work aims to evaluate the early myocardial changes in an animal model of doxorubicin-induced cardiotoxicity.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 after 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, nHill). Sirius-red, hematoxylin-eosin and TUNNEL stained samples, were used to quantify left (LV) and right ventricular (RV) fibrosis, cardiomyocytes cross sectional area and apoptotic nucleus, respectively. Titin isoform expression, phosphorylation and degradation were quantified. DOX-HF group presented cardiac hypertrophy as evidenced by the increase in heart weight normalized to body weight (2.38±0.09 vs 2.17±0.06 g/kg) and by the increased RV and LV cardiomyocyte cross-sectional 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±1.9mN/mm^2 vs 16.5±1.1mN/mm^2) without significant differences in passive tension (3.8±0.5 vs 3.1±0.3mN/mm^2). Myofilaments sensibility to Ca2+ was not changed by doxorubicin (pCa50: 5.7±0.2 vs 5.8±0.1; nHill: 1.9±0.2 vs 1.8±0.2). DOX-HF group showed a decrease in total titin phosphorylation (49.0±6.1 vs 85.2±9.9%), more pronounced in the stiff N2B isoform (62.6±9.1 vs 31.0±4.4%), besides the increase in N2BA: N2B isoform ratio (0.3±0.1 vs 0.5±0.1). On the other hand, the percentage of apoptotic nuclei was similar between groups (2.1±1.3 vs 3.5±1.8%). 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%) and a tendency in the RV (12.0±1.6 vs 9.0±1.2%). This work describes novel and early myocardial effects of doxorubicin-induced cardiotoxicity, including changes at the level of cardiomyocytes and myofilaments (titin). These early changes precede the initial echocardiographic diagnosis of cardiomyopathy, emphasizing the need for an early detection of cardiac damages associated to cancer treatments that provide therapeutic adjustments and prevent the progression of cardiomyopathy.

P3636 | BENCH
Doxorubicin impairs the insulin-like growth factor-1 axis in H9c2 cells

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Background: Increasing evidence indicates that anthracyclines cause a depletion of resident cardiac progenitor cells, thereby preventing the turnover of cardiomyocytes that underlies the regenerative capacity of the heart. Insulin-like growth factor-1 (IGF-1) has previously been shown to promote the survival of cardiomyocyte precursor cells by activating type 1 IGF receptor (IGF-1R). Within the myocardium, IGF-1 action is modulated by IGF binding protein-3 (IGFBP-3), which sequesters IGF-1 away from IGF-1R.
Methods: The H9c2 cell line was used as a model of cardiomyocytes with proliferative and differentiative potential. Cells were treated for 24 hours with 0.1, 0.5, and 1 μM doxorubicin, a concentration range comparable to that observed in patients after bolus infusion of the drug. In some experiments, exposure to doxorubicin was preceded by pre-treatment with the antioxidant agents, N-acetylcysteine (NAC; 50 μM for 1 h), dexrazoxane (20 μM for 3h), and carvedilol (10 μM for 1h), or the p53 inhibitor, pifithrin- alpha (PFT-α; 5 μM for 1h). Oxidative stress and apoptosis were assessed by flow cytometry for fluorescent dichlorofluorescein and annexin V stained cells, respectively. Expression of IGF-1R and IGFBP-3 was evaluated by RT-PCR and western blot.
Results: Consistent with the established pro-oxidant activity of anthracyclines, dichlorofluorescein fluorescence rose after incubating H9c2 cells with doxorubicin. Oxidative stress was associated with a significant increase in apoptosis. Exposure to doxorubicin also resulted in a dose-dependent decrease in mRNA and protein levels of IGF-1R. By contrast, IGFBP-3 expression dose-dependently increased. All these effects were counteracted by pre-treatment with NAC, dexrazoxane, and carvedilol. Doxorubicin-induced apoptosis was also antagonized by PFT-α, indicating the involvement of p53. Since p53 is a transcriptional repressor of IGF-1R and an inducer of IGFBP-3, we hypothesized that doxorubicin modulation of IGF-1R and IGFBP-3 was also p53-mediated. Indeed, pre-treatment of H9c2 cells with PFT-α prevented the decrease in IGF-1R and the increase in IGFBP-3.
Conclusions: Treatment with doxorubicin down-regulates IGF-1R and up-regulates IGFBP-3 via p53 in the H9c2 cell model. This may contribute to anthracycline-induced apoptosis through the inhibition of IGF-1 action. Further studies are needed to confirm our findings in human cardiac progenitor cells and explore the possibility of manipulating the IGF-1 axis to protect against anthracycline cardiotoxicity.

P3637 | BENCH
Glucose regulated protein 78 inhibits doxorubicin cardiomyopathy by modulating autophagy and cell death

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Purpose: Cancer treatment with the anthracycline doxorubicin (Dox) is limited by the development of cardiomyopathy. Dox seems to induce cell death by autophagy and apoptosis, however, the exact molecular mechanism is still unclear. Interestingly, some cancer cells evade Dox treatment by upregulation of the endoplasmic reticulum (ER) chaperone Glucose Regulated Protein 78 (GRP78). Initially discovered as ER stress protein, a role of GRP78 in apoptosis and cell survival has emerged during the last years. We therefore wanted to investigate the effects of a gene therapeutic treatment with GRP78 on Dox induced cardiomyopathy in vivo and in vitro.
Methods: Isolated neonatal rat ventricular cardiac myocytes were treated with 1μM doxorubicin. GRP78 expression was modulated by siRNA mediated knockdown and treatment with a recombinant adeno-associated virus serotype 6 (AAV6-GRP78). Cell death and apoptosis were determined by ToxiLight Assay, TUNEL assay and Caspase-3 cleavage. For the in vivo study C57Bl6 mice were injected with AAV9-GRP78 and treated with 20mg/kg Doxorubicin over 4 weeks. Cardiac function was determined by intraventricular pressure volume measurements. All samples were analyzed by western blotting and realtime-PCR.
Results: In our in vitro model we could show, that Dox treatment leads to a short-time downregulation of GRP78 and activates apoptosis as indicated by elevated cell death, TUNEL positive cells and cleaved caspase-3. Additionally, autophagy regulator beclin-1 mRNA expression was decreased. While GRP78 knockdown further increased caspase-3 activation and cell death, AAV mediated overexpression of GRP78 protected cells from these Dox effects. In our mouse model therapeutic GRP78 gene transfer improved cardiac function after Dox treatment. Ejection fraction and systolic pressures where increased when compared with Dox treated control animals. Molecular assessment of ventricular samples showed that GRP78 gene transfer altered the expression of beclin-1 and caspase-3 cleavage. We therefore conclude that GRP78 protects hearts from Dox by influencing autophagy and apoptosis.
Conclusion: Dox induces cardiac dysfunction via induction of cell death. Our experiments implicate a role of GRP78, as it is downregulated by Dox treatment and gene transfer with the endoplasmic reticulum Chaperone GRP78 protects Dox treated mice via modulation of autophagy and apoptotic signaling. Our findings could have implications not only for Dox cardiomyopathy, but also other cardiac diseases in which autophagy and cell death are main contributing factors.

P3638 | BEDSIDE
The clinical characteristics and outcomes of patients with amphetamine associated cardiomyopathy in New Zealand

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Purpose: Amphetamine use is a global health issue and amphetamine associated cardiomyopathy (AAC) is becoming an increasingly recognized entity. Despite this, the characteristics and outcome of these patients are poorly understood. We therefore aim to describe the characteristics and outcome of patients with AAC, admitted to a tertiary hospital from a multi-ethnic population in New Zealand.
Methods: Patients admitted with heart failure and echocardiographic evidence of cardiomyopathy between 2011 and 2014 were retrospectively identified and recruited if they have documented history of amphetamine abuse and is thought to be the most likely cause of cardiomyopathy when all other causes of heart failure have been excluded on clinical grounds. Baseline characteristics, investigations and clinical outcomes were collected by interrogating local hospital electronic medical record.
Results: A total of 15 patients were identified over a follow-up period of 1.5 years. The mean age was 36 years with a male predominance (n=14, 93%). The majority of patients were of indigenous Maori ethnicity. At presentation 40% of patients were in pulmonary oedema and 20% were in cardiogenic shock. 27% of patients required Intensive care unit (ICU) admission for inotropic support (3 patients) and mechanical ventilation (2 patients).
The ECG was abnormal in 73% of patients predominantly with T wave inversion. Baseline echocardiograms showed severe left ventricular (LV) dilation (mean LV end-diastolic dimension (LVEDD) - 6.7cm) and all patients had at least moderate to severe LV dysfunction (mean LVEF – 16%).
ACE-inhibitor, beta-blocker and spironolactone therapy were commenced on 67% of patients. Despite optimal heart failure therapy, follow up echocardiogram on 7 patients continued to show severe LV dilation (mean LVEDD - 7.2cm) and severe LV dysfunction.
Two patients (13%) died from end stage heart failure during the follow up period.
Conclusions: AAC was seen in young patients, predominantly in indigenous

Maori. They present initially with severe cardiomyopathy, often requiring ICU admission. Severe LV dilation and dysfunction persisted despite heart failure therapy and mortality is high.

P3639 | BEDSIDE
Left ventricular strain assessing by means of two-dimensional speckle tracking as a strong early predictor of cardiotoxicity during breast cancer chemotherapy with anthracyclines

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Purpose: The effectiveness of breast cancer treatment increases with each decade. However, the efficacy is undermined by potentially life-threatening cardiotoxicity. This is a pilot study focused on the predictive role of early alteration of strain assessed by means of speckle tracking for further cardiotoxicity caused by chemotherapy.
Methods: Patients (n=97) with diagnosed breast cancer were selected for the study. Heart failure was a criterion for exclusion. Patients were studied before treatment, 1 day after the first cycle, 1 day after the last anthracyclines cycle, and on the last day of radiotherapy, 6 and 12 months after chemotherapy cessation. Cardiotoxicity was defined as a cardiac dysfunction with any signs or symptoms of congestive heart failure and the decline of 5% or more in an ejection fraction (EF) of less than 55%, or asymptomatic dysfunction with 10% decline in EF to less than 55%. Strain was assessed by speckle tracking method in apical 2-, 3- and 4-chamber views. This study was approved by Internal Ethic Committee and conforms to the principles of the Declaration of Helsinki.
Results: During the study 11 (11.3%) patients developed cardiotoxicity, Ejection fraction decreased (62±5% to 59±5%, 62±6% to 60±4%, 63±6% to 52±3%) 6 months after chemotherapy in the whole group, in those without endpoint and with cardiotoxicity respectively. At the baseline there were no differences in age, past history, admitted drugs and also in echocardiography parameters such as EF (the mean was 62%, 62%, 63%, p=0.52) and speckle tracking (the median was: -20.1%, -19.6% and -20.2%, p=0.68) for the whole group, those without endpoint and with cardiotoxicity respectively. In those patients who developed cardiotoxicity 6 months or 12 months after the end of chemotherapy, speckle tracking measured 4 and 10 months earlier to that point was: -16.6±2% and -17.2±0.7% respectively. In comparison, in the group without cardiotoxicity it was: -20.2±1.8% and -20.8±1.6%. The sensitivity and specificity of speckle tracking measurements just after radiotherapy with cut-off equal to -18.5% for prediction of cardiotoxicity development in the next 4 months was 91% and 85% respectively. Area under curve (AUC) was 0.971. Strain assessment by means of speckle tracking can also predict cardiotoxicity after chemotherapy 10 months in advance with the sensitivity of 81% and specificity of 85% (AUC 0.903).
Conclusion: Left ventricular strain assessed by means of two-dimensional speckle tracking can be a useful method in oncology for cardiotoxicity prediction during breast cancer treatment.

P3640 | BEDSIDE
Impaired exercise capacity after anthracycline treatment in asymptomatic survivors of childhood acute lymphoblastic leukemia

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Purpose: Little is known about the effect of anthracycline therapy on future exercise capacity, measured by maximal oxygen uptake (VO2max), after treatment of childhood acute lymphoblastic leukemia (ALL). In a cross-sectional study of very long-term survivors of childhood ALL, mean 23±8 years post diagnosis, we wanted to compare VO2max in survivors exposed and unexposed to anthracycline treatment.
Methods: Treatment data were collected from medical records. Echocardiography was performed in all survivors, before they performed maximal exercise on a bicycle, with continuous measurement of respiratory gas exchange and calculation of VO2max.
Results: Exposed survivors had received a cumulative isotoxic doxorubicin dose of median 120 mg/m^2 (range 40-485). Unexposed survivors were older, thus having lower values of expected VO2max. Mean body weight and gender distribution did not differ between the treatment groups. In all, 55% of exposed survivors had reduced VO2max, compared to only 17% of unexposed survivors ($p<0.001$). VO2max did not have any statistical association with other treatment variables. However, we observed significant correlations between exercise capacity and measures of left ventricular function, such as ejection fraction (p=0.001), global longitudinal strain (0.015) and diastolic tissue Doppler velocities ($p<0.001$).
Conclusions: In survivors of childhood ALL, previous anthracycline treatment is associated with impaired exercise capacity, possibly related to late cardiotoxicity.

	All survivors (n=132)	Exposed (n=103)	Unexposed (n=29)	p-value
Age at diagnosis (years)	6.3±4.0	6.8±4.2	4.7±2.7	0.013
Age at exam (years)	29.4±7.1	27.5±6.4	36.1±5.0	<0.001
Female (number)	65 (49%)	48 (76%)	17 (58%)	0.253
Body weight (kg)	76.5±17.9	76.0±18.2	78.0±17.2	0.599
VO2max (ml/kg/min.)	34.7±8.4	34.5±8.5	35.2±8.3	0.711
VO2max (% of predicted)	85±19	83±19	94±18	0.004
Reduced VO2max (number)	62 (47%)	57 (55%)	5 (17%)	<0.001

P-values are for the comparison between survivors exposed and unexposed to anthracycline therapy. VO2max: maximal oxygen uptake.

P3641 | BEDSIDE
Additional value of two-dimensional and three-dimensional speckle tracking echocardiography in detecting early cardiotoxicity of anthracycline and trastuzumab in breast cancer patients

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Purpose: The present study aimed at assessing the diagnostic power of both 2D and 3D Speckle Tracking Echocardiography (STE) in comparison with standard echo Doppler in detection of early signs of cardiotoxicity of anthracycline (ANT) and trastuzumab (TRS) in breast cancer patients.
Methods: Thirty-five consecutive women (mean age = 47.5 years) with breast cancer were treated by sequential protocols including ANT (epirubicin, cumulative dose = 489±74 mg/m^2) + cyclophosphamide and/or 5-fluorouracil for 3-4 cycles, followed by 18 cycles of TRS (mean cumulative dose = 877.4±306 mg/kg). At baseline (before starting treatment), after ANT completion (3 months) and after the first 4 TRS cycles (3 additional months) all the patients underwent complete standard echo Doppler exam, 2D STE with measurement of global longitudinal strain (GLS) and both 3D volumetric (left ventricular volumes and EF) and 3D STE echo with determination of GLS, global circumferential strain (GCS), global area strain (GAS) and global radial strain (GRS). Patients taking cardiac drugs before and/or after cancer therapy were excluded from the study.
Results: All the patients completed the cycles of chemotherapy. None complained about symptoms and/or signs of heart failure. Among standard echo Doppler parameters, 2D EF was not significantly changed by treatments (baseline: 63.5±3.64%, ANT: 63±4.4%, TRS: 62.9±3.9%) whereas E/e' ratio was higher after ANT (7.1±0.8) than at baseline (6.3±1.5) ($p<0.01$) but not significantly different between baseline and TRS (6.8±1.8) (p=0.09). 2D STE-derived GLS was lower after ANT (-21.8±2.7%, $p<0.02$) and during TRS (-21.1±2.3%, $p<0.01$) than at baseline (-22.9±2.7%). Three-dimensional EF did not change significantly by both ANT and TRS. Among 3D STE parameters, GLS (ANT: $p<0.05$, TRS: $p<0.01$), GCS (both $p<0.01$), GAS (ANT: $p<0.05$, TRS: $p<0.01$) and GRS (ANT: $p<0.05$, TRS: $p<0.01$) were all significantly reduced in comparison with baseline. Worthy of note, 2D STE was feasible in all the patients (100%) whereas the feasibility of 3D volumetric and 3D STE assessment was 80% and 69% respectively.
Conclusions: Our study demonstrates the potential superiority of both 2D and 3D STE in diagnosing subclinical cardiotoxicity of both anthracycline and trastuzumab in breast cancer patients but also the much greater feasibility of 2D STE in this clinical setting. Among standard echo Doppler parameters, E/e' ratio shows a particular trend, with an increment which achieves the statistical significance only after ANT as a possible marker of acute and likely transient cardiotoxicity.

P3642 | BENCH
The effects of a bradykinin b1 receptor antagonist on the development of hypertensive organ damages in SHR model

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Purpose: It is well known that currently used non-steroidal anti-inflammatory drugs have adverse effects on cardiovascular morbidity and mortality. Therefore we aimed to test the cardiovascular effects of a novel analgesic compound in a preclinical study using spontaneously hypertensive rats.
Methods: The test substance was administered in rat chow test diet containing a concentration of 120 ppm or 400 ppm of FGY1153, or control diet containing no active ingredient. The treatment started at the age of 11 weeks and lasted for 26 weeks. Body weight and food consumption were measured weekly; blood pressure measurements were performed at Weeks 0, 13 and 26, echocardiography was performed at Weeks 0 and 26. We investigated the hypertensive organ damages on heart, carotid artery and aortic segments with light microscopy, electron microscopy and Western blot analysis.
Results: The treatment did not affect blood pressure. Echocardiography showed that the treatment decreased the degree of left ventricular hypertrophy (FGY120 Septum (S): 1.90±0.04 mm, $p<0.01$; Posterior wall thickness (PWT): 1.82±0.01 mm, $p<0.05$; FGY400 S: 1.88±0.02 mm, $p<0.01$; PWT: 1.81±0.04 mm, $p<0.05$ vs. Control group S: 2.09±0.04 mm; PWT: 1.94±0.02 mm) in both treated groups. The activity of signal transduction factors of TGF-β and SMAD2 decreased sig-

Echocardiographic parameters

	SHR Week 0	Control Week 26	FGY120 Week 26	FGY400 Week 26
Septum (mm)	1.66±0.01	2.09±0.04	1.90±0.04**	1.88±0.02**
Post. wall (mm)	1.58±0.02	1.94±0.02	1.82±0.01*	1.81±0.04*
LVESV (ml)	88.72±3.33	141.56±5.89	111.69±4.15*	127.31±8.66
EF (%)	68.48±0.75	62.16±1.24	67.10±1.33*	63.36±1.37

*p<0.05, **p<0.01 vs. Control group.

nificantly in FGY1153 treated groups (TGF-β: FGY120 30.43 dens%, p<0.01 vs. Control: 40.76 dens%) (SMAD2: FGY120 26.12 dens% p<0.05 vs. Control: 37.50 dens%). The intima-media thickness of great vessels and the amount of vascular wall collagen content did not decrease significantly in treated animals.

Conclusions: In conclusion, long-term administration of the FGY1153 did not have any deleterious effects in SHR model. Moreover, we could observe some protective effect of FGY1153 against hypertensive cardiovascular remodeling despite having no antihypertensive effect. Inhibition of the TGF-β-SMAD signaling may be an important mechanism in the background of this effect.

P3643 | BEDSIDE
Impaired left ventricular diastolic function in adult survivors of childhood acute lymphoblastic leukemia treated with anthracyclines

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Purpose: Anthracycline therapy carries a dose dependent risk of late cardiotoxicity. Left ventricular (LV) diastolic dysfunction is thought to precede systolic dysfunction. Tissue Doppler imaging (TDI) with measurement of peak early diastolic velocities of the mitral annulus (e') is recommended to detect diastolic dysfunction. Several recent, smaller studies of childhood cancer survivors have failed to show reduced e' associated with anthracycline therapy. We wanted to test the hypothesis that antracycline therapy leads to LV diastolic dysfunction in the very long term.

Methods: In a cross-sectional study of 138 childhood acute lymphoblastic leukemia (ALL) survivors, mean 23 years after diagnosis, echocardiography with measurement of e' was performed, and compared to 138 randomly selected, healthy controls matched 1:1 for gender, age, body weight and systolic blood pressure.

Results: ALL survivors and controls had equal body weight and systolic blood pressure. Survivors had lower e' than controls. Anthracycline treated survivors (median cumulative dose 120 mg/m^2) were younger than the other survivors, but e' did not differ between survivor groups (table). However, anthracycline treated survivors had lower e' than age-matched controls (p>0.001, table), whereas anthracycline naïve survivors and age-matched controls had equal e' (p>0.5). LV ejection fraction did not differ between survivors and controls, but was lower in anthracycline treated survivors compared to other survivors.

Conclusions: Anthracyclines lead to impaired LV diastolic function in the long term. As e' decreases with age, age-matched controls are necessary to detect the premature decline in diastolic function found after anthracycline therapy.

P3644 | SPOTLIGHT
Genetic variants in antracicline biotransformation genes and risk of cardiotoxicity

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Purpose: It is well established that elevation in Cardiac Troponin I (cTnI) level after high-dose chemotherapy predicts delayed heart failure. The aim of this study is to analyzed the possible role of genetic polymorphisms for enzymes involved in Antracicline (ANT) metabolism, to predict cTnI elevation after treatment with non-high dose of Epirubicin (EPI).

Methods: Using QIAamp DNA purification system (QIAGEN, Milano, Italy), genomic DNA is extracted from blood of early breast cancer pts treated with EPI (90 mg/m^2 for 3 or 4 cycles every 21 days) with or without radiation and hormone therapy. The presence of a known heart disease and previous treatment with ANT or exposure to mediastinal irradiation are exclusion criteria for the study protocol. DNA samples are genotyped for single-nucleotide polymorphisms (SNPs) by TaqMan®SNP genotyping assay (Life Technologies, Monza MB, Italy), which was designed to detect variants of a single nucleic acid sequence, without quantifying the target. The presence of two probes in each reaction allows genotyping of the three possible variants at the SNPs site in the target sequence. Complete cardiac evaluation and serial blood measurement of cardiac biomarkers is performed at baseline, every 3 weeks during ANT treatment and every 3 months during 1-year follow-up. Plasma cTnI is determined using LOCI method on a Dimension Vista system (Siemens Healthcare Diagnostic); we consider "elevated" any cTnI value exceeding the cut-off level of 0.02 ng/mL.

Results: Sixty-six patients were considered in this preliminary analysis. During ANT treatment (mean cumulative dose 313.1±45.3 mg/m^2), an increase in cTnI plasma level (≥0.02 ng/mL) was found in 13 pts (19.7%; group A); in all these pts cTnI plasma level persisted elevated also at 3 month follow-up. In the remaining 53 pts (80.3%; group B), cTnI concentration was normal during all scheduled controls. Comparing clinical, laboratory, ECG and Echocardiographic parameters collected at baseline we didn't find any significant difference between the two groups. Of the 6 SNPs for 3 key ANT biotransformation genes included in this analysis, homozygosis for the "protective variants" rs4148808 [C/T] for ABCB4 transporter, rs7853758 [A/G] and rs885004 [A/G] for SLC28A3 gene were present in the 5.6% of pts in the group B, while were absent in all patients in the group A.

Conclusion: Genetic analysis combined with serial cTnI measurements could be able to predict individual susceptibility for ANT-induced cardiotoxicity. The meaning of these finding might be elucidated at the end of follow-up.

P3645 | BEDSIDE
Influence of mTOR inhibitors on left ventricular hypertrophy and diastolic function in kidney transplant recipients

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Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality among renal transplant recipients. The mammalian target of rapamycin (mTOR) inhibitors have shown cardioprotective effects in experimental studies but their influence on CVD in renal transplantation is unclear. The aim of study is to assess of left ventricular (LV) mass and diastolic function among kidney transplant recipients treated with mTORihibitors (sirolimus and everolimus)

Methods: The study group consisted of 15 mean age 60 years kidney transplant recipients treated with mTOR inhibitors and steroids. The control group consisted of 16 at age 54 years kidney transplant recipients received calcineurin inhibitor, mycophenolate mofetil and steroids matched for gender, duration of pretransplantat dialysis, time after transplantation, eGFR and BMI. The incidence of hypertension and diabetes were similar in both groups. In all patients echocardiographic examination acording to ASA was performed The LV mass was calculated by formula 0.8(1.04[(LVED + LVPW + IVS)^3] - (LVED)^3 and indexed for body surface area. The cut-off of 115g/m^2 for man and 95g/m^2 for women was defined as LV hypertrophy.

Results: The diastolic diameter of LV and LV mass were significantly higher in study group. The LV hypertrophy was significantly more frequent in study group The systolic function was normal in the all patients. There were significant differences in diastolic function between two groups:IVRT was significant longer in study group, lateral early diastolic annular velosity (e lat) was significantly smaller in study group and E/e ratio was significantly higher in study group. Logistic regression analysis revealed that LV hypertrophy was related only with mTOR inhibitor therapy (OR 8.7 95% CI: 1.01-75.5 p=0.048)
The results were shown in Table 1

Table 1

	Time after KTx (years)	eGFR (ml/min)	LVd (mm)	LVmass ASE	% pts with LV hypertrophy	e lat (cm/s)	E/e	IVRT (ms)
Study group	9.6	40.2	52.8mm	278.4	31.2%	8.3	9.9	95.8
Control group	6.7	48.2	48.5	213.2	80.0%	10.7	7.5	85.8
p	0.09	0.1	0.04	0.01	0.01	0.04	0.04	0.04

Conclusion: The treatment with m TOR inhibitors in kidney transplant recipients was related with left ventricular hypertrophy and impaired of left ventricular diastolic function.

Abstract P3643 – Table 1

	Survivors (n=138)	Controls (n=138)	p-value	Anthracyclines (n=107)	Controls (n=107)	p-value	No anthracyclines (n=31)	p-value (vs other survivors)
Age at exam	29.5±7.2	29.8±7.4	0.667	27.5±6.6	27.9±7.0	0.618	36.3±4.8	<0.001
Heart rate	66±11	65±11	0.319	67±11	65±11	0.132	63±10	0.080
e' septum	11.1±2.8	12.6±2.5	<0.001	11.0±2.7	13.0±2.5	<0.001	11.1±3.2	0.924
E/e' average	6.0±1.5	5.6±1.3	0.015	6.1±1.5	5.4±1.2	0.001	5.8±1.3	0.454
EF	57±6	57±5	0.614	56±4	57±6	0.162	60±5	<0.001

e': tissue Doppler peak early diastolic velocity of the mitral annulus; EF: ejection fraction.

PROGNOSIS: KEY POINTS I

P3647 | BEDSIDE
The prognosis of patients hospitalized for heart failure the Polish population of the ESC Heart Failure Pilot Registry

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Background: Heart failure (HF) is a major cause of hospital admissions, especially in an elderly population. The costs of hospitalization in patients with HF absorb a growing proportion of health care funds.
Objective: To determine the clinical characteristics and prognosis of patients hospitalized with heart failure.
Method: The study included patients hospitalized for HF in the Polish centers participating in the ESC EURObservational Research Programme: The Heart Failure Pilot Survey, for which complete clinical data as well as full 12 month follow-up were available.
Results: The analysis included 650 patients (56% of all included in the register) with a mean age of 67.9±13.3 years, 64.5% men, mostly with angiographically documented ischemic origin heart failure (60.5%). In 42.4% of cases it was the first hospitalization for HF. The most common presentation at admission was decompensated heart failure (78%), 8% of patients had pulmonary edema on admission. Average NYHA class at admission was 3.0±0.7 and mean left ventricular ejection fraction was 28.9±7.7% (from 11 to 76%). Most of patients were smokers (former or present: 68.6%), have hypertension (66%) and overweight (mean BMI 28.2±5.3, from 16 to 50 kg/m^2). Chronic kidney disease was present in 23%, atrial fibrillation in 39.1%, diabetes mellitus in 35.5% and COPD in 12.7% of patients. 27.2% of patients have history of prior PCI, 13.3% prior CABG and 10.2% prior stroke.
The in-hospital mortality was 2.6%. During the 12 month follow-up the re-hospitalization rate was 48.3% and the one-year survival rate was 84.6%.
Conclusions: In patients hospitalized with heart failure we found a high prevalence of risk factors and comorbidities, which significantly influences the prognosis. Within one year after hospital discharge more than half of patients die or will be re-hospitalized.

P3648 | BEDSIDE
A simple online risk calculator: prediction of survival in Asian patients with heart failure

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Purpose: Risk models have been developed to predict survival in the heart failure patient. However, some are complex and none designed for use in Asians. We aim to develop a simple online risk calculator to predict 1 and 2 year survival in Asian patients with heart failure.
Methods: Consecutive patients admitted to our institution for heart failure from Jan 2008 to Dec 2009 were included. All patients were followed-up for 2 years. Overall mortality was obtained from the national registry of deaths. The risk score was derived from a multivariate Cox model and this was validated in another local institution.
Results: A total of 1392 patients and 729 patients were included in the derivation and validation cohort respectively. The accuracy of the model was good (see Table 1). The risk calculator and the variables included are available online.
Conclusions: The risk calculator provides a good estimate of 1 and 2-year survival in Asian patients with heart failure from readily obtainable clinical characteristics. Furthermore, the calculator is easily available online and is simple to use and may potentially impact management.

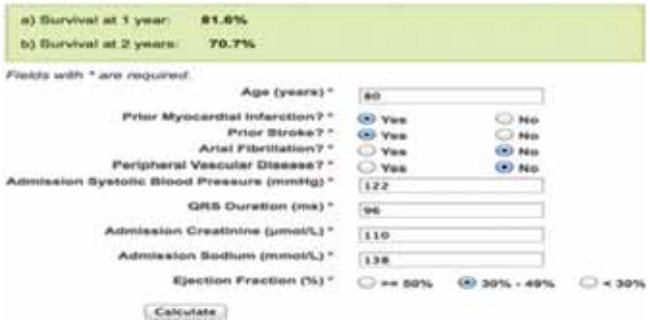

Figure 1. Online risk calculator.

Table 1. Performance of risk model

	Derivation cohort (n=1392)	Validation cohort (n=729)
1-year survival (actual vs predicted)	78.3% vs 84.3%	75.2% vs 78.4%
2-year survival (actual vs predicted)	68.1% vs 72.0%	64.1% vs 71.6%
1-year receiver operating curve (95% CI)	0.731 (0.699–0.764)	0.669 (0.623–0.715)
2-years receiver operating curve (95% CI)	0.725 (0.697–0.754)	0.681 (0.640–0.722)

P3649 | SPOTLIGHT
The CardShock risk score for prediction of mortality in cardiogenic shock- results from the prospective CardShock study

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Aim: To develop a risk prediction score for short term mortality in cardiogenic shock (CS) in the contemporary era.
Methods: The CardShock study prospectively enrolled 220 patients with CS. Predictors of in-hospital death, identified through multiple stepwise logistic regression analyses, were used to build a score for mortality risk stratification. The risk score included: age >75 years, confusion (1 point each), ACS etiology, previous MI, LVEF<40% (2 points each), previous CABG (3 pts), and blood lactate levels (<2, 2-4, >4 mmol/L; 0,1,3 pts respectively). Performance of the risk score was assessed by crude mortality rates and c-statistic.
Results: Patients were on average 67 years, 74% were men. Mean systolic blood pressure was 78 mmHg, heart rate 93 bpm. CS was caused by ACS in 81% of cases. There were 81 in-hospital deaths (37%) and 90-day mortality was 42%. The distribution of the population and in-hospital mortality according to risk class is shown in Figure 1. The risk score exhibited good overall discrimination both for prediction of in-hospital and 90-day mortality with a c-statistic of 0.87 (95%CI 0.83-0.92; p<0.001) and 0.86 (95% CI 0.81-0.91; p<0.001), respectively. Patients with risk scores 0-5 (43% of the cohort) had low (<20%) 90-day mortality. The intermediate group (scores 6-8; 44%) had bad prognosis (50% mortality), whereas 25/26 patients in the high risk category (scores 9-14; 13%) died. In this high risk group, more than 50% of deaths occurred within 2 days from detection of shock.

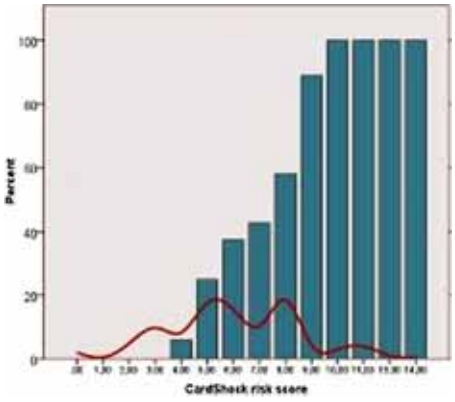

Figure 1. The CardShock risk score.

Conclusion: Cardiogenic shock is still associated with poor prognosis. A practical risk score, consisting of seven easily identifiable factors, can be used for risk stratification of short-term mortality. This might aid clinicians in rapid decision making during acute intensive care.

P3650 | BEDSIDE
The systemic inflammation-based Glasgow Prognostic Score as a predictor of prognosis in patients with acute decompensated heart failure

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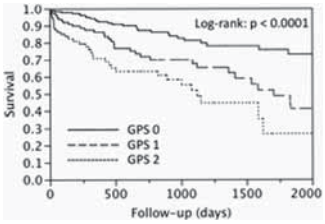
Purpose: The Glasgow Prognostic Score (GPS), combination of C-reactive pro-

tein (CRP) and serum albumin concentration, provides predictions of prognosis in patients with cancer. Both systemic inflammatory response and malnutrition are also common in patients with heart failure (HF). We evaluated the GPS of patients with acute decompensated heart failure (ADHF).
Methods: 502 patients with ADHF were classified into 3 groups by GPS (0; CRP <1.0 mg/dL and albumin >3.5 g/dL, 1; CRP >1.0 mg/dL or albumin <3.5 g/dL, 2; CRP >1.0 mg/dL and albumin <3.5 g/dL). The prognoses of 3 groups were investigated retrospectively.
Results: In-hospital mortality of GPS 0, GPS 1, and GPS 2 were 1.7%, 5.2%, and 14.8%, respectively. During the follow-up periods (605±682 days), 106 patients (21.1%) died. Relative to a GPS of 0, the hazard ratios for all-cause death were 1.76 (95% CI: 1.08–2.87) for a GPS of 1 and 2.97 (95% CI: 1.82–4.85) for a GPS of 2 in the age- and sex-adjusted Cox proportional hazard model.



Conclusions: The GPS, which is based on systemic inflammation, is useful for predicting the prognoses of hospitalized patients with ADHF.

P3651 | BENCH
Predictive clinical score evaluation in a population with ICD implanted for primary prevention and low left ventricular ejection fraction

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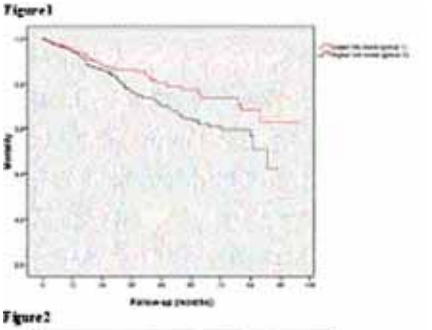
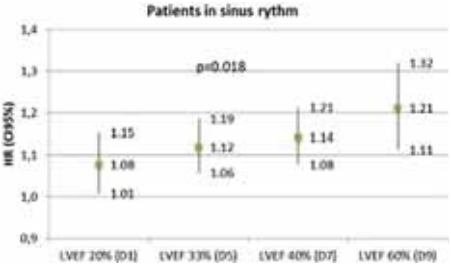
Purpose: Left ventricular dysfunction,estimated by ejection fraction (EF) quantitation, is a major factor in decision making for implantable defibrillator (ICD) therapy in primary prevention for sudden death in patients with ischemic/non-ischemic dilated cardiomyopathy (DCM). EF has low specificity if taken as the only indicator for a decision. An accurate identification and extensive clinical prognostic factors is necessary for better stratification model. The Seattle Heart Failure Model (SHFM) has a predictive ability providing valuable information regarding short, intermediate and long-term survivals. We have evaluated SHFM in a limited cohort of patients with heart failure, low EF and primary prevention ICD therapy.
Methods: 396 subjects (325 Male and 71 Female; mean age 67.1±10.1 years) with ischemic or idiopathic DCM and EF of 26.4±8%, implanted with an ICD in primary prevention between 2006 and 2012, has been retrospectively quantified by SHFM score at implant, attributing patients to 2 groups: 1) lower risk score (=<18% mortality prevision at 1 year) (124 patients); 2) higher score (>18% mortality prevision at 1 year) (282 patients). During follow up time period we have evaluated mortality and appropriate ICD discharges, with correlated Kaplan-Meier survival curves.
Results: The mean follow up was of 44.7±24.8 months (49.8 months/patient). The Kaplan-Meier survival curves (Fig. 1) demonstrated a higher mortality trend in patients with higher score (group 2, p=0.05 vs. group 1); the curves began to diverge after 2 years. ICD discharges were appropriately distributed in a similar way to both groups (Fig. 2) (P=0.8).
Conclusions: SHFM clinical score could indentify patients with medium/long term higher risk of mortality in primary prevention ICD indication better than EF alone.



P3652 | BEDSIDE
Prognostic value of heart rate according to rythm and systolic function in heart failure patients

D.A. Pascual Figal[1], A. Ferrero[2], J. Alvarez-Garcia[2], J. Delgado[3], P. Garcia-Pavia[4], R. Vazquez[5], R. Bover[6], T. Puig[2], J.R. Gonzalez-Juanatey[7], J. Cinca[2] on behalf of REDINSCOR. *[1]University Hospital Virgen De La Arrixaca, Murcia, Spain; [2]Hospital de Sant Pau, Barcelona, Spain; [3]University Hospital 12 de Octubre, Madrid, Spain; [4]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain; [5]University Hospital Puerta del Mar, Cadiz, Spain; [6]Hospital Clinic San Carlos, Madrid, Spain; [7]University Hospital of Santiago de Compostela, Santiago de Compostela, Spain*

Background: Heart rate (HR) is currently considered as a risk factor for death and hospitalization in patients with chronic heart failure (HF) and left ventricular ejection fraction (LVEF) ≤35%. However, the impact of the interaction between heart rhythm and LV systolic dysfunction is not well established.
Purpose: To evaluate in a large population with chronic heart failure, the effect of HR on prognosis as a function of baseline rhythm and LVEF.
Methods: A population of 2507 patients [age 67 (13), male 69%] with established diagnosis of chronic HF was prospectively included in the database of the National Network of Heart Failure (REDINSCOR). All baseline characteristics were recorded at enrollment, including heart rate (HR) obtained from the electrocardiogram performed at the inclusion visit. Events were also prospectively registered.
Results: At baseline, HR was median of 75 bmp (Q1:65, Q3:85), LVEF was median of 33% (Q1:25, Q3:41) and 1595 (64%) were in sinus rhythm. At 5 years, 829 (33%) patients died, 775 (31%) were hospitalized with HF and 1277 (51%) presented death or HF hospitalization. HR, examined as +10 bpm, was independently associated with a higher risk of death [1.06 (1.01-1.11), p=0.014], HF hospitalization [1.06 (1.01-1.11), p=0.023] and any event [1.06 (1.02-1.10), p=0.003]. However, this risk was only significant among patients in sinus rhythm at inclusion. Hazard ratio also showed a positive relationship with LVEF. Patients with sinus rhythm and preserved LVEF (>60%) had the higher risk. By contrast, HR did not reach significance as risk factor among patients without sinus rhythm [1.02 (0.96 – 1.08].



Conclusions: The prognostic impact of higher HR was restricted to patients in sinus rhythm, however this association occurred regardless of LV systolic dysfunction.

P3653 | BEDSIDE
Heart failure and the soluble prorenin receptor (sPRR): results from the CIBIS-ELD trial

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The prorenin receptor (PRR) is a transmembrane protein that binds prorenin and renin, leading to their activation and activation of the local renin-angiotensin system (tissue RAS). Interestingly, cardiomyocyte-specific ablation of PRR resulted in lethal heart failure (HF), indicating an important role in this setting. A soluble form of the prorenin receptor (sPRR) is found in plasma that is able to bind and activate prorenin, the inactive proenzyme form of renin. Hence sPRR may be a usefull pathophysiological marker of a RAS activity. Aim of the present analysis was to determine distribution patterns of sPRR receptor plasma levels in the setting of HF. An ELISA to detect sPRR was developed by CellTrend. The sPRR receptor was measured in the CIBIS-ELD trial population (n=556,72.2±5.4 years, 66% male). The CIBIS-ELD trial was an investigator-initiated multi-centre randomised trial with patients with moderate to severe diastolic or systolic chronic HF.198

healthy volunteers without relevant cardiovascular diseases served as controls (58.5±7.4 years, 33% male). Levels of sPRR were log-transformed before analysis and are reported as log(Units). The plasma levels of sPRR in patients with ejection fraction <55% (0.42±0.41) or LVEDD >55 mm (0.45±0.42) were statistically significant higher compared to the control group levels (0.32±0.38) ($p<0.01$). This difference remained significant in a multivariate analysis. sPRR levels negatively correlated with 6 minute walk test distance r= -0.08 (p=0.003). Statistically higher concentrations of soluble PRR were found in patients with a left ventricular end diastolic diameter (LVEDD) >55mm in comparison to those with a normal LVEDD ($p<0.001$). Patients with signs of renal impairment (creatinine >1.2 mg/dl) demonstrated statistically significant higher levels of sPRR compared to healthy volunteers ($p<0.001$). sPRR, as a novel diagnostic tool, should be further evaluated as a possible diagnostic biomarker of heart failure.

P3654 | BEDSIDE

Prognostic value of right ventricular systolic function in cardiac amyloidosis according to its etiology

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Purpose: Right ventricular (RV) systolic echocardiographic parameters are routinely used in chronic heart failure to identify patients with bad prognosis. There is a lack of data in the specific context of cardiac amyloidosis.
Methods: Among a cohort of 229 patients consecutively referred to our amyloidosis network for a diagnosis work-up, we identified 107 patients, by a standard two-dimensional echocardiography, with increased interventricular septal (IVS) thickness ≥12mm and all RV systolic function echocardiographic parameters measurable [tricuspid annular plane systolic excursion (TAPSE), lateral tricuspid annulus peak systolic wave (St') measured by tissue Doppler imaging and global and regional RV longitudinal strain (LS)] of whom 62 had cardiac amyloidosis (CA) with a proven biopsy and 45 had a negative biopsy (controls).
Results: The mean±SD age, of the 107 selected patients, was 68.8±13.7 years, 76% were male, mean left ventricular ejection fraction was 54±14%, and mean IVS thickness was 14.9±5mm. There was no difference between the two groups. Origine of amyloidosis was transthyretin-related hereditary (ATTR, n=26), senile (wild type TTR, n=16) or linked to immunoglobulin light chain (AL, n=20). CA patients had significant lower TAPSE (16±5mm vs 20±6mm, $p<0.001$) and St' (8.8±3.3 vs 10.4±4.1, p=0.04) than controls. There was no difference in global or segmental RVLS between CA and controls. Among CA, TAPSE and St' were correlated with all RVLS values ($p<0.01$ for all). Finally, among patients with CA during one year of follow-up, TAPSE, St', were significantly lower in patients presenting outcome (death, cardiogenic shock or acute cardiac decompensation), compared to those who did not, whereas global and segmental RVLS were not.
Conclusions: Standard two-dimensional RV systolic echocardiographic parameters are impaired in cardiac amyloidosis and more relevant than RVLS to identify patients at higher risk of outcome.

P3655 | BENCH

Comparison and identification of early clinical, biological and echocardiographic prognostic markers in transthyretin and AL cardiac amyloidosis

T. Damy[1], A. Jaccard[2], A. Guellich[1], D. Lavergne[2], S. Rappeneau[1], J.F. Deux[1], L. Hittinger[1], V. Frenkel[1], V. Plante-Bordeneuve[1], D. Mohty[2]. *[1]AP-HP - University Hospital Henri Mondor, Creteil, France; [2]University Hospital of Limoges, Limoges, France*

Background: Amyloidosis is a lethal infiltrative disease characterized by fibrils deposition in the extracellular matrix. The most common types of amyloidosis are primary (AL), hereditary transthyretin (mTTR) and senile transthyretin (WT-TTR) amyloidosis. Amyloidosis prognosis depends on cardiac dysfunction. Identifying patients at higher risk of events are needed.
Aims: Define the clinical, biological and echocardiographic variables and thresholds predictors of bad prognosis in cardiac amyloidosis (CA).
Method: Analysis of 266 patients referred for suspected amyloidosis in two university centers.
Results: Of the 266 referrals, 198 were considered having CA, of whom AL, m-TTR and WT-TTR prevalence were respectively 60%, 29% and 11%. The median (IQR) age, NT-proBNP and LVEF of CA were respectively 69 (60,76), 3027 (673,7155) and 60 (48,66). 66% were male and 40% were in NYHA III-IV classes. NT-proBNP was correlated to interventricular septal thickness (IVST) reflecting the severity of the infiltration (R=0.34; p=0.0001). IVST was higher in m-TTR and WT-TTR than in AL ($p<0.0001$) but NT-proBNP was higher in AL (p=0.0001). 53 patients were dead or had heart transplant at 1 year. m-TTR CA had better 1 year survival (Chi square log rank =14.0; p=0.01). Using multivariate Cox proportional model only NT-proBNP (>8000pg/ml) NYHA (III-IV), cardiac output (<4l/min) and pericardial effusion were independent predictors of prognosis.
Conclusions: NT-proBNP and cardiac output are powerful predictors of mortality in CA whatever the type. NT-proBNP increase depends of the type of CA and is not correlated with the severity of the infiltration.

P3656 | BEDSIDE

Peripheral monocyte count predicts long-term mortality in patients with decompensated systolic heart failure

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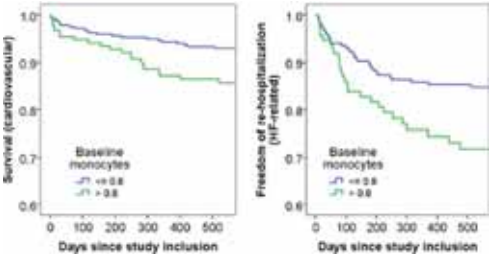
Purpose: Monocytes are an essential component of immune defense and contribute to tissue remodeling. So far, only few studies evaluated prognostic implications of monocytes in the peripheral blood in heart failure (HF). We studied this issue in patients hospitalized for cardiac decompensation.
Methods: Participants of the extended INH study were eligible if they had a differential blood count performed at the index hospitalization. A monocyte count >0.8/ml was considered increased, and patients were grouped accordingly (≤/>0.8/ml). Follow-up (FUP) for all-cause and cardiovascular mortality (ACM, CVM) and all-cause and HF-related hospitalization (ACH, HHF) was performed at 180 and 540 days after discharge.
Results: 478 patients were enrolled (mean age 65.8±12.4 years, 24% female, 35% NYHA III/IV). A monocyte count >(≤)0.8/ml was found in 155 (323) patients. At the 180 days FUP a monocyte count >0.8/ml failed to predict ACM (hazard ratio 1.5, 95% confidence interval 0.8-2.9, p=0.27), CVM (1.6, 0.7-3.7, p=0.24), ACH (1.2 0.8-1.6, p=0.34) and HHF (1.7, 0.9-3.0, p=0.1). However, at the 540 days FUP baseline monocytes >0.8/ml predicted ACM (2.1, 1.4-3.2, p=0.001), CVM (2.1, 1.2-3.8, p=0.01), ACH (1.3, 1.0-1.7, p=0.03) and HHF (1.9, 1.2-3.2, p=0.01) in univariable analysis. After adjusting for age, sex, anemia, NYHA class, renal dysfunction, diabetes and NT-proBNP monocytes >0.8/ml remained an independent predictor of ACM (1.8, 1.1-2.9, p=0.02). Significance was lost for CVM (1.5, 0.9-2.9, p=0.2), ACH (1.2, 0.9-1.6, p=0.18) and HHF (1.3, 0.7-2.4, p=0.36) in multivariable analysis.



Conclusions: After cardiac decompensation for systolic HF monocytes in the peripheral blood seem of long-term prognostic significance. This indicates a potential role of this cell population in HF progression.

P3657 | BEDSIDE

Echocardiographic features and survival in a large cohort of systemic sclerosis patients

L. Gargani[1], G. Agoston[2], S. Guiducci[3], A. Moreo[4], L. Bazzichi[5], E. Bruschi[6], O. Epis[6], S. Bombardieri[5], M. Matucci Cerinic[3], E. Picano[1]. *[1]CNR, Institute of Clinical Physiology, Pisa, Italy; [2]University of Szeged, Cardiology, Szeged, Hungary; [3]Careggi University Hospital (AOUC), Florence, Italy; [4]Niguarda Ca' Granda Hospital, Cardiology, Milan, Italy; [5]University of Pisa, Dept. of Internal Medicine, Rheumatology & Immunoallergology Units, Pisa, Italy; [6]Niguarda Ca' Granda Hospital, Rheumatology, Milan, Italy*

Purpose: Cardiac and pulmonary involvement in systemic sclerosis (SSc) are frequent, and affect the prognosis of the disease. Prevalence of cardiac involvement is highly variable in studies, according to the different definitions and tools employed to detect it. Our aim was to assess the prevalence and prognostic meaning of some established echocardiographic and lung ultrasound parameters in a large cohort of SSc patients.
Methods: In a prospective multicenter study (4 Italian and 1 Hungarian Hospitals), 376 SSc pts (age=54±14 yrs, 91% females), after a thorough clinical evaluation, underwent a comprehensive 2D echocardiogram and lung ultrasound to assess B-lines, a sonographic sign of pulmonary fibrosis. Peripheral echo reading

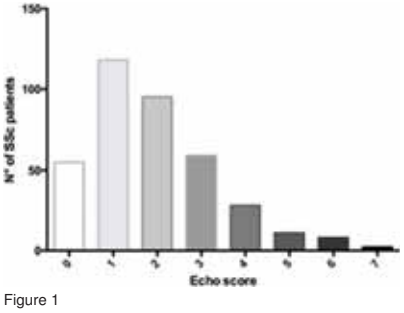


Figure 1

was performed by accredited cardiologists. A cardiopulmonary echo score was built with 7 items (each from 0= normal to 2= markedly abnormal, with a range 0-14), including ejection fraction, E/e', tricuspid annular plane systolic excursion (TAPSE), tricuspid regurgitation maximal velocity (TVR), pericardial effusion, mitral or aortic valvular heart disease (VHD) and B-lines number.
Results: At least one ultrasound imaging abnormality was present in 85% pts (see figure). Ejection fraction ≤50% was present in 3.4% pts, E/e' ≥13 in 8.7%, TAPSE <16 mm in 5.2%, TVR≥290 cm/sec in 16% and ≥340 cm/sec in 0.08%, pericardial effusion in 6.5%, a more than mild aortic or mitral VHD in 9.5%, and a more than mild degree of B-lines in 37%. During 5-year follow-up 5 patients died. Cox-regression analysis showed that the cardiopulmonary echo score was an independent predictor of mortality (HR 3.1, 95%C.I. 1.2-7.7) among clinical and imaging parameters.
Conclusions: An echo score integrating cardiac and pulmonary biomarkers is a strong, independent predictor of mortality in SSc patients.

P3658 | BEDSIDE
Reduced level of thrombin receptor (PAR-1) autoantibodies in chronic heart failure: new insights?

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Autoantibodies (AA) against G-coupled receptors were found in heart failure and hypertension. Several studies have shown that these AA activate receptors and contribute to disease progression. We have recently developed an ELISA for the detection of autoantibodies against PAR1-Receptor (AA-PAR1) and could show that AA-PAR-1 are present in the systemic circulation. We hypothesized that autoantibodies against PAR1-Receptor (AA-PAR1) are upregulated in patients with heart failure.
An ELISA to detect AA-PAR1 was developed by CellTrend. 556 patients from the CIBIS-ELD trial (72.2±5.4 years, 66% male) with heart failure (HF) were investigated. 198 healthy controls (58.5±7.4 years, 33% male) were studied for comparison. Levels of AA-PAR1 were log-transformed before analysis and are reported as log(Units). Strikingly, AA-PAR1 levels were significant higher in controls, compared to HF patients (0.277±0.39 vs. 0.65±0.194 $p<0.0001$. A positive correlation for ejection fraction was observed for the entire cohort r=0.161, $p<0.001$ while a negative correlation to left ventricular enddiastolic volume r= -0.122, $p<0.001$. We found a striking positive correlation to e-wave and a negative correlation to left atrial size, indicating that AA-PAR are reduced with progressive diastolic dysfunction. AA-PAR1 levels correlated with 6 minute walk test distance r=0.214 $p<0.001$
Hence, autoantibodies against the Thrombin receptor (PAR-1) were reduced in patients with heart failure compared to age-matched healthy controls. The functional relevance of AA-PAR1 has to be elucidated in HF. Further studies have to evaluate the relevance of this new biomarker.

PROGNOSIS: KEY POINTS II

P3660 | BEDSIDE
Fragility in heart failure patients: a key determinant of survival

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Background: Heart failure (HF) is a chronic condition with poor prognosis and is highly prevalent among older people. Due to this fact, fragility is often present among HF patients. However, even young HF patients show a high degree of fragility. The effect of fragility on long-term prognosis in HF patients, irrespective of age, remains unexplored.
Objective: To assess the influence of fragility on long-term prognosis in outpatients with HF.
Methods: At least one abnormal evaluation among four standardized geriatric scales was used to identify fragility. Predefined criteria for such scales were: Barthel Index <90; OARS scale <10 in women and <6 in men; Pfeiffer Test >3 (±1, depending on educational grade); and ≥1 positive response for depression on the abbreviated Geriatric Depression Scale (GDS).
Results: We assessed 1,314 consecutive outpatients with HF (27.8% women, median age 69 years [P25–75: 59–76 years]). Etiology was mainly ischemic heart disease (53.7%), followed by dilated cardiomyopathy (11.9%). Patients were mainly in NYHA functional class II (62.4%) or III (31.1%). Fragility was detected in 581 (44.2%) patients. Median follow-up was 4.9 years [P25–75: 2.5–8.4] for living patients. 626 deaths were documented. Fragility and all of its components were significantly associated with decreased survival in the univariate analysis. Abnormal OARS scale and Barthel index were the individual items of fragility with worse hazard ratio. In a comprehensive multivariable Cox regression analysis, fragility remained independently associated with survival in the entire cohort, and in age and left ventricular ejection fraction subgroups.

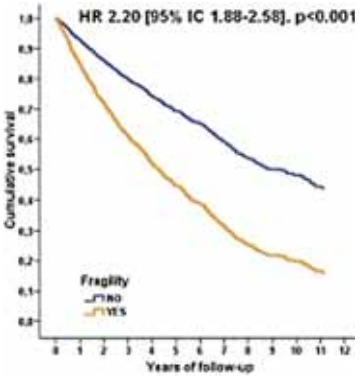

Figure 1. Fragility and survival.

Conclusion: Fragility is a key determinant of survival in ambulatory patients with HF across all age strata.

P3661 | BEDSIDE
Prevalence, clinical characteristics and prognosis of non-ischemic cardiomyopathy patients without left ventricular dilatation

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Purpose: We sought to determine the prevalence of patients without left ventricular (LV) dilatation among patients with non-ischemic cardiomyopathy (NICM), and to compare clinical characteristics and prognostic determinants of patients with and without LV dilatation.
Methods: 648 consecutive patients (463 males, age 55±15 years) with NICM were studied with cardiovascular magnetic resonance. Late gadolinium enhancement (LGE) was used for myocardial fibrosis detection. LV volumes, mass and ejection-fraction were quantified using short-axis cine images. According to reference values, patients were dichotomized according to the presence or absence of LV dilatation. Patients underwent clinical follow-up, for the end-point of a composite of cardiovascular death, admission for heart failure, worsening of NYHA class, and aborted sudden cardiac death. For survival analysis, patients without LV dilatation were compared to an age- and LV ejection-fraction-matched group of patients with LV dilatation (n=250; matching 1:2).
Results: 125 (19%) NICM patients did not have LV dilatation. Compared to patients with LV dilatation, they were younger, had shorter duration of disease and milder NYHA class ($P<0.05$ for all). There was no significant difference in the cause of cardiomyopathy between the two groups (P=0.179). Patients without LV dilatation had higher LV ejection-fraction (45±8 vs 33±12%,$P<0.001$) and showed less frequently LGE (31 vs 41%,P=0.041). During a median follow-up of 23 months (25th-75th: 11-39), 66 (26%) and 24 (19%) patients with (matched group) and without LV dilatation, respectively, experienced the composite end-point (HR: 1.279, 95%CI: 0.794-2.061, P=0.311). No significant differences between the two groups were observed regarding the achievement of the end-point. In patients without LV dilatation, LGE occurrence was associated with a 3-fold increased likelihood of developing the composite end-point (HR: 3.508, 95%CI: 1.387-8.875, P=0.008) after correction for age, LV ejection-fraction and cardiac index.
Conclusions: Subjects without LV dilatation represent a non-negligible proportion of NICM patients and show a more favourable clinical profile than patients with LV dilatation. Nonetheless, they have comparable prognosis to patients with LV dilatation of similar age and degree of systolic dysfunction. Furthermore, LGE is a strong and independent prognostic predictor in NICM patients without LV dilatation.

P3662 | BEDSIDE
The role RV-LV delay to predict time to first heart failure hospitalization and mortality with cardiac resynchronization therapy

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Purpose: Cardiac resynchronization therapy (CRT) is an effective therapy for patients with left ventricular (LV) systolic dysfunction, heart failure (HF) and QRS prolongation. However, despite the benefits of CRT, the non-responder rate remains challenging. LV electrical delay measured at the LV pacing site has been shown as a strong predictor of remodeling and quality of life. However, the predictive value of electrical delay for clinical outcomes has not been assessed in prospective trials. Accordingly, this study was designed to evaluate the relationship between RV-LV duration and HF hospitalization or death.

Methods: A total of 1342 patients enrolled in PEGASUS (66% male, mean age 67±11 years, LV ejection fraction (LVEF): 23% ± 7%, QRS duration 158±29 ms, 68% LBBB) were analyzed. The RV-LV duration was defined as the time interval from the peak of the RV electrogram (EGM) to the peak of the LV EGM. The time to first HF event and/or death during one year follow up were assessed. Multivariate cox proportional hazards modeling was performed to evaluate the relationship of RV-LV with event free survival, adjusting for baseline covariates.
Results: The median value of RV-LV value for this cohort was 67 ms. Patients with longer RV-LV had a 30% lower risk of HF or death (p=0.03) after adjustment for baseline covariates (Fig. 1). The absolute reduction in HF hospitalization at 12 months was 6.4% with longer RV-LV as compared to shorter RV-LV.

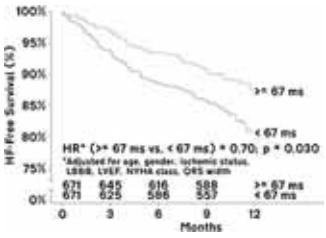

Figure 1

Conclusions: Baseline electrical dyssynchrony, as assessed by RV-LV duration, predicted the clinical responses to CRT. The RV-LV duration can be easily measured at implant and by CRT devices and may provide a simple means of selecting/optimizing LV stimulation site and possibly maximizing CRT response.

P3663 | BEDSIDE
The optimum heart rate and blood pressure control in chronic heart failure patients varies with the heart rhythm

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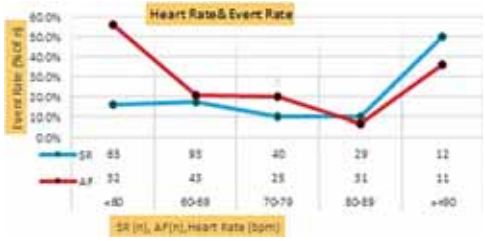
Purpose: Evaluating the optimum heart rate (HR) and blood pressure (BP) associated with lowest mortality and readmission rates in patients with chronic heart failure with reduced ejection fraction (HFREF), both in sinus rhythm (SR) and in atrial fibrillation (AF).
Method: We retrospectively analysed clinical data on 428 consecutive HFREF patients discharged over 2 yrs. from our heart failure service on completion of treatment. Mortality and readmission data (adverse events) were collected for a mean follow up period of 17 months after discharge.
Results: 56.1% patients were in SR and 33.2% in AF. Mean age was 69 yrs. in SR and 75.5 yrs. in AF. 77.5% patients in AF were male and 68% in SR. Mortality and readmission was 12.7% & 14.1% in AF and 10.4% & 7.1% in SR. Average EF (34%), NYHA class (2.4), HR (68 bpm), systolic BP (SBP, 125 mmHg), diastolic BP (DBP, 71mmHg) and patients on beta blockers (86%) were similar in the 2 groups.
Patients in SR had lower mortality (OR 0.80) and lower readmissions (OR 0.46) than the AF subgroup. In SR, HR <80bpm was associated with lower mortality (OR 0.72) and readmission (OR 0.63). HR <70bpm did not confer additional survival benefit (OR 0.98). In the AF subgroup a HR of 70-90 bpm had the best prognosis. HR <70 bpm was associated with increased mortality (OR 5.68) as was HR >90 (OR 10.1).
SBP <100mmHg and DBP <60mmHg was associated with 2 fold increase in adverse events in all the patients. Strict BP control in patients in SR (SBP 110-130mmHg and DBP 60-80mmHg) was associated with 50% reduction in adverse events as compared to a higher BP. Patients in AF had the best outcome if they had higher BP (SBP >130mmHg and DBP>70mmHg).



HR control in SR & AF and adverse events.

Conclusion: Strict BP and HR control in SR improves prognosis while a higher HR and BP is needed for the same in patients with AF.

P3664 | BENCH
Circulating matricellular protein osteonectin as a marker of 3-years survival in patients with ischemic symptomatic moderate-to-severe chronic heart failure

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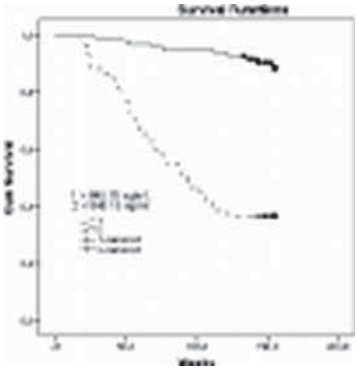
Background: Secreted protein acidic and rich in cysteine (SPARC) plays a key role in post-synthetic procollagen processing in heart failure myocardium.
Aim: To evaluate the prognostic value of circulating OSN for cumulative survival in patients with ischemic chronic heart failure (CHF).
Methods: A total of 154 patients with ischemic symptomatic moderate-to-severe CHF were enrolled in the study on discharge from the hospital. Observation period was up to 3 years. Blood samples for biomarkers measurements were collected. ELISA methods for measurements of circulating level of all biomarkers were used. Concentrations of OSN for cumulative survival cases due to advanced CHF was tested.
Results: During a median follow-up of 2.18 years, 21 participants died and 106 subjects were hospitalized repetitively. Medians of circulating levels of OSN in survival and died patient cohort were 670.96 ng/ml (95% confidence interval [CI] = 636.53-705.35 ng/ml) and 907.84 ng/ml (95% CI = 878.02-937.60 ng/ml). ROC analysis has been shown that cut off point of OSN concentration for cumulative survival function was 845.15 ng/ml. Figure demonstrates a significantly divergence of Kaplan-Meier survival curves in patients with high (>845.15 ng/ml) and low (<845.15 ng/ml) concentrations of OSN.
We found that OSN had independently predicted all-cause mortality (OR = 1.23; 95% CI = 1.10–1.36; P<0.001), CHF-related death (OR = 1.46; 95% CI 1.22–1.80; P<0.001), and also CHF-related rehospitalisation (odds ratio [OR] = 1.92; 95%confidence interval [CI] = 1.77 – 2.45; P<0.001) within 3 years of observation period.


Kaplan-Meier curves in patients with CHF

Conclusion: Increased circulating SPARC family member OSN associates with increased 3-years CHF-related death, all-cause mortality, and risk for recurrent hospitalization due to advanced CHF.

P3665 | BENCH
SELDI-TOF-MS Peaks identified as independent biomarkers of mid-term cardiac mortality in patients with stable chronic heart failure: Design and validation of a statistical score

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Background: Risk stratification of patients with stable chronic heart failure (CHF) is critical to better identify those who may benefit the most from invasive strategies such as heart transplantation.
Methods: To identify biomarkers related to cardiac mortality in CHF, we performed a proteomic analysis using high throughput surface enhanced laser desorption ionization - time of fight - mass spectrometry (SELDI-TOF-MS). Plasma samples were pre-treated to access the deep proteome of patients and analyzed in duplicates. The proteomic analyses was first performed in a case (died from cardiac cause within 3 years) /control (still alive at 3 years) study including 198 patients with a left ventricular ejection fraction (LVEF) <45%. A statistical score was developed in this derivation population using the support vector machine technique. The score was then validated in an independent cohort of 344 consecutive patients (cardiac death at 3 Years) with CHF.
Results: We detected 203 peaks by SELDI-TOF-MS analysis in the derivation population. When duplicates data are taken into account, 125 peaks had a relevant (>0.5) intraclass coefficient variation. After Bonferroni's correction (significant P value set at 0.00025), 42 peaks were differentially expressed between cases and controls. Altogether, 25 peaks fit both criteria and were entered into a support vector machine model to develop a score to predict cardiac mortality. This score was validated in the cohort population. The level of the score was higher in patients with cardiac death as compared to those who were still alive at 3 years: 0.55 vs. 0.45 (p=0.002). After adjustment on main documented predictors in CHF (NYHA, BNP, LVEF, and VO2 peak), the score was still significantly associated

with cardiac mortality (p=0.005). Of note, the use of this score on top of other predictors allows a good reclassification of patients with or without mid-term cardiac mortality: P value for integrated discrimination improvement at 0.01 and for net reclassification improvement at 0.0005. When associated to other predictors, the score was able to predict cardiac mortality with an area under curve at 0.88 by using receiving operator curve analysis.
Conclusion: Proteomic analysis of low abundance plasma proteins is highly promising to identify new prognostic biomarkers in CHF. After adjustment on well-known predictors in CHF, our study allowed to develop a score significantly and independently associated with mid-term cardiac mortality.

P3666 | BEDSIDE
Recurrent hospitalization due to heart failure in stable outpatients at risk of or with atherothrombosis

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Background: Heart failure (HF) is the leading cause of hospitalization and readmission in many hospitals worldwide. Previous studies have shown that early readmission in patients hospitalized for HF is associated with high morbidity, mortality, and healthcare expenditures, however, there are limited data on late readmissions. Our objective was to evaluate the frequency and factors associated with readmission during long term follow up.
Methods: Of the 68,236 patients enrolled, 45,227 patients were followed up to 4 years in the Reduction of Atherothrombosis for Continued Health (REACH) Registry, a large international study of patients with established ischemic events (CAD, CVD, and PAD) or multiple risk factors. Comorbid diseases, demographics, medications, and laboratory parameters were evaluated.
Results: Out of 45,277 patients, 6,085 patients had a history of HF at baseline, and of those, 1,610 patients experienced at least one recurrent HF hospitalization during the follow-up (26.5%). Among 38,503 patients without a history of HF, 1,703 patients were diagnosed with new HF (4.4%). The yearly percentage of recurrent HF was 6-10 fold higher than that of newly diagnosed HF and was consistently high throughout 4 years. Among patients with HF at baseline, patients with recurrent HF events were older (73.2 vs. 71.9 yr), had more DM (58.9% vs. 48.5%), more CKD (54.5% vs. 47.6%), more AF (36.5% vs. 27.5%) and more MI patients (56.0% vs. 53.1%). By year 4, the cumulative all-cause mortality rate was 30.8% among those with baseline HF who had recurrent HF vs. 19.6% in those with baseline HF but without subsequent hospitalization for HF.

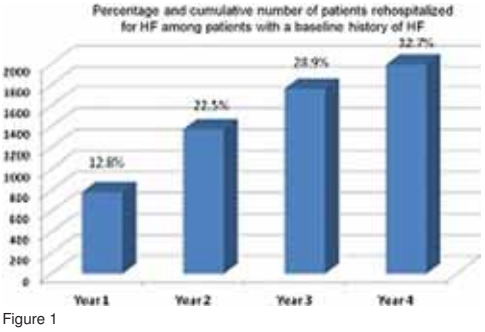

Figure 1

Conclusions: This analysis provides estimates of the risk of heart failure hospitalization in patients with and without heart failure at baseline.

P3667 | BEDSIDE
Hear rate as an independent predictor of mortality in patients with heart failure: results from the Norwegian Heart Failure registry

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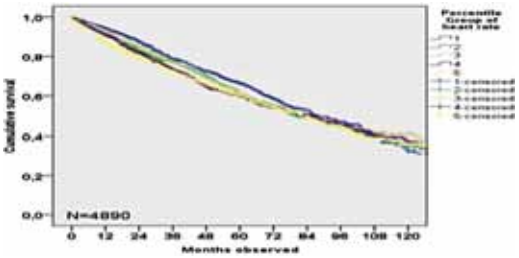
Purpose: To evaluate whether heart rate is an independent predictor of mortality in patients with heart failure (HF).
Methods: Hospital outpatients with HF were enrolled at stable follow-up with a measurement of heart rate and extensive demographic data, and followed for all cause mortality with complete update for all patients.
Results: There were 4890 patients (Sinus rhythm 2974), with mean age 70.4±11.8 years, 28.5% women, included from 2000 to 2012 in the analyses. The median follow-up was 58 months in survivors. Adherence to evidence-based medication was high: >90% was prescribed a beta blocker and an ACE-I/ARB and 27% an aldosterone blocker. In multivariate linear regression heart rate was related to type of rhythm, age, daily diuretic dose, gender, presence COLD/asthma, beta blocker use, NYHA class, coronary artery disease as the main cause for HF, diabetes mellitus, and use of ACE-I/ARB. In univariate Cox regression analyses of time to mortality heart rate was not a predictor (HR 1.004; 95% CI 1.000-1.008; P=0.069). However, in multivariate Cox regression analyses heart rate was a strong predictor of mortality (HR 1.006, 95% CI 1.001-1.010; P=0.008). This was adjusted for age, beta blocker use, NYHA class, daily dose diuretic, diabetes mellitus, gender, coronary artery disease as the main reason for HF, ACE-I/ARB use. Similarly for patients with sinus rhythm this was also significant (HR 1.009, 95% CI 1.003-1.014; P=0.004).). This result was adjusted for age, beta blocker use, NYHA class, daily dose diuretic, diabetes mellitus and gender.



Kaplan-Meier curve of quintiles of HR.

Conclusion: In this cohort of patients receiving optimal medical treatment at specialized out-patient HF clinics, an increased heart rate was as strong independent predictor of an increased risk of death independent of the type of rhythm.

P3668 | BEDSIDE
ST2 in ambulatory heart failure patients: prognostic marker beyond pathophysiological profile

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Background: ST2 has been identified as a novel biomarker involved, at least partially, in three patophysiological pathways: (1) cardiac stretch, (2) fibrosis and remodelling, and (3) inflammation. Serum concentrations of ST2 provide important prognostic information in heart failure (HF). However, the relative weight of ST2 in each of the aforementioned pathways and up to which point its prognostic value is affected by the different degree of stretch, inflammation or fibrosis-remodelling is unknown.
Aim: To examine whether ST2 levels improve HF risk-stratification relative to the concentrations of other biomarkers representative of these pathophysiological pathways: NTproBNP (stretch), galectin-3 (fibrosis-remodelling), and hs-CRP (inflammation).
Patients: 876 patients (71.5% men, mean age 68.3 ± years) were studied. Mean LVEF was 35.9% ± 13.6. Most patients were in NYHA class II (65.9%) or III (25.8%). Mean follow-up was 4.2±2.1 years.
Results: ST2 levels were higher as NTproBNP, hs-CRP, and Galectin-3 concentrations increased (p for trend <0.001 in all cases). ST2 correlation was highest with NTproBNP (r=0.32, p<0.001) and lowest with Galectin-3 (r=0.17, p<0.001). 386 patients died during follow-up. ST2 (above/below the median) remained an independent prognosticator of risk at every tertile of the other three biomarkers (Fig. 1). This was observed even after adjustment for age, sex, LVEF, NYHA functional class and ischaemic aetiology of HF.

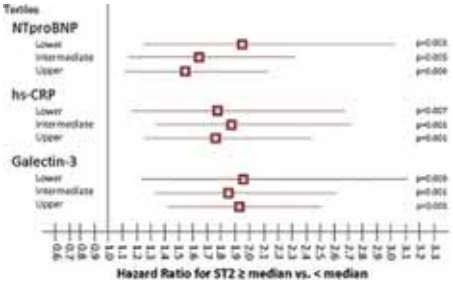

Figure 1

Conclusions: ST2 provides most-valuable long-term risk stratification information in HF above and beyond the degree of stretch, inflammation and fibrosis-remodelling reported by NTproBNP, hs-CRP and Galectin-3.

P3669 | BEDSIDE
Independent and incremental value of renal resistance index in predicting mortality among heart failure outpatients

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The aim of this study was to define the independent and incremental role of a

novel marker of renal perfusion impairment (Renal Resistance Index, RRI) in predicting mortality among CHF outpatients.
We enrolled 250 outpatients (78% males, 64±13 years, NYHA class 2.2±0.6, left ventricular ejection fraction, LVEF, 34±10%) with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (>1 month) and in conventional therapy. All patients underwent a clinical evaluation, a routine chemestry, an echocardiogram and a renal echo-Doppler. Pulsed Doppler flow recording was performed at the level of a segmental renal artery and RRI was then calculated from the peak systolic Doppler flow velocity and the end-diastolic Doppler flow velocity.
During follow-up (21.4±11.3 months) 33 patients died, 25 from cardiovascular causes (19 deaths due to heart failure worsening, 1 after arrhythmic storm and 7 for other cardiovascular causes), 6 for non cardiovascular causes. RRI was associated with events at univariate (HR: 1.11; 95%CI: 1.06-1.17, p<0.001, C-index 0.73) as well as at multivariate Cox regression analysis (HR: 1.06; 95%CI: 1.01-1.12; p: 0.023; C-index: 0.78) after correction for the independent predictors of the reference model, i.e. LVEF, GFRMDRD and logNT-proBNP. The addition of RRI to the reference model significantly improved reclassification according to both NRI (45%; 95%CI: 8-82%; p: 0.016) and IDI (0.018; 95%CI: 0-0.037; p=0.05). Figure 1 shows Kaplan-Meier curves according to RRI cut-off of 75.

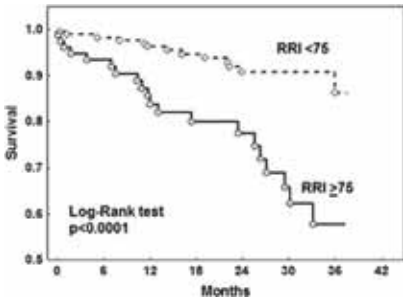

Figure 1

In conclusion, our findings demonstrate the independent and incremental role of RRI in predicting mortality among CHF patients thus suggesting its possible utility in daily clinical practise in order to better characterise patients with cardio-renal syndrome.

P3670 | BEDSIDE
Kidney injury molecule-1 (KIM-1): additional prognostic value on top of NT-proBNP and hs-TnT in chronic heart failure, a 5 year follow-up

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Background: Patients with chronic heart failure are often characterized by the cardiorenal syndrome (CRS). Urinary kidney injury molecule-1 (KIM-1), a novel marker of kidney injury, was shown to be a predictor of prognosis in chronic heart failure. The aim of the present study was to assess whether KIM-1 adds additional prognostic value to the established blood markers NT-proBNP and high-sensitive Troponin T (hs-TnT) during long-term follow-up.
Methods: KIM-1 was assessed from urinary samples of 149 individuals with chronic heart failure. NT-proBNP and hs-TnT were measured from serum samples. After 5 years of follow up, data regarding all-cause mortality and rehospitalisation for congestive heart failure were obtained.
Results: KIM-1 (binary cutpoint median of 1100 ng/g urinary creatinine) as well as NT-proBNP (binary cutpoint 900 pg/mL) and hs-TnT (binary cutpoint 14 pg/mL) were each significant predictors for all-cause mortality (each p<0.01) and a combined endpoint of all-cause mortality and rehospitalisation for congestive heart failure (each p<0.005). In a cox regression analysis, each marker was a significant predictor for both endpoints, independently from NYHA and EF (each p<0.05; GFR and age each p = n.s.). The combination of all three markers showed additive diagnostic value in comparison to each marker alone and the combination of hs-TNT and NT-proBNP. Of note, no death occurred in the subgroup with below-threshold concentrations of all three markers. On the other hand, if all three markers were positive, mortality was 63,2% after 5 years (Fig. 1).
Conclusions: The novel renal biomarker KIM-1 extends the long-term prognostic value of NT-proBNP and hs-TnT in chronic heart failure and allows further differentiating between low and high risk patients.

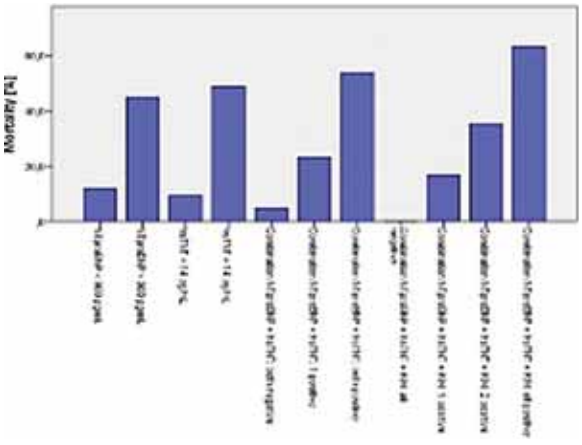

Figure 1. Mortality.

P3671 | BEDSIDE
Asymptomatic peripheral arterial disease is an independent predictor for reduced exercise capacity in patients with chronic heart failure

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Background: It is well known that symptomatic peripheral arterial disease (PAD) is strongly associated with increased risk for cardiovascular events and mortality. On the other hand, reduced exercise capacity is an independent predictor for increased mortality in patients with chronic heart failure (CHF). Although CHF patients who have symptomatic PAD show decreased exercise capacity, it is still unknown whether asymptomatic PAD contributes to its reduction in them. The purpose of this study was to investigate whether asymptomatic PAD reduced exercise capacity in CHF patients.
Methods: We recruited 347 consecutive patients with compensated CHF who underwent a cardiac rehabilitation during the hospitalization. We studied 223 patients (71 females) aged 65±14 years in this study after excluding patients with PAD of Fontaine stage 2 or more, hemodialytic patients, patients with atrial fibrillation, or those who needed assistance for walking at hospital discharge. Patients were defined to have an asymptomatic PAD, when their ankle-brachial index (ABI) measured during the hospitalization showed ≦0.90. Patients were divided into two groups based 0.90 of ABI: PAD(+) and PAD(–) groups. We measured blood hemoglobin, albumin and brain natriuretic peptide (BNP) on admission, and assessed patients' characteristics including estimated glomerular filtration rate, left ventricular ejection fraction and duration of hospital stay. We also measured quadriceps isometric strength (QIS) and one leg standing (OLS) time as parameters of motor function, and six-minute walk distance (6MWD) as a parameter of exercise capacity at the hospital discharge. We compared all parameters between the two groups. Multiple regression analysis was used to detect the predictors for reduced 6MWD.
Results: Forty two patients (13 females) aged 68±16 years were in the PAD(+) group. The QIS and OLS time were significantly lower in the PAD(+) group than in the PAD(–) group (P<0.05, respectively), and showed 85% and 68% of those measured in the PAD(–) group, respectively. The 6MWD was significantly lower in the PAD(+) group than in the PAD(–) group (340±133 m vs. 423±104 m, P<0.001). There were no significant differences in the other parameters between the two groups. Multiple regression analysis identified age (β=-0.191), duration of hospital stay (β=-0.130), BNP (β=-0.179), QIS (β=0.184), OLS time (β=0.134), and ABI≦0.90 (β=-0.137) as significant independent predictors for 6MWD (P<0.05, respectively) (R2=0.52).
Conclusion: Asymptomatic PAD was an independent predictor for reduced exercise capacity in patients with CHF.

SCANNING HORIZON IN HEART FAILURE

P3673 | BEDSIDE
Serial measurements of high-sensitive C-reactive protein predict prognosis of ambulant chronic heart failure patients: results of the Bio-Shift study

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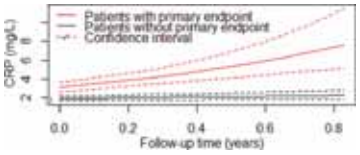
Purpose: C-reactive protein (CRP) is an inflammatory marker with prognostic value in chronic heart failure (CHF) patients. We aimed to investigate long-term CRP patterns in CHF patients, as well as their value for determining prognosis.
Methods: From 2011 to 2013, 263 ambulant CHF patients were included in 2 hospitals in our country. CRP was measured at baseline and every 3 months. The primary endpoint (PE) comprised heart failure (HF)-hospitalization and cardiovascular mortality. The association between CRP pattern and the PE was assessed by a statistical method that combines a mixed model, describing temporal evolution of CRP, with Cox proportional hazards regression.
Results: Mean age was 67 (SD 13) years, 72% were men and 27% were in NYHA class III–IV. During a median follow-up of 1.0 (IQR 0.6-1.4) years 886 blood sam-

ples were drawn, with a median of 3 (IQR 2-5) per patient. The PE was reached in 41 patients (16%). Median baseline CRP was 2.0 (IQR 0.9-4.8) mg/L. Baseline CRP was higher in patients with PE than in patients without (3.3 (IQR 1.3-6.7) mg/L vs. 1.9 (IQR 0.8-4.1) mg/L; p=0.02). Age- and sex adjusted hazard ratio (HR) for doubling of baseline CRP was 1.32 (95% CI 1.08-1.62). In patients with a PE, age- and sex adjusted CRP increased linearly over time (figure). The median of the last CRP before a PE was 6.5 (IQR 2.6-12.1) mg/L. The temporal CRP pattern was associated with increased risk of PE: doubling of CRP over time resulted in 1.86 times increased risk (95% CI 1.43-2.49).



Temporal patterns of CRP.

Conclusions: Temporal patterns of CRP are associated with HF-hospitalizations and cardiovascular mortality in CHF patients. CRP increased linearly before the occurrence of an event, whereas in stable patients the CRP pattern remained steady over time.

P3674 | BEDSIDE
The prognostic value of plasma galectin-3 in chronic heart failure patients treated with mineralocorticoid receptor antagonists

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Objective: Galectin-3 (Gal-3) is considered as a myocardial fibrosis biomarker with prognostic value in heart failure (HF). Since aldosterone is a neurohormone with established fibrotic properties, we aimed to investigate if mineralocorticoid receptor antagonists (MRAs) would modulate the prognostic value of Gal-3.
Methods and results: In a cohort of 353 consecutive chronic HF patients admitted between 2007 and 2013, 127 received an MRA. Two equal groups were formed by propensity score matching, consisting of patients treated with an MRA (MRA-Plus, n=101) or not (MRA-Neg, n=101). Propensity scores differed by less than 0.25 of the standard deviation of the logit of the propensity score based on cardiovascular risk factors, clinical and biological parameters. Gal-3 levels were measured in baseline samples. The primary endpoint of all-cause mortality was reached in 31 out of 202 patients, with a median follow-up time of 1.13 years (range 0.01 to 6.17).
Median Gal-3 levels were similar in MRA-Plus (14.4 ng/mL; IQR 12.3 – 19.8) and MRA-Neg groups (14.0 ng/mL; IQR 9.9 – 19.3) (P=0.132). In multivariable Cox proportional hazard regression analysis Gal-3 was an independent predictor for all-cause mortality in both MRA-Plus (HR 5.80; 95% CI 1.98 – 16.95, P=0.001).and MRA-Neg groups (HR 5.00; 95% CI 1.36 – 18.40, P=0.016).
Survival analysis showed no significant difference between MRA-Plus and MRA-Neg groups in patients with low Gal-3 (≤17.8 ng/mL; P=0.509) as well as high Gal-3 (>17.8 ng/mL; P=0.5393).
Conclusions: Gal-3 has strong prognostic value in chronic HF, irrespective of treatment with MRAs. The significance of the observed lack of an interaction between Gal-3 and treatment effect of MRAs remains to be elucidated.

P3675 | BEDSIDE
The role of left ventricular global function index for the prediction of cardiac complications in thalassemia major

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Purpose: Cardiac complications are one of the main causes of death in thalassemia major (TM) patients. Recently, the MESA study showed the strong predictive value of the left ventricular global function index (LVGFI) evaluated by cardiovascular magnetic resonance (CMR) in the prediction of the of cardiovascular events. LVGFI is a functional parameter integrating structural as well as mechanical behaviour derived from the analysis of cine SSFP images.
We evaluated the predictive value of LVGFI and other CMR parameters for cardiac complications in thalassemia major (TM).
Methods: We followed prospectively 537 white TM patients enrolled in the MIOT network. Fifty patients were excluded from the analysis because a cardiac complication was present at the time of the first CMR. All prognostic variables associated with the outcome at the univariate Cox model were placed in the multivariate model and were ruled out if they did not significantly improve the adjustment.
Results: At baseline the mean age was 29.5±9.0 years and 222 patients were males. The mean follow-up time was 58±18 months. After the first CMR only the 37.8% of the patients did not change the chelation regimen or the frequency/dosage. We recorded 40 cardiac complications: 19 episodes of HF, 19 arrhythmias, all supraventicular hyperhyperkinetic, and 2 pulmonary hypertensions. A LVGFI<37% was a significant univariate prognosticator of cardiac complications (HR=3.42, 95%CI=1.56-7.52, P=0.002). The other significant univariate prognosticators were myocardial iron overload (MIO), atrial dilatation, ventricular dysfunction evaluated by the left ventricular ejection fraction (LVEF), and myocardial fibrosis. Serum ferritin and liver iron by T2* MR were not predictive factors for cardiac complications.
In the multivariate analysis the independent predictive factors were a LVGFI<37% (HR=3.08, 95%CI=1.32-7.20, P=0.010), an homogeneous pattern of MIO (compared to no MIO) (HR=3.95, 95%CI=1.56-10.04, P=0.001), and myocardial fibrosis (HR=3.45, 95%CI=1.68-7.09, P=0.001).
Conclusions: We detected few cardiac events thanks to a CMR-guided, patient-specific adjustment of the chelation therapy. A LVGFI<37%, severe and homogeneous MIO, and myocardial fibrosis identify patients at high risk of cardiac complications globally considered. Importantly, the dysfunction evaluated by the LVEF lose its predictive value for cardiac complications when included in a multivariate model.

P3676 | BEDSIDE
Heart failure epidemiology, management and prognosis in over 80 years old patients: A cohort study in the French national healthcare insurance database

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Aims: Part of over 80 year's old heart failure (HF) patients is increasing. These patients are poorly studied. The present study undertook a real-life analysis of various aspects of the evolution of over 80 yo HF patients' admissions in France between 2008 and 2011.
Methods and results: Analysis was based on the "General Sample of Beneficiaries", a continuously updated representative sample of the population covered by the French national health insurance system. All admissions with HF as principal diagnosis were selected for descriptive and survival analysis with 48 months' follow-up. Over 80 patients represented 53% of hospitalizations for HF. In over 80 patients in-hospital mortality was 11% and mean 12-, and 24-months survival 62.3% (range, 59.1-65.4) and 48.2% (44.8-51.5). Only prescription levels for beta-blockers (BB) (p=0.02) increased during the follow-up period. Only 5% of patients received associated angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARB) + BB + mineralocorticoid receptor antagonists (MRA). During this period there was no increase of ACEi and ACEi/ARB+BB+MRA prescription at discharge (p=0.48 and p=0.87, respectively). On multivariate analysis, atrial fibrillation [HR: 0.77 (0.65–0.91), p=0.003], female gender [HR: 0.80 (0.67–0.95), p=0.01] and the associations ACEi/ARB+BB+MRA [HR: 0.49 (0.29–0.85), p=0.01] and ACEi/ARB+BB [HR: 0.54 (0.43–0.68), p<0.001] were associated with improved survival, in contrast to denutrition [HR: 1.64 (1.27–2.13), p<0.001] and cardiogenic shock [HR: 3.11 (1.78–5.46), p<0.001].
Conclusion: These real-life HF data advance our knowledge of prognostic factors, management and the impact of implementing guidelines, which are often poorly followed in this population whereas the present study confirms their benefit.

P3677 | BENCH
Predictive value of circulating endothelial-derived apoptotic microparticles in patients with ischemic symptomatic moderate-to-severe chronic heart failure

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Background: Chronic heart failure (CHF) is considered as a leading cause of morbidity and mortality in worldwide. Endothelial dysfunction has been shown to play a critical role in the clinical manifestations of CHF. Recent studies suggested that injure of endothelial monolayer due to any reasons leads to dramatic increase of circulating level of endothelial-derived apoptotic microparticles (EMPs). We postulated that EMPs might be discussed as prognostic factors in CHF, but their predictive value in patients with symptomatic ischemic CHF has not been defined.
Aim: To evaluate the prognostic value of circulating endothelial-derived microparticles for cumulative survival in patients with ischemic CHF.
Methods: A total of 154 patients with ischemic symptomatic moderate-to-severe CHF were enrolled in the study on discharge from the hospital. Observation period was up to 3 years. Blood samples for biomarkers measurements were collected. Flow cytometry analysis for quantifying the number of EMPs was used. EMPs number for cumulative survival cases due to CHF was tested. Additionally, all-cause mortality, and CHF-related death were examined.
Results: During a median follow-up of 2.18 years, 21 participants died and 106

subjects were hospitalized repetitively. Medians of circulating levels of EMPs in survived and died patient cohort were 0.286 n/mL (95% confidence interval [CI] = 0.271-0.309 n/mL) and 0.673 n/mL (95% CI = 0.65-0.74 n/mL) (P<0.001). Number of circulating EMPs was distributed into Quartiles (Q): Q1 (<0.341 n/mL), Q2 (0.342-0.514 n/mL), Q3 (0.521-0.848 n/mL), and Q4 (>0.850 n/mL). ROC analysis has been shown that cut off point of EMPs number for cumulative survival function was 0.514 n/mL. Area under cure was 0.913 (Std. error = 0.025; 95% CI = 0.863-0.962), sensitivity and specificity were 89.6% and 69.7% respectively. It has been found a significantly divergence of Kaplan-Meier survival curves in patients with high quartile (EMPs number >0.514 n/mL) of EMPs numbers when compared with low quartiles. Using a stepwise model selection method for multivariable prediction model we have been investigated that EMPs number alone and combination of EMPs number with NT-pro-BNP remained statistically significant predictors for all-cause mortality, CHF-related death, and CHF-related rehospitalisations, whereas combination of EMPs with both NT-pro-BNP and LVEF did not.

Conclusion: Increased circulating EMPs associates with increased 3-year CHF-related death, all-cause mortality, and risk for recurrent hospitalization due to CHF.

P3678 | BEDSIDE
Prognostic impact of systolic blood pressure and its changes during titration of medication in patients with chronic heart failure with reduced ejection fraction

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Background: In patients with heart failure (HF), low systolic blood pressure (SBP) is a marker of poor prognosis. However, the prognostic impact of changes in SBP during titration of HF medical treatment is not well known.
Methods: Patients enrolled in the randomized, controlled multicenter Trial of Intensified Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF) with left ventricular ejection (LVEF) <45% [n=499, age 76±8 years, LVEF 30±8%] were included in this post-hoc analysis. The effects of baseline SBP and changes in SBP from baseline to 6 months during titration of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (RAS inhibitors) and beta-blockers on 18 months outcomes (survival, HF hospitalization-free survival) were examined.
Results: The mean ± SD baseline SBP in all patients was 118±18 mmHg. A lower baseline SBP was associated with higher mortality {hazard ratio (HR) 0.82 [95% confidence interval (CI) 0.78- 0.97] per 10mg increase, p=0.01}. Patients in the lowest quartile of SBP (SBP ≤105 mmHg, n=127) had a significantly higher risk of death (HR 1.78, 95% CI 1.17-2.70, p=0.007) than patients in the upper three quartiles (mean SBP =126±14 mmHg). The increase in SBP during titration of medication from baseline to 6 months was directly correlated with better outcome [HF hospitalization and death: HR 0.86, 95% CI 0.78- 0.95, per 10 mmHg increase; p=0.003], even after adjustment for LVEF, NT-proBNP, age and NYHA class. Patients in the lowest quartile of SBP with the SBP failing to increase by ≥10mmHg or to >105 mmHg were 3.2 times more likely (p<0.001) to die or be hospitalized for HF compared to others in the lowest quartile of SBD. In patients with baseline SBP>105 mmHg, a decrease in SBP by ≥10mmHg from baseline to 6 months was an independent predictor of adverse events (mortality: HR 2.49, 95% CI 1.21-5.11, p=0.01; death or HF hospitalization: HR 1.68, 95% CI 1.09-2.59, p=0.02) and this was not significantly influenced by changes in beta-blockers and RAS inhibitor doses.
Conclusion: In patients with HF low baseline SBP (≤105 mmHg) and a lack of increase in SBP by 10 mmHg or to >105 mmHg during titration of HF medication is a predictor of poor prognosis. In HF patients with SBP >105mmHg a decrease in SBP by ≥10mmHg during titration of HF therapy identifies those with poor outcome. The prognostic value of SBP and its changes was independent of other established risk factors.

P3679 | BEDSIDE
The third heart sound predicts mortality in heart failure with normal ejection fraction

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Background: Presence of the third heart sound (S3) is associated with impaired left ventricular (LV) function and acute decompensated heart failure. Previous large scale studies also characterized the prognostic role of S3 in heart failure (HF) patients with reduced ejection fraction (EF). Whether S3 provides long-term prognostic information in heart failure with normal EF (HFNEF) remains unknown. We currently test the hypothesis S3 predicts adverse outcomes in HFNEF.
Methods: We consecutively studied 290 acute heart failure patients (mean age 78±10 years, 39% male, NYHA class IIIorIV) with normal EF (EF≧50%, mean 60±6%). S3 was assessed by acoustic cardiography within 48 hours on admission. All patients were prospectively followed up for 1 year. End points were defined as 1) all-cause mortality; 2) heart failure related rehospitalization; 3) composite of 1) or2).
Results: S3 was detected in 48 (16.6%) patients. There were no differences between presence and absence of S3 groups in terms of gender, heart rates, history of IHD, COPD, PVD, AF, HT and medications. Patients with absence of S3 were older (79±10 vs. 74±13 year, p=0.013) and had higher SBP (155±39 vs. 138±28 mmHg, p=0.018). In Kaplan-Meier analysis, patients with presence of S3 had higher mortality (Log-rank Chi square = 10.956, p=0.001). In multivariate logistic regression which were adjusted for age, gender, BP, LVEF, history of IHD, COPD, HT, DM, AF, PVD and medications, S3 significantly predicted 1 year mortality from all causes (p=0.009, odd ratio (OR) 4.266, 95% CI: 1.443, 12.613), but didn't predict rehospitalization (p=0.689,OR 1.218,95%CI: 0.463, 3.204) and composite end points (P=0.054, OR 2.764, 95%CI: 0.983, 7.770).

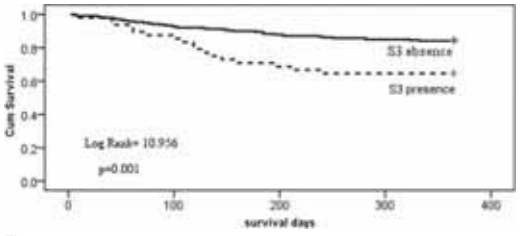

Figure 1

Conclusion: In HFNEF, S3 independently predicts 1-year mortality, but is not related to HF rehospitalizaiton.

P3680 | SPOTLIGHT
Impact of exercise training and testosterone replacement on skeletal muscle atrophy and muscle sympathetic nerve activity in heart failure patients with hypogonadism

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Purpose: Testosterone deficiency is common in advanced heart failure (HF) leading to skeletal muscle atrophy. Our hypothesis was that aerobic training alone or associated with testosterone replacement, could reduce skeletal muscle fiber atrophy and muscle sympathetic nerve activity (MSNA), improve body composition, functional capacity and quality of life (QoL) in patients with HF and hypogonadism.
Methods: Twenty-four patients, functional class III, total testosterone (<271 ng/dL) and free testosterone (<131pmol/L), ejection fraction (EF) <45% (Echocardiography), were randomized into 3 groups: Training (TR, n=9), Testosterone (T, n=8) and Training+Testosterone (TR+T, n=7). Patients performed pre and post 4 months: 1) MSNA, microneurography; 2) Biopsy, immunohistochemistry (vastus lateralis; type I and IIX fibers); 3) Body composition, dual X-ray absorptiometry; 4) Cardiopulmonary exercise on a bike and 5) QoL, Minnesota questionnaire. Exercise training on bicycle, 3 times/week, between anaerobic threshold and respiratory decompensation point, and undecylate testosterone (intramuscular).
Results: There was no difference between TR, T and TR+T groups for age (54±4, 51±4 and 52±3 years) and EF (28±2, 28±4 and 22±2%), respectively. MSNA decreased within TR+T (49±4 vs. 34±3 bursts/min; P<0.05) and TR (61±4 vs. 32±2 bursts/min; P<0.05). MSNA in bursts/100 heart beats decreased within TR+T group (80±7 vs. 50±4 bursts/100HB; P=0.05). Cross-sectional area (CSA) of type I fibers increased within TR+T group (2.487±329 vs. 3.637±347 μm, P=0.04). CSA of type I fibers increased in TR+T group compared to TR and T (3.637±347 vs. 2.567±238 vs. 2.628±178 μm; P<0.03, respectively). CSA of type IIX fibers was not different between groups. Lean mass increased within TR+T group (58±3 vs. 63±4 kg; P=0.02). Lean mass increased both TR and TR+T groups compared to T group (57±3 vs. 50±3 kg; P<0.001 and 63±4 vs. 50±3 kg; P<0.001, respectively). VO2 peak increased in TR, T and TR+T groups (14.76±1.60 to 18.06±2.26; 18.31±1.87 to 20.34±2.08 and 17.61±1.37 to 20.63±2.72 ml/kg/min; P<0.01, respectively). However, maximal power (Watts) increased in TR+T group (75±6 to 129±20 Watts; P=0.001) and it was higher compared to TR and T groups (129±20 vs. 87±8 vs. 73±18 Watts; P<0.01, respectively). QoL improved in TR and TR+T groups (57±7 to 23±6 and 70±7 to 13±3 score; P<0.03, respectively).
Conclusion: Although functional capacity improved in all groups, TR+T reduced skeletal muscle atrophy, decreased MSNA, improved lean muscle mass and QoL. This combined therapy signals a new approach to clinical management in HF patients.

P3681 | BEDSIDE

Dose target dose matter for outcome in systolic heart failure in the elderly (>75 years) ? analysis of 5-year cause-specific mortality and its relation with highest tolerated doses (dose-elderly)

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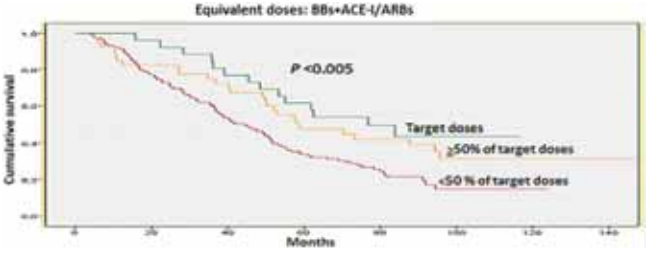
Objective: To identify the optimal doses of neurohormonal drugs in elderly patients (>80 years) with systolic heart failure

Methods: A total of 184 patients with systolic heart failure and left ventricular ejection fraction <40%, referred to our dedicated CHF outpatient clinic were consecutively included. No exclusions applied. All guideline-recommended medications were uptitrated to highest tolerable doses during at least 3 months period.

Results: 64% of patients were received <50% target doses of both agents (BBs and ACEI/ARBs),whereas only14% of patients received target doses of both agents. When only one agent is concerned, half of patients received <50% target dose of BBs and 21% received target doses for BBs. In case of ACE-I/ARBs, 26% received <50% target doses and 53% received target doses. In term of all cause mortality, those patients who received target doses had higher survival rate compared with those <50% target doses. But there was no difference, neither between target doses and ≥50% target doses nor between <50% target doses and ≥50% target doses. Above applies for either ACEI/ARBs or BBs. No significant differences founded in heart rate and NYHA class between different groups after up-titration. Comorbidities were studied witout any statistical significant differences between different dosegroups.



Kaplan-Meier survival curves.

Conclusion: Our findings demonstrate that target doses, regardless of BBs or ACEI/ARBs, are mostly effective in octogenarians (>80 years old), despite that this is only achievable in a small group. This is the case even for those reached highly tolerable dose but still less than target dose.Both heart rate and NYHA were comparable between different dose levels. This implies that if heart rate target has been achieved, target doses is more beneficial than other doses.

P3682 | BEDSIDE

Cardiovascular function and prognosis of patients with heart failure coexistent with chronic obstructive pulmonary disease

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Background: Chronic obstructive pulmonary disease (COPD) causes systemic inflammation and is frequently associated with cardiovascular diseases. COPD often coexists with heart failure (HF), and is considered to be associated with adverse outcomes in HF patients. However, cardiovascular function and detailed all-cause mortality of HF with COPD remain unclear.

Methods and results: Consecutive 378 patients admitted for HF who underwent spirometry were divided into 3 groups: HF without COPD (Non-COPD group, n=272), HF with mild COPD (GOLD I group, n=82), and HF with moderate COPD (GOLD II group, n=24). The GOLD II group, as compared to Non-COPD group, had higher serum troponin T level (P=0.009) and greater cardio-ankle vascular index (P=0.032). In contrast, BNP, right ventricular and right atrial areas, and systolic and diastolic function of the right and left ventricle did not differ between the two groups. In addition, rates of cardiac (P=0.049), non-cardiac (P=0.001), and all-cause mortality (P=0.002) were higher in GOLD II group than in Non-COPD and GOLD I groups. Importantly, in the Cox proportional hazard analyses, the GOLD stage II was an independent predictor of cardiac (P=0.038), non-cardiac (P=0.036), and all-cause mortality (P=0.015) in HF patients.

Conclusions: HF patients coexistent with moderate COPD (GOLD stage II) have greater myocardial damage, greater arterial stiffness, and higher cardiac and non-cardiac mortality.

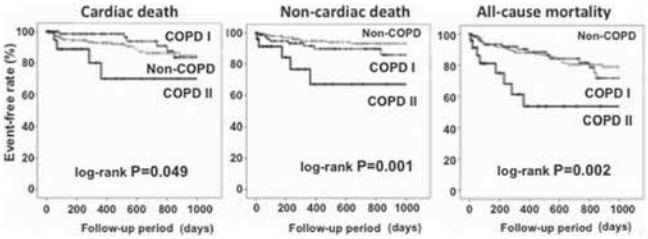

Figure 1. Kaplan-Meier curves.

P3683 | BEDSIDE

Worsening of renal function one year after discharge is a strong predictor of prognosis in ADHF patients

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Purpose: Renal dysfunction is one of the strongest risk factors for prognosis of acute decompensated heart failure (ADHF). In the real world, however, renal function is labile during the management of ADHF. Although some earlier works reported the analyses using the baseline serum creatinine level (SCr) or worsening of SCr during hospitalization, significance of worsening of renal function (WRF) after discharge is not investigated well.

Methods: Among 611 consecutive patients with ADHF who emergently admitted to our hospital between January 2007 and December 2012, we measured SCr three times (on admission, at discharge and one year after discharge) in 233 patients. The patients were divided into 2 groups according to WRF, defined as an absolute increase in SCr >0.3 mg/dl (>26.5 μmol/l) in combination with ≥25% increase in SCr at a year after discharge compared with the values at discharge.

Results: During a mean follow-up of 35.4 months, 48 patients showed WRF and 185 did not. There were 66 deaths from all causes, including 38 deaths from cardiovascular causes. Kaplan-Meier analysis showed that all-cause and cardiovascular mortality were significantly higher in patients with WRF than without WRF (log-rank P<0.0001 and P<0.0001, respectively) (Fig. 1). In a multivariate analysis with clinical and laboratory variables, including BNP, Hb and eGFR at discharge, WRF was the independent predictor for all-cause and cardiovascular death (HR, 2.42; 95%CI, 1.41-4.11; P=0.015, HR, 4.50; 95%CI, 2.23-9.25; P<0.0001, respectively). At discharge, Hb was lower (P=0.0336) and BNP was higher (P=0.0023) in patients with WRF.

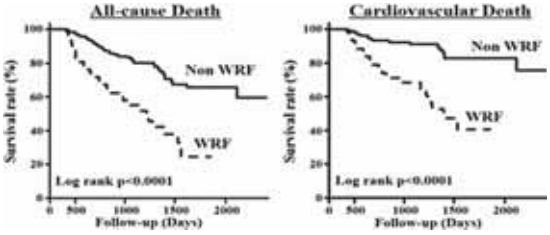

Figure 1. Kaplan-Meier survival curves.

Conclusions: Worsening of renal function after one year, not during hospitalization, is strong predictor of all-cause and cardiovascular mortality in patients with ADHF.

P3684 | BEDSIDE

Predictors of early and late readmission risk in outpatients with chronic heart failure

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Purpose: Prevention of hospital readmissions is a major challenge in the management of heart failure (HF). Most stratification models are based on data extracted from inpatients but information based on ambulatory HF patients is scanty. The aim of this study was to develop a score predicting 1-month and 1-year risk of readmission for worsening of HF and evaluate its performance based on gender and age.

Methods: A cohort of 2,507 ambulatory patients with chronic HF was prospectively followed for a median of 27 months. Clinical, echocardiographic, ECG, and biochemical parameters were used in a multivariable Cox model analysis to develop a risk score for readmissions for worsening of HF. Thereafter, the score predictors were assessed by gender and age.

Results: Predictors of 1-month readmission were: a) elevated NT-proBNP (>1000 ng/l), b) left HF signs and c) estimated glomerular filtration rate <60 ml/min/m^2. Predictors of 1-year readmission were: a) elevated NT-proBNP

(>1000 ng/l), b) anaemia, c) left atrial size >26 mm/m^2, d) heart rate >70 beats/minute, e) left HF signs and f) estimated glomerular filtration rate<60 ml/min/m^2. The Kaplan-Meier curves distinguished a low-risk group (<1% event rate) and a high-risk group (>5% event rate) for 1-month HF readmission risk, and a low-risk group (6% event rate), intermediate-risk group (17.3% event rate) and a high-risk group (29.5% event rate) for 1-year HF readmission risk. Stratifying the score by gender and age, our model performed better in males and middle-aged (<65 years old) patients, improving up the C-statistic index from 0.69 to 0.73 and from 0.68 to 0.69 for 1-month and 1-year readmission model, respectively.
Conclusions: Early and late readmission for worsening of HF can be predicted using proven prognostic variables that are routinely collected in outpatient management of chronic HF.

PROGNOSIS

P3686 | BEDSIDE
Low EPA/AA ratio was independent risk factor of non response to therapy with acute decompensated heart failure

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Background: Heart failure is characterized by several abnormalities of sympathetic cardiac activity that can be assessed by 123I metaiodobenzylguanidine single photon emission computed tomography (MIBG SPECT).
We investigated to predictor of responder for heart failure patients.
Method: From 2011 to 2012 consecutive 104 patients with ADHF (acute decompated heart failure) were enrolled.
After conventional therapy for ADHF, they were assessed by MIBG SPECT.We defined that RG (responder group) was BNP decreased under 200 within 2weeks, and NRG (non responder group) was over 200. we compared RG with NRG by multi factor (Gender, Age, 3%ODI, Smoker, Alcohol, CRF (Chronic renal failure), PAD (periph), AF, HTN, DM, Dyslipidemia, Obesity, EF <40%, post HM ratio <1.8, Eicosa Pentaenoic Acid (EPA) /Arachidonic Acid (AA) <0.3 (because median of it was 0.3.))
Results: Using multi-variant analysis, PAD (peripheral artery disease), DM (Diabetes Mellitus), Obesity, EF (Ejection Fraction) <40%, post Heart Mediastinum (HM) ratio <1.8, EPA/AA ratio were remained independently associated with RG (BNP <200 within 2 weeks).
OddsRatio (OR) of PAD was 16.4, (95% CI was 1.8 to 332; p=0.01) and OR of DM was 4.6, (CI: 1.2 to 22.5; p=0.03). Furthermore, OR of EF <40% was 5.5, (CI: 1.4 to 25.7; p=0.01), OR of post HM ratio was 6.24, (CI: 1.5 to 32.3; p=0.01) and OR of EPA/AA ratio was (3.92, CI: 1.1 to 16.9; p=0.04).
Conclusion: Low EPA/AA ratio was independent risk factor of non response to therapy with acute decompensated heart failure, along with Low Output Syndrome, and post HM ratio <1.8.

P3687 | BEDSIDE
Prediction of mortality using quantification of renal function in acute heart failure: Direct comparison of four formulas estimating glomerular filtration rate

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Background: Renal dysfunction increases the risk of death in acute heart failure (AHF). Four different formulas (Cockroft-Gault, MDRD-4, MDRD-6, CKD-EPI) have been developed to estimate glomerular filtration rate (eGFR). It is unknown, wether is superior to predict death in AHF.
Methods: 1104 unselected AHF patients presenting to the Emergency Department were enrolled (55% men; median age 79 years, IQR: 70 to 85 years), with a median left ventricular ejection fraction of 45% (IQR: 30% to 58%). Serum creatinine was measured at presentation. Renal insufficiency was defined as eGFR<60ml/min/1.73m^2. The primary objective was to evaluate the accuracy of the different eGFR equations to predict short-term (90 days) and long-term mortality risk. The median follow-up period was 363 days (IQR: 221 to 679 days).
Results: Over the study period 445 patients (40.3%) died, 148 of them (13.4%) within 90 days. All four eGFR equations were independent predictors of 90-day mortality and long-term mortality. When comparing the eGFRs derived with the four formulas with each other, Cockcroft-Gault showed statistically significant higher prognostic accuracy for both short- and long-term risk of death as quantified by the area under the time-dependent receiver operator characteristic curve, which was significantly higher for the Cockroft-Gault formula (0.70 vs 0.65 in MDRD-4 with 90 days cut-off time, and 0.64 vs 0.61 in MDRD-4 with 2 years cut-off time, p<0.05). These findings were confirmed in the predefined subgroups of women, patients with severe systolic left ventricular dysfunction and the elderly. MDRD-6 had the lowest accuracy.
Conclusion: In patients with AHF, Cockcroft-Gault formula was the most accurate for predicting short- and long-term mortality.

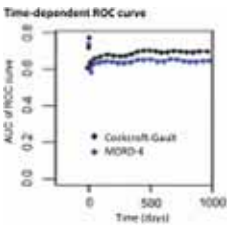
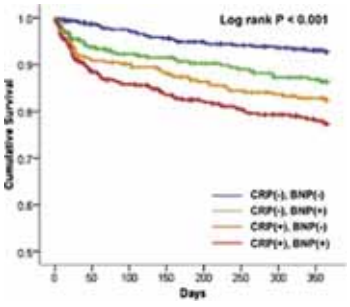


Figure 1

P3688 | BEDSIDE
Prognostic value of C-reactive protein as an inflammatory and N-terminal probrain natriuretic peptide as a neurohumoral marker in acute heart failure (from the korean heart failure registry)

J.J. Park[1], D.-J. Choi[1], C.-H. Yoon[1], I.-Y. Oh[1], S.-J. Park[2], E.-S. Jeon[1], J.-J. Kim[3], M.-C. Cho[4], S.C. Chae[5], K.-H. Ryu[6] on behalf of the KorHF Registry. *[1]Seoul National University Bundang Hospital, Division of Cardiology, Seongnam, Korea, Republic of; [2]Samsung Medical Center, Seoul, Korea, Republic of; [3]Asan Medical Center, Seoul, Korea, Republic of; [4]Chungbuk National University College of Medicine, Cheongju, Korea, Republic of; [5]Kyungpook National University Hospital, Daegu, Korea, Republic of; [6]Konkuk University Hospital, Seoul, Korea, Republic of*

Purpose: The neurohumoral and inflammatory pathways are regarded as the main mechanisms for the progression of heart failure. We sought to investigate the prognostic value of high sensitivity C-reactive protein (hs-CRP) and N-terminal probrain natriuretic peptide (NTproBNP) by evaluating their relation with 12-month mortality rate in the Korean Heart Failure (KorHF) registry.
Methods: KorHF registry is a Korean, prospective, multicenter registry designed to reflect "real world" clinical data of Korean patients admitted for AHF (June 2004 to April 2009, n=3,200).
Results: In 1,608 patients with acute heart failure (AHF), the median hs-CRP and NT-proBNP values were 0.77 mg/dl (interquartile range 0.29 to 2.84) and 4,638 pg/ml (interquartile range 1,945 to 10,852), respectively. During the 12-month follow-up, 213 patients (13.3%) died. The mortality rate increased from the lowest to the highest hs-CRP quartiles (Q1 7.4%, Q2 9.5%, Q3 16.9%, Q4 19.3%, p<0.001) and NT-proBNP quartiles (Q1 7.0%, Q2 13.4%, Q3 11.6%, Q4 20.4%, p<0.001). After adjustment, both hs-CRP (hazard ratio [HR] 1.811, 95% confidence interval [CI] 1.138 to 2.882) and NT-proBNP (HR 1.971, 95% CI 1.219 to 3.187) were independent predictors of 12-month mortality among others. When combining both hs-CRP and NT-proBNP and stratifying the patients according to their median values, patients with elevation of both hs-CRP and NT-proBNP values had 2.4-fold increased hazards (HR 2.382, 95% CI 1.509 to 3.761) compared with those without elevation of both markers.



Twelve-month mortality

Conclusions: In Korean patients with AHF, patients with increased levels of both hs-CRP and NT-proBNP had worse clinical outcomes. The combination of the neurohumoral and inflammatory markers may provide a better strategy for risk stratification of Asian patients with AHF.

P3689 | BEDSIDE
Prothrombin activity is a novel and powerful prognostic marker in patients not taking oral anticoagulants with acutely decompensated heart failure

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Background: Where prothrombin activity is used to monitor patients on anticoagulation, it is a universal indicator of liver disease severity. Although liver congestion is caused by and prothrombin activity is known to be decreased in heart failure, its significance in patients with acutely decompensated heart failure (ADHF) has not been clarified. The present study was conducted to investigate the impact of prothrombin activity on cardiovascular outcomes in patients with ADHF from prospective registry of our institution.
Method: Of 280 consecutive patients admitted for ADHF, subjects who were not taking oral anticoagulants including vitamin K antagonists, direct thrombin

inhibitors, and direct factor Xa inhibitors on arrival at hospital were examined. Heparin was not administered to any patients before blood collection. Patients with known history of liver disease were excluded from the analysis, and consequently, a total of 150 patients was enrolled in the study. Patients' basic characteristic data including sex, age, past medical history, medications, as well as blood exam results, were analyzed. The primary endpoint was a composite of all-cause death or readmission for heart failure.
Results: Of the 150 patients (77±12 years, 95 male), 17 patients (11%) underwent adverse cardiovascular event including death or hospital readmission for heart failure during a mean follow up period of 157 days. There were no significant differences in age, sex, use of ACE inhibitors/ARB and β-blockers, serum Na, creatinine and hemoglobin levels between patients with adverse event and those without. Prothrombin activity was significantly lower in the event group (59±5% vs. 85±2%, $p<0.0001$). Kaplan-Meier survival curves demonstrated that decreased prothrombin activity of <70% was associated with poor clinical outcome in ADHF patients ($p=0.004$). Cox proportional hazards regression analysis showed that decreased prothrombin activity is an independent predictor of cardiovascular event (OR=3.8, $p=0.02$) among variables including age, sex, serum Na concentration, serum creatinine, and plasma brain natriuretic peptide levels, and left ventricular ejection fraction.
Conclusion: Decreased prothrombin activity on admission is a novel and powerful predictor of short-term adverse cardiovascular outcome in ADHF patients without anticoagulants, suggesting the impact of liver dysfunction on disease process of heart failure.

P3690 | BEDSIDE
Low T3 syndrome: a strong predictor of mortality in patients with acute decompensated heart failure

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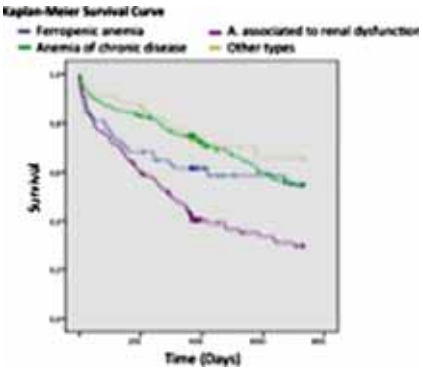
Low thyroid hormone concentration, in particular low T3 serum levels, is a common finding in critically ill patients, including those with cardiac disorders. This non-thyroidal illness syndrome has been associated with an adverse prognosis.
Aims: To assess low T3 concentration impact in prognosis of patients admitted for NYHA class III/IV acute decompensated heart failure.
Methods: Three hundred and forty eight consecutive patients were included in the analysis. Demographic and clinical variables were analyzed. Thyroid tests were measured at admission. Low T3 syndrome was defined as T3 concentration <0.79 ng/ml. In-hospital and 90-day prognosis were reported.
Results: Low T3 serum concentration was detected in 239 patients (68.6%). TSH concentrations did not differ between patients with low or normal T3 levels (median 2.1 and 2.08, respectively, p=NS). Patients with low T3 were older (70.3 vs. 64.6 years old, respectively, $p<0.05$), with worse prior renal function ($p<0.05$), more hyponatremia (Na+<136 meq/L) (52.4 vs 33.7%, respectively, $p<0.01$) and more anemia (40.3 vs. 24.3%, respectively, $p<0.01$). No differences were noticed in cardiac rhythm and heart rate at admission. Left ventricular function was similar in both groups.
Regarding treatment, 22.9% of patients were on amiodarone at admission. Patients with low T3 were more frequently treated with amiodarone than those with normal thyroid status (28 vs 17%, respectively, $p<0.05$). More in-hospital complications were observed among patients with low T3, including worsening heart failure (22.6 vs. 12.1%, $p<0.05$).
In-hospital mortality was 8.6%; and 12.4% at 90 days.
Independent predictors of death at 90 days were low T3 (OR 3.93 – 95%CI 1.5 – 10.3, $p<0.005$), diuretic resistance (OR 3.32, 95%CI 1.23–8.4, $p=0.01$) and use of inotropes (OR 3.18, 95%CI 1.1–8.8, $p<0.05$). Although low T3 was associated with a higher number of in-hospital deaths (28 vs. 2 patients, respectively, OR 5.04; 95%CI 1.1–22.9; $p<0.05$), neither mortality nor re-admission differences were detected after discharge.
Conclusion: Abnormal thyroid function is prevalent among NYHA class III/IV patients admitted for acute decompensated heart failure. Low T3 level at admission is strongly associated with adverse events and mortality during hospitalization. Whether thyroid dysfunction is an adaptative mechanism or contributes to worsening/ exacerbation of cardiac disease is not well understood, yet.
It seems it is time to encourage safety and efficacy assessment of thyroid T3 and/or T4 replacement in this high risk population.

P3691 | BEDSIDE
Does the etiology of anemia matter regarding its impact on survival in acute heart failure? Insights from a prospective study

Z.L. Moreno Weidmann, R. Twerenbold, F. Stallone, T. Herrmann, K. Pershyna, L. Krivoshei, Y. Tanglay, C. Mueller. *University Hospital Basel, Cardiovascular Research Institute of Basel (CRIB), Basel, Switzerland*

Background: Anemia is associated with worse survival in patients with acute heart failure (AHF). However, it is unknown whether the etiology of anemia matters regarding its impact on survival. Our aim was to examine the association among different types of anemia and short-term (90 days) and long-term (2 years) survival.
Methods: In a cohort of 1159 unselected patients with AHF (43% women, median age 80 years) enrolled in a prospective study, 497 (43%) had anemia. Median hemoglobin were 100g/l (interquartile range: 100 to 117g/l), 15% of them had a hemoglobin <80g/l. Logistic regression, Kaplan-Meier survival analyses and Cox regression were used to assess the association of anemia subtypes with survival.
Results: According to their analytic characteristics, patients were categorized in four groups: 13% ferropenic anemia, 45% anemia of chronic disease, 30% associated to renal dysfunction and 12% other type. Hemoglobin levels were similar in the four predefined groups. Overall, survival was 88% at 90 days and 56.5% at two years follow up. When comparing the four types, ferropenic anemia and anemia associated to renal dysfunction had statistically significant lower survival rates as compared to the two other subtypes ($p<0.01$). These findings remained statistically significant after adjusting for renal function, left ventricular systolic function, age and other comorbidities.



Conclusion: Etiology of anemia should be considered as an important modifier of the impact of anemia on survival in patients with AHF.

P3692 | BEDSIDE
Lessons from acute decompensated heart failure patients in korea (KorAHF) registry

S.E. Lee[1], H.J. Cho[1], H.Y. Lee[1], E.-S. Jeon[2], J.-J. Kim[3], S.-H. Baek[4], S.-M. Kang[5], D.-J. Choi[6], S.C. Chae[7], B.-H. Oh[1] on behalf of KorAHF Investigator. *[1]Seoul National University Hospital, Internal medicine, Seoul, Korea, Republic of; [2]Samsung Medical Center, Internal medicine, Seoul, Korea, Republic of; [3]Asan Medical Center, Internal medicine, Seoul, Korea, Republic of; [4]Seoul St. Mary's Hospital, Internal medicine, Seoul, Korea, Republic of; [5]Yonsei Cardiovascular Center, Cardiology, Seoul, Korea, Republic of; [6]Seoul National University Bundang Hospital, Internal medicine, Seongnam, Korea, Republic of; [7]Kyungpook National University Hospital, Internal medicine, Daegu, Korea, Republic of*

Background: The prevalence of heart failure has been rapidly increasing in Korea and its influence on mortality, morbidity and the cost of health care is growing fast. To reduce the health burden of heart failure and to improve the care system and clinical guidelines, it is essential to verify the patients' profile, current trends of management, and outcome.
Objectives: Korean acute heart failure registry aims to evaluate clinical characteristics, management, hospital course, predictors of mortality, and short-term and long-term outcomes of patients hospitalized for acute heart failure syndrome (AHFS) in Korea.
Methods: The patients hospitalized for AHFS in ten tertiary university hospitals have been consecutively enrolled between March, 2011 and July, 2013. The study is expected to complete the enrollment of at least 5,000 patients in 2014 and to follow up until 2016. This analysis was performed to investigate the baseline characteristics, management, short-term outcomes and predictors of in-hospital mortality.
Results: 4,183 patients were analyzed at this moment. The mean age was 69±14 years old; 54% were male; 51% were de novo HF; 59% had underlying hypertension; 35% had diabetes mellitus. 83% of patients presented with NYHA III-IV dyspnea and the mean left ventricular ejection fraction (EF) was 39±16%. Ischemia was both the leading cause (38%) of HF and the most frequent aggravating factor (24%). Parenteral diuretics and inotropes were administered in 74% and 32% of patients, respectively. Angiotensin converting enzyme inhibitors/angiotensin receptor blockers and beta-blockers were prescribed at discharge in 66% and 49% of the patients, respectively. The mean length of hospital stay was 9 days and mean cost for an admission was about 9,164,200 Korean Won. In-hospital mortality was 6.14% (including 1.38% of patients who underwent urgent heart transplantation). After discharge, 90-day mortality was 4.2% and rehospitalization was 15%. Multivariable logistic regression revealed that lung congestion, renal failure, Q wave, RBBB, SBP<100 and Na<135 were important predictors for in-hospital mortality. In subgroup analysis, in contrast to HFrEF (≤40%), patients with HFpEF (≥50%) were predominantly female and showed different predictors of poor outcome.
Conclusion: The data from KorAHF demonstrate specific characteristics of AHFS in Korea, an unmet need for analysis of patient heterogeneity and socioeconomic burden of hospitalization. Therefore, findings of KorAHF may have important therapeutic implications to improve outcome of AHFS.

P3693

ABSTRACT WITHDRAWN

P3694 | BEDSIDE
Prognostic value of Tpeak-Tend interval in patients with acute heart failure syndrome

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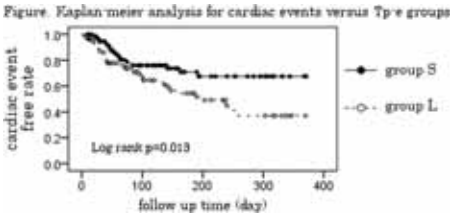
Purpose: Recently it has been reported that long Tpeak-Tend interval (Tp-e) is associated with the occurrence of life-threatening arrhythmias. However, little is known about whether Tp-e predicts prognosis in acute heart failure (HF) patients. We investigated the relation between Tp-e and prognosis in acute HF syndrome patients.
Methods: From January 2013 to November 2013, a total of 201 consecutive acute HF patients (86 males, mean age of 78.4 years) were enrolled. The patients were divided into two groups on the basis of the Tp-e on admission: group L (n=102, Tp-e $\geq$ median: 108ms) and group S (n=99, Tp-e $<$ median). We followed up all patients for the occurrence of cardiac events: cardiac deaths and re-hospitalizations for worsening HF. The mean follow up period was 161days.
Results: The mean of left ventricular ejection fraction (EF) was 43.6% and plasma brain natriuretic peptide (BNP) level was 1083pg/ml. There were no significant difference in age, sex or EF between group L and S. Plasma BNP level was significantly higher in group L than that in group S (p=0.037). During follow up periods, 30 patients in group L and 18 patients in group S experienced re-hospitalization for worsening HF. Cardiac death occurred in 14 patients in group L and 4 patients in group S. Three patients in group L and 2 patients in group S experienced life-threatening arrhythmias. The probability of cardiac event-free survival in group L was significantly lower than that in group S (Figure). Multivariate analysis identified Tp-e as an independent predictor of cardiac events (hazard ratio, 1.98; 95% confidence interval, 1.17 to 3.35; p=0.011).
Conclusion: The long Tpeak-Tend interval is a potentially useful indicator of poor prognosis in patients with acute HF syndrome.



P3695 | BEDSIDE
Rapid shallow breathing worsens prior to heart failure decompensation

A. Capucci[1], G. Molon[2], M.R. Gold[3], Y. Zhang[4], R. Sweeney[4], V. Averina[4], J.P. Boehmer[5] on behalf of MultiSENSE Study investigators. *[1]Università Politecnica delle Marche, ancona, Italy; [2]Sacro Cuore hospital, negrar, Italy; [3]Medical University of South Carolina, Charleston, United States of America; [4]Boston Scientific, St Paul, United States of America; [5]Penn State Milton S. Hershey Medical Center, Hershey, United States of America*

Introduction: Respiratory distress is one of the primary drivers for heart failure (HF) hospitalization. Respiratory rate (RR) and minute ventilation (MV), as monitored by implanted devices, have demonstrated changes leading to admissions. Since patients often present with rapid shallow breathing, we hypothesize that a rapid shallow breathing index (RSBI) will better reflect respiratory distress than either RR or MV.
Method: Multisensor Chronic Evaluations in Ambulatory Heart Failure Patients Study (MultiSENSE) enrolled patients implanted with cardiac resynchronization therapy devices. The device was reprogrammed to trend RR and tidal volume (TV) derived from transthoracic impedance. MV and RSBI were calculated as MV = RR'TV, RSBI = RR/TV. HF events (HFEs) were defined as HF admissions or unscheduled visits with intravenous HF treatment. All HFEs were adjudicated. For each HFE, the average of a 7-day pre-event period (Evt) and a baseline period (BL, 35 to 63 days pre-event) were calculated. Percentage change (% chg = [Evt-BL]/BL) was determined for each event. The mean % chg was tested against 0 using paired t-test ($p<0.05$).
Results: Fifty-two of the 528 patients enrolled (age 66.4±10.8, 72.7% male, EF 29.3±11.5%) experienced 69 HFEs. Daily mean RR was elevated significantly prior to HFEs (3.4%, p=0.005) while daily mean TV and MV did not change significantly (-1.7% and 0.4% respectively). Daily RSBI showed the largest change among all respiratory parameters, and increased by 5.0% (p=0.012).

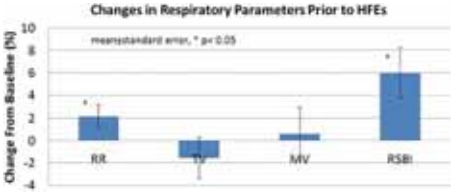


Figure 1. Respiratory signal changes prior to HFEs.

Conclusion: Data from MultiSENSE study showed that rapid shallow breathing measured by RR and RSBI changed significantly before HF events, suggesting that these measures might be useful in early identification of worsening heart failure status.

STRUGGLES WITH THE LIPID-GUIDELINES IN CLINICAL PRACTICE

3816 | BEDSIDE
Is it really necessary to review the role of statin therapy in primary prevention? Application of the new ACC/AHA guidelines on blood cholesterol on a population registry

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Purpose: The new guidelines of the American College of Cardiology (ACC) and American Heart Association (AHA) on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk significantly expand the indications for statin therapy in primary prevention. Our aim is to: (1) inquire, in a wide population registry, the percentage of individuals who should have been under statin therapy for primary prevention according to the novel ACC/AHA guidelines; (2) determine the relative risk reduction of 10-year ASCVD that could be obtained if these individuals had had optimal control of total cholesterol levels.
Methods: Employing our center's registry on acute coronary syndrome (ACS), we estimated the number of individuals who should have been previously put on statin therapy for primary prevention according to their risk factors. We stratified our population on the 3 groups established by the ACC/AHA guidelines for primary prevention: (group 1) any individual with $\geq$21 years of age and LDL $\geq$190mg/dL; (group 2) diabetic individuals aged between 40-75 years with LDL 70-189 mg/dL; (group 3) non-diabetic individuals aged between 40-75 years with

LDL 70-189 mg/dL and 10-year atherosclerotic cardiovascular disease (ASCVD) risk ≥7.5% estimated by pooled cohort equations delivered by the ACC/AHA. The pooled cohort equation to calculate the 10-year ASCVD considers: age, sex, race, total cholesterol level, HDL-cholesterol level, systolic blood pressure, anti-hypertensive drug therapy, diabetes and smoking.
Results: A total of 1154 patients (P) were included in this study. We identified 792 P (68.6%) who fell in one of the 3 groups highlighted above who meet criteria for statin therapy in the context of primary prevention. The percentage of P who should have been under statin therapy and were not was: 90.5% for group 1 (124 P), 88.9% for group 2 (126 P), 85.6% for group 3 (456 P). Assuming that an optimal cholesterol level could have been reached with statin therapy, this would have represented a 12.1% relative risk reduction on 10 year ASCVD for these individuals.
Conclusions: This study suggests that a large percentage of individuals who suffer ACS and had no prior cardiovascular event should have been previously placed on primary prevention with statin therapy if the new ACC/AHA guidelines had been followed. The impact of optimally controlled cholesterol levels in these individuals would be a 12.1% relative risk reduction on 10-year ASCVD.

3817 | BEDSIDE
Treat dyslipidemia according to current ESC/EAS and recent ACC/AHA guidelines: evidence from a lipid clinic

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Purpose: There is a paucity of data regarding attainment of goals of lipid-lowering treatment according to current European (ESC/EAS) and recent American (ACC/AHA) guidelines. Therefore, we aimed to assess the "reality" of achieving these targets in subjects attending an Outpatient University Hospital Lipid Clinic.
Methods: This was an observational study of subjects treated for dyslipidemia. A total of 1,000 adult individuals consecutively referred and followed-up for a period of at least 3 years were studied. The proportion of patients achieving LDL-C targets according to ESC/EAS guidelines were recorded, along with the percentages of appropriate lipid-lowering treatment proposed by ACC/AHA guidelines. In this study, SCORE was used instead of 10-y atherosclerotic cardiovascular disease (ASCVD) risk calculation. As it has recently been reported, a risk of ASCVD event of 7.5%, would correspond to a 2.5% risk for cardiovascular (CV) death in 10 years according to the SCORE model.
Results: A total of 1,000 subjects were studied. Of those, 48% were considered "very high", 41% "high" and 11% "moderate" CV risk according to ESC/EAS guidelines. LDL-C targets were achieved in 25%, 52% and 57% of patients, respectively.
According to the American guidelines, 21% of patients were diagnosed with ASCVD. Almost half of these patients with age ≤75 years were receiving "high"-intensity statin, while 32% and 61% of those being older than 75 years were on "high"- and "moderate"-intensity statin, respectively. Of patients without ASCVD and baseline LDL-C ≥190 mg/dL (28%), 45% were treated with "high"-intensity statin. Of patients with type 2 diabetes, age 40-75 years and baseline LDL-C 70 – 190 mg/dL (6%), 58% had a SCORE ≥2.5%. Of those, 24% were on "high"-intensity statin, while 21% and 67% of those having SCORE <2.5% were treated with "high"- and "moderate"-intensity statin, respectively. Finally, 12% and 74% of patients with SCORE ≥2.5% not classified as above (14%), were receiving "high"- and "moderate"-intensity statin, respectively.
Conclusion: In the setting of a specialized lipid clinic, 25% of patients at "very high" and almost 50% of those at "high" and "moderate" risk achieve therapeutic goals according to the European guidelines. On the other hand, the proportions patients receiving "appropriate-intensity" statin therapy according to ACC/AHA guidelines are relatively high in all patient groups.

3818 | BEDSIDE
To what extent do high-intensity statins reduce low-density lipoprotein cholesterol in the four statin benefit groups identified by the ACC/AHA 2013 guidelines? A VOYAGER meta-analysis

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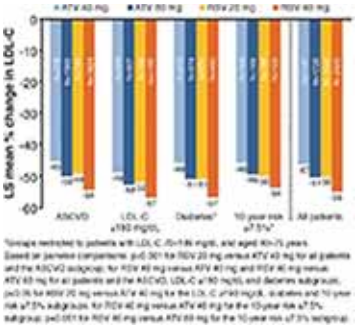
Introduction: The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines identify 4 patient groups who benefit from moderate- or high-intensity statin treatment: 1) atherosclerotic cardiovascular disease (ASCVD); 2) baseline LDL-C ≥190 mg/dL; 3) diabetes; and 4) 10-year ASCVD risk ≥7.5% (no ASCVD or diabetes). High-intensity statins, anticipated to reduce LDL-C by ≥50%, are rosuvastatin (RSV) 20–40 mg and atorvastatin (ATV) 40–80 mg.
Objectives: Individual patient data (n=32,258) from the VOYAGER meta-analysis of 37 studies are used to analyse LDL-C reduction with these doses in each statin benefit group.
Methods: The least-squares mean (LSM) % change from baseline in LDL-C was compared during 8496 patient exposures to RSV 20–40 mg, and ATV 40–80 mg in the 4 patient groups. Comparisons were made using a single mixed-effects model using only data from studies directly comparing treatments by randomised design. The analyses include only patients who would be candidates for high-intensity statin treatment based on the guidelines.
Results: LSM % reductions in LDL-C in all patients considered candidates for high-intensity statin and in the 4 statin benefit groups are shown in the figure. Reductions in LDL-C for RSV 20 mg and 40 mg were greater than for ATV 40 mg, overall and in each benefit group, and for RSV 40 mg were greater than for ATV 80 mg overall and in 3 of the 4 benefit groups (all $p<0.05$; figure). In the ASCVD group, 41%, 60%, 58% and 71% treated with ATV 40 mg, ATV 80 mg, RSV 20 mg and RSV 40 mg had a ≥50% reduction in LDL-C from baseline, with similar results seen in the other groups.



Conclusions: The choice and dose of statin has an impact on LDL-C reduction for patients requiring high-intensity statin therapy within each statin benefit group.

3819 | BEDSIDE
Statin treated patients at very high cardiovascular risk: Are the majority close to LDL-C <70 mg/dl?

A.K. Gitt[1], B. Ambegaonkar[2], P. Brudi[2], M. Horack[3], B. Vanneste[2], D. Lautsch[4] on behalf of DYSIS-Study-Group. *[1]Herzzentrum Ludwigshafen + Institut f. Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany; [2]Merck, Whitehouse Station, United States of America; [3]Institut f. Herzinfarktforschung Ludwigshafen, Ludwigshafen am Rhein, Germany; [4]Merck, Vienna, Austria*

Background: International societies such as the EAS, ESC and IAS set the recommendation for LDL-C to be <70 mg/dl in cardiovascular very high risk patients. It is unknown how many % of statin treated patients actually reach various thresholds. We further evaluated the median distance to this treatment target.
Objectives: EAS/ESC guidelines for dyslipidemia and the IAS position paper recommend a LDL-C treatment target of <70 mg/dl for patients at very high cardiovascular risk. We evaluated whether statin treated patients reach LDL-C <70 mg/dl or a less stringent threshold of <100mg/dl as per country treatment targets in place when the data were collected.
Methods: The cross sectional, observational study DYSIS examined lipid goal attainment among statin-treated (monotherapy as well as combination therapy) patients in Canada, Europe and Middle East countries at very high cardiovascular risk due to suffering from coronary heart disease, diabetes, chronic kidney disease or peripheral atherosclerotic disease.
Results: 26,846 patients were at very high cardiovascular risk defined by guideline criteria. 20.3% reached the treatment target <70 mg/dl, while 68.8% had LDL-C levels >80 mg/dl, 62.9% >85 mg/dl; 55.1 44.9% >100 mg/dl and 29.1% >115 mg/dl. Mean LDL-C was 100,6±37,5 mg. Statin (various molecules) doses equivalent to simvastatin 20 mg and 40 mg were predominantly used (34.2% and 37.2%); higher doses of statins were used in 17.0% and combination of statin with ezetimibe use was 11.7%. In the 19.648/24.651 patients who did not reach the current treatment target, median distance to LDL-C <70 mg/dl was 34,0 mg/dl (IQR 16,0,-58,0mg/dl).
Conclusions: Despite ongoing statin therapy, the large majority of patients at very high cardiovascular risk who participated in DYSIS did not reach the <70 mg/dl threshold. Distance to target was substantial (34 mg/dl) and likely could be reduced with strongly intensified therapy such as higher dose statins and/or in combination with cholesterol absorption inhibition.

3820 | BEDSIDE
Association between statin pre-treatment and LDL-C levels on the incidence of STEMI presentation among ACS patients: data from the ACS Israeli survey (ACSIS) 2002-2010

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Background: STEMI is thought to occur as a result of vulnerable coronary plaque rupture. Statins posses hypolipidemic and pleotrophic effects and can stabilize coronary plaque.

Aim: To determine the association between LDL-C levels,with or without statin use on the presentation of patients with ACS (STEMI/NSTEMI).
Methods: Data was drawn from the Acute Coronary Syndrome Israeli Survey (ACSIS), a biennial survey with data on all ACS patients hospitalized in all CCU/Cardiology departments in Israel.Data from years 2002-2010 was used.The incidence of STEMI presentation was calculated according to LDL-C levels on admission and statin use prior to the index event.
Results: Among 6793 ACS patients, 2761 (41%) were on statin and 4032 were statin naïve prior to the index event.The proportion of STEMI vs NSTEMI at presentation was significantly lower among statin treated vs. statin naïve patients (35.5% vs. 57.3%, $p<0.0001$).
At each LDL-C level, the proportion of STEMI was significantly lower among patients on statins (Table, $p<0.0001$ for all comparisons).
LDL-C<70mg/dl was associated with a lower proportion of STEMI presentation only in patients on statin, but not in statin naïve patients (33.1% vs. 56.9%, $p<0.0001$).Multivariate analysis (adjusting for the propensity score for statin use including baseline pertinent variables,chronic medications,statin use and LDL-C levels)revealed that statin use was independently associated with lower STEMI presentation (OR=0.79, $p<0.0001$), but LDL-C<70mg/dl was not (OR=1.16, p=0.27). Similar results were obtained when analyzing separately patients with or without prior cardiovascular disease.

	LDL-C (mg/dl)					
	<50	50–69	70–100	101–130	>130	All
Patients on statin	(n=132)	(n=430)	(n=1053)	(n=668)	(n=478)	(n=2761)
STEMI (n,%)	38 (28.8)	148 (34.4)	354 (33.6)	235 (35.1)	207 (43.3)	982 (35.5)
Statin naïve patients	(n=70)	(n=199)	(n=898)	(n=1037)	(n=1558)	(n=4032)
STEMI (n,%)	38 (54.3)	115 (57.8)	496 (55.2)	771 (74.3)	892 (57.3)	2312 (57.3)

Conclusions: In patients with ACS, statin use but not LDL-C level is associated with lower incidence of STEMI. These findings can be explained by the pleotropic effect of statins.

3821 | BEDSIDE
The theoretical effect of the use of high intensity statin doses on the 1.8 mmol/l LDL-cholesterol goal attainment rate in the MULTI GAP 2013 study

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Aim: The American guidelines are of primary relevance for the rest of the world. For the past several years there has been a great expectation for the appearance of the ATP IV guideline. Two major issues of the joint recommendations of the ACC/AHA cholesterol announced in the fall of 2013 were the rejection of the treatment target values and nomination of statins intensity groups. In the present paper there were investigated that using the data of an observational study the what would be the 1.8 mmol/l LDL-cholesterol achievement rate in patients with cardiovascular event taking high intensity statins.
Methods: In the MULTI-GAP (MULTI Goal Attainment Problem) surveys conducted annually since 2007 the effectiveness of lipid lowering therapies among high-risk patients was monitored by retrospective data analysis using structured questionnaires. From MULTI GAP 2013 we used the data of patients taking 20 or 40 mg rosuvastatin and 40 or 80 mg atorvastatin.
Results: The mean LDL-cholesterol level of the 1712 patients of MULTI GAP 2013 was 2.64 mmol/l, the 1.8 mmol/l goal achievement rate was 21,2%. The number of patients and 1.8 mmol/l attainment rate in groups taking 10, 20, 40 mg rosuvastatin 103, 256, 68, and 25.2%, 20,3% 22.1%, respectively. In the groups 20, 40, 80 mg atorvastatin were 186, 240, 49, and 21,0%, 23.3% and 20,4%, respectively.
Conclusions: The 1.8 mmol/l LDL-cholesterol goal attainment is very poor in the MULTI GAP 2013. The statins doses were selected according to the baseline cholesterol levels. In a theoretical use of 'high intensity statin doses" in about half of patients presently taking low or moderate statin doses would effect a slightly better goal achievement but overall this rate remained very poor.

3822 | BEDSIDE
Titration of statins and adding ezetimibe could help to substantially increase target value attainment on a population level - a DYSIS based model

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Background: While achievement of recommended LDL-C levels is low in clinical practice, we evaluated how it could be increased by titrating and switching statins to the highest available dose or adding ezetimibe.
Objectives: The European societies EAS and ESC set an LDL-C target value of <70 mg/dl for patients at very high cardiovascular risk. In clinical practice, the rate of attainment of this value is low. We therefore examined to which extent the attainment level would increase if statin doses were titrated up to higher doses or ezetimibe, a cholesterol absorption inhibitor was added.
Methods: The cross sectional, observational study DYSIS examined lipid goal attainment among statin-treated (monotherapy as well as combination therapy) very high cardiovascular risk (defined as per 2011 EAS/ESC guidelines, including patients suffering from coronary heart disease, diabetes, chronic kidney disease or peripheral atherosclerotic disease) patients in Canada, Europe and Middle East countries. Data were collected under real life conditions in physicians' offices and hospital outpatient wards. Study period was between 2008-2012. Based on an individual approach, we modeled uptitration of statins (to the maximum dose) as well as addition of ezetimibe. In the scenario for uptitration of statins, LDL-C reduction was 6% per titration step vs. 25% for adding ezetimibe. This model takes into account the average additional reductions after initial standard dose statin therapy as observed in multiple studies.
Results: 26.846 patients were at very high cardiovascular risk defined by guideline criteria. 20.3% reached the treatment target <70 mg/dl. Titration to maximum Simvastatin dose (80 mg/dl, or equivalent Atorvastatin 40 mg) helped increasing this value to 27.3%; by switching all patients to Atorvastatin 80 mg, 33.7% would have reached the target. Addition of ezetimibe led to an increase of target value attainment to 44.9%. Finally, by adding ezetimibe after initially switching to Atorvastatin 80 mg, 61.1%, 73.8% and 87.9% would have reached LDL-C <70 mg/dl, <80 mg/dl and <100mg/dl respectively in this DYSIS based model.
Conclusions: In clinical practice, target value attainment is low, but could be increased from 1 out of 5 patients to 2 out of 3 patients by titrating statin dose and adding ezetimibe.

3823 | BEDSIDE
Future risk of coronary heart disease due to uncontrolled hyperlipidemia in early adulthood

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Purpose: Current European and American cholesterol guidelines emphasize overall risk and therefore tend to be less aggressive at treating hyperlipidemia in younger adults. Our hypothesis is that risk of coronary heart disease (CHD) relates to the cumulative exposure of the arterial wall to atherogenic lipoproteins over time.
Methods: This hypothesis was tested using a landmark analysis of adults free of CHD at age 53-57 in the Offspring Cohort of the Framingham Heart Study (n=1514). The association between cumulative number of years of hyperlipidemia (non-HDL ≥160) over 20 years prior to age 53-57 and future risk of CHD was evaluated using multivariable cox proportional hazards modeling. Subgroup analyses were performed specifically on adults that would not quality for statin therapy under current American guidelines.
Results: At median follow-up (15 years), adults with the longest exposure to hyperlipidemia (11-20 years) by age 53-57 had a 16.4% CHD event rate, compared to 7.0% for adults with 1-10 years and 6.2% for adults who never had hyperlipidemia ($p<0.001$, Fig. 1). CHD risk increased by 41% for each decade of exposure to hyperlipidemia (HR 1.41, 95% CI 1.07-1.86), even after adjusting for standard risk factors (smoking, age, hypertension, blood pressure treatment, sex, and diabetes) and baseline non-HDL. This association was also seen in adults with low predicted 10-year CHD risk (<7.5%) not recommended for statin therapy (HR 1.63, 95% CI 1.04-2.56).

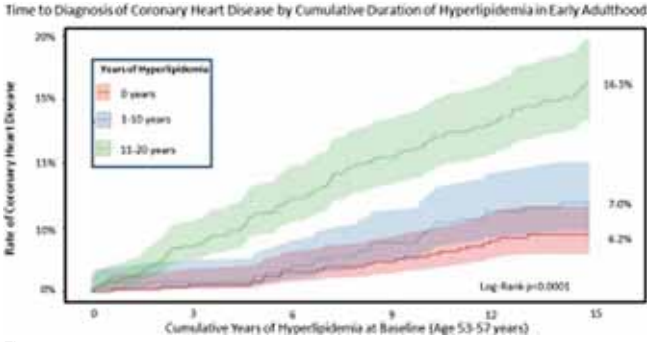

Figure 1

Conclusions: Cumulative exposure to hyperlipidemia in early adulthood substantially increases future CHD risk after age 50 in a dose-responsive relationship, even in adults with otherwise low predicted CHD risk. These data support more aggressive targeting of young adults with hyperlipidemia for primary prevention of CHD.

3824 | BEDSIDE

Prevalence of familial hypercholesterolemia and cardiovascular risk management among patients with acute coronary syndromes: a prospective Swiss cohort study

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Purpose: Familial hypercholesterolemia (FH) is associated with the occurrence of premature coronary heart disease (CHD) or sudden cardiac death and intensive preventive strategies are therefore highly recommended. However, the prevalence of FH among patients presenting with acute coronary syndromes (ACS) as well as the quality of secondary prevention are still insufficiently studied.
Methods: We studied 3660 patients with ACS included in the SPUM-ACS study, a contemporary prospective cohort involving 4 university hospitals in Switzerland, from 2009 to 2012. Diagnosis of FH was assessed at baseline using clinical and cholesterol criteria from the Dutch Lipid Clinic Network classification, as recommended by the World Health Organization. At one year we assessed: 1) ideal cholesterol management, defined as plasma LDL-cholesterol below 1.8 mmol/l or 50% LDL-cholesterol decrease or use of high-intensity statin (atorvastatin 40-80mg, rosuvastatin 20-40 mg); 2) ideal blood pressure control, defined as a systolic below 140 mmHg and a diastolic below 90 mmHg; 3) ideal glucose control, defined as fasting plasma glucose below 5.6 mmol/l or HbA1c below 7% for adults with diabetes; 4) smoking cessation for smokers; 5) 5% or more weight reduction for adults with obesity or overweight; 6) ideal drug adherence, defined as the concomitant use of 3 cardioprotective drugs: aspirin, statin and either angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or beta-blockers; and 7) attendance to cardiac rehabilitation.
Results: At the time of hospitalization for ACS, 392 (10.7%) patients would be diagnosed with FH, including 350 (9.6%) with possible FH, 39 (1.1%) with probable FH, and 3 (0.1%) with definite FH. Mean age (standard deviation) of patients with FH was 53 (10) years, 21% were women, 55% were current smokers, 9% had diabetes and 10% reported pre-existing cardiovascular disease. Among 1103 young adults with premature CHD, defined as an ACS occurring before 55 years for men and before 60 years for women, 309 (28%) would be diagnosed with FH. Over one year, 3 ACS patients with FH died. In 389 adults with FH who survived, one-year targets were achieved in 73% for lipid management, 76% for blood pressure control, 58% for glucose control, 47% for smoking cessation, 20% for weight control, 86% for drug compliance; and 81% for cardiac rehabilitation.
Conclusions: In approximately 10% of adults presenting with ACS and 30% of young adults with premature CHD familial hypercholesterolemia can be diagnosed. Identification of FH at the time of ACS is essential to optimize long-term secondary prevention.

3825 | BEDSIDE

Long term follow-up in patients with homozygous familial hypercholesterolemia; 13-year xperience of an university hospital lipid clinic

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Purpose: Familiar Hypercholesterolemia (FH) is genetic disease characterized with extremely high levels of cholesterol leading to cholesterol deposition in skin and tissues and premature atherosclerosis due to defective LDL receptors. In homozygous individuals (HoFH) cardiovascular events could develop at very early ages. Current literature gives information on short term follow-up especially good results with effective lipid apheresis. This study was conducted to evaluate the long term real clinical experience with adult HoFH patients.
Methods: Seventeen HoFH patients (11 women, 6 men) who are being followed between the years 2000-2013 in a University Lipid clinic were included. All data including clinical characteristics, family history, lipid levels, treatment, lipid apheresis, cardiovascular events, complications etc. were obtained retrospectively from the patient chart records.
Results: Mean age was 31±10 years during the admission to our Clinic. First diagnosis age was 25±14. At the time of diagnosis, mean cholesterol level was 625±136 mg/dl. Admission complaints were dermatologic (41%) and ischemic symptoms (41%) and 3 patients (18%) were diagnosed during family screening. All patients had had admitted to dermatologists due to skin depositions. 65% of the patients' parents had consanguineous marriage. Xantomas were present in 59%, aortic valve pathology in 59%, and carotid artery plaques in 47%. Coronary artery disease was documented in 59%. Though all patients had indication for lipid apheresis, only 10 patients received this treatment due to high refusal rate. Age at first apheresis was 27±12 (min 10-max 42) and the adherence to apheresis was 60%. With 2-year regular apheresis the skin depositions were vanished, however the carotid atherosclerosis and aortic pathology showed progression in all patients. During the 43±42 months follow-up, 4 patients died (mean age 25±5), and 3 patients were lost to follow-up. All deaths had cardiac origin.
Conclusions: 1. Diagnosis is especially late in HoAH patients. Because of the delayed treatment of lipid apheresis, atherosclerosis and aortic stenosis progress in these patients. The awareness of the physicians and knowledge of the public is warranted. 2. Though apheresis is a lifesaving therapy for patients with HoFH, in real clinical practice the adherence to apheresis is low in long term follow-up due to the invasive nature of the treatment. New treatments are urgently needed for these patients.

GENOME EDITING: NOVEL TRANSIENT AND PERMANENT TREATMENT OPTIONS

3826 | BENCH

Signatures of recessive alleles and susceptibility to coronary artery disease - Genome-wide homozygosity analysis

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Introduction: Runs of homozygosity (ROH) - long segments (typically >1Mb) of uninterrupted sequences of >100 consecutive homozygous SNPs are recognised markers of recessive variants in human DNA. Such variants have been largely ignored by genome-wide association studies (GWAs) that examined primarily alleles operating under additive mode of inheritance in complex diseases.
Purpose: We explored differences in genetic architecture of homozygosity between patients with coronary artery disease (CAD) and CAD-free controls in a large multi-centre CARDIoGRAM Consortium.
Design: Approximately 2.5 million single nucleotide polymorphisms (SNPs) from previously conducted GWAs in 10,548 patients with CAD and 10,273 CAD-free controls were used to identify and characterise ROH and their distribution across all 22 autosomes in 9 cohorts of white European ancestry. This was followed by analysis of association between measures of homozygosity and CAD in 20,821 subjects.
Results: Each individual had on average 32.1±8.7 ROH in their DNA. The stretches of homozygous SNPs have an average length of 1370.7±489.0 kb and cover an average total length of 44.1±15.0 Mb (approximately 1.6% of the human genome). Compared to CAD-free controls, CAD patients had approximately 0.7 excess of ROH - each additional ROH was associated with approximately 1% increase in the risk of CAD (OR=1.01, 95% CI: 1.006-1.014, $P=2.57x10^{-6}$). An average ROH was 5.2 kb longer in CAD patients than in controls. Globally, the average total length of ROH covering autosomal genome was approximately 1162.0 kb longer in patients with CAD compared to controls (95% CI: 758.4-1565.7, $P=1.70x10^{-8}$).
Conclusion: This study provides the first evidence for an excess of homozygosity in CAD. Our data also suggest that recessive variants may be an important factor in the genetic architecture of CAD.

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Methyltransferase Set7 induces NF-kB-dependent vascular inflammation and dysfunction in visceral fat arteries of obese individuals

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Purpose: Cardiovascular diseases are largely prevalent in obese subjects and account for high morbidity and mortality. Methylation of histones is emerging as a key mechanism regulating gene transcription. The methyltransferase Set7 induces a specific monomethylation of lysine 4 at histone 3 (H3K4m) on NF-kB promoter, leading to its upregulation and increased transcription of inflammatory genes. Epigenetic modifications driven by environmental factors may alter the expression of pro-atherosclerotic genes thus contributing to the inflammatory milieu observed in obese subjects. The present study was designed to investigate whether epigenetic signatures induced by Set7 contribute to obesity-related vascular disease phenotype.
Methods: Small visceral fat arteries (VFA) were isolated from 10 obese and 10 age-matched healthy subjects undergoing bariatric surgery and cholecystectomy, respectively. Organ chamber experiments were performed to assess endothelium-dependent relaxations to acetylcholine (Ach, 10-9 to 10-4 mol/L). mRNA and protein expression were assessed by real-time PCR and immunoblotting. Chromatin immunoprecipitation (ChIP) was performed to investigate epigenetic modifications on NF-kB promoter. Correlation between variables were made by Spearman analysis. Data are expressed as percentage of control.
Results: Maximal endothelium-dependent relaxations were impaired in VFA from obese as compared with controls (64.9%±4.8 vs 93±2.9, $p<0.01$). Set7 gene expression was significantly increased in vessels isolated from obese subjects (194%±18 vs. controls, $p<0.01$). Interestingly, Set7-dependent H3K4m on NF-kB p65 promoter was found in obese patients but not in control subjects. This epigenetic mark was associated with upregulation of NF-kB p65 and increased expression of inflammatory genes VCAM-1, ICAM-1 and MCP-1. Of note, Set7

expression negatively correlated with maximal Ach-induced relaxation (r= -0.69, p<0.01).
Conclusions: Upregulation of methyltransferase Set7 in obese subjects may participate to vascular inflammation and endothelial dysfunction. We show that H3K4m induced by Set7 causes NF-kB upregulation and transcription of inflammatory molecules. Targeting Set7 may contribute to reduce vascular risk in obese patients.

3828 | BENCH
The Spen gene - a novel candidate gene in pathogenesis of dilated cardiomyopathy

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Dilated cardiomyopathy (DCM) is a severe cardiac disease which indispensably results in decreased left ventricular function and finally heart failure. Staying untreated its five year mortality rate is fifty percent. Moreover DCM is the major cause for heart transplantation both, in adults and children. Due to the fact that in about 30 percent genetic causes contribute to the pathogenesis of DCM it is crucial to detect and evaluate possible candidate genes. Genome-wide association studies (GWAS) suggest a single nucleotide polymorphism which maps to a region on chromosome 1p36.13 associated with the development of dilated cardiomyopathy. This region encompasses several genes, amongst others the Spen homolog, transcriptional regulator (Spen) gene. The biological significance of Spen in the context of heart function is completely unknown to date. Morpholino-mediated gene knock-down in zebrafish offers an excellent method to evaluate the role of Spen gene and its influence on pathogenesis of DCM. Therefore, we identified Spen in zebrafish and conducted zebrafish Spen gene-specific knockdown experiments. Interestingly, we found a DCM-like phenotype. More than 90% of MO-Spen-injected embryos develop pericardial edema, bradycardia, and severe heart failure. Spen deficient larvae display highly impaired fractional shortening and decrease in blood flow. Coupled with these findings, electric conduction is disturbed in MO-Spen-injected zebrafish. While MO-Spen-injected zebrafish hearts are bradycardic at 48 hours post fertilization (hpf) only, from 60 hpf onwards hearts reveal higher grade AV-blockades and these electric abnormalities augment in complete atrial and ventricular fibrillation at 72 hpf, sequentially. Electric stimulation reveals that during early embryonal stages the heart rate can be increased through electrical stimulationen but usually triggers the development of AV-blockades if higher frequent stimuli are applied.
In summary, with regard to the GWAS findings our data suggest a significant role of Spen gene function as a novel candidate in pathogenesis of dilated cardiomyopathy.

3829 | BENCH
Cardiac I-1c over-expression with reengineered AAV improves cardiac function in swine ischemic heart failure

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Purpose: Cardiac gene therapy has emerged as a promising option to treat advanced heart failure. Advances in molecular biology and gene targeting approaches are offering further novel options for genetic manipulation of the cardiovascular system. The aim of this study was to improve cardiac function in chronic heart failure by over-expressing constitutively active inhibitor-1 (I-1c) using a novel cardiotropic vector generated by capsid reengineering of adeno-associated virus (BNP116).
Methods: One month after a large anterior myocardial infarction, 20 Yorkshire pigs randomly received intracoronary injection of either high-dose BNP116.I-1c (1.0 x 1013, n=7), low-dose BNP116.I-1c (3.0 x 1012, n=7), or saline (n=6). Changes in cardiac function and volumes were evaluated before the gene transfer and 2 months after using 3-dimensional echocardiography and high fidelity pressure-volume catheter.
Results: Mean left ventricular ejection fraction increased by 5.7% (38.8±7.7 to 40.4±6.2) in high-dose group, and by 5.2% (43.3±6.9 to 45.5±10.1) in low-dose group, whereas it decreased by 7% (37.2±4.0 to 34.5±6.3) in saline group (Figure). Additionally, preload-recruitable stroke work obtained from pressure-volume analysis demonstrated significantly higher cardiac performance in high-dose group. Likewise, other hemodynamic parameters including stroke volume and contractility index indicated improved cardiac function after the I-1c gene transfer. Furthermore, BNP116 showed a favorable gene distribution pattern for targeting the heart and de-targeting the liver.
Conclusion: I-1c over-expression using BNP116 improves cardiac function in a clinically relevant model of ischemic heart failure.

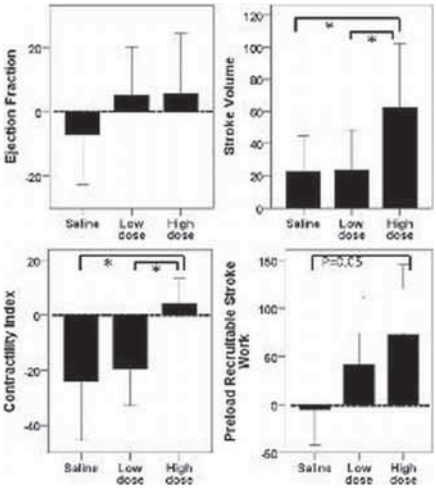

Figure 1

3830 | BENCH
Viral-delivered gene therapy for treatment of CPVT

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Catecholaminergic polymorphic ventriculartachycardia (CPVT) is a lethal human arrhythmia provoked by exercise or emotional stress. It is mediated by abnormal calcium release from the sarcoplasmic reticulum through “leaky” ryanodine channels. Beta-adrenergic blockers are the therapy of choice for human CPVT but they fail to achieve complete arrhythmia control in some of the cases. Gene therapy is a potential treatment for genetic and other diseases associated with inadequate expression of a key protein. We established a new gene-delivery system to target CASQ2 knock-out mice suffering from CPVT2. CASQ2 gene was cloned into pAAV-IRES-hrGFP plasmid. AAV9 recombinant vectors were generated by co-transfecting the expression plasmid into the AAV-293 cells with pHelper (carrying adenovirus-derived genes) and pAAV-RC (carrying AAV-9 replication and capsid genes), which express the transacting factors required for AAV replication and packaging in the AAV-293 cells. Viral particles were purified from crude cell lysates, concentrated and injected into the left ventricle of 12-14-week-old mice. Mice underwent provocation testing for arrhythima 7 weeks post viral infection. Cryosections staining demonstrated that cardiac muscle and lung tissues were CASQ2 and GFP positive while liver and spleen were GFP negative in the infected mice. Calsequestrin protein expression was elevated in the hearts of infected CASQ2 knock-out mice (n=10) compared to controls. A dose-dependent reduction in abnormal ventricular beats was observed in mice that expressed AAV9-delivered myocardial CASQ2 protein (R2=0.723, p<0.005). Viral gene-delivery eliminated sustained ventricular tachycardia in all infected mice (p=0.012) while more than 33% of the normal protein level was required to prevent non-sustained VT (n=5, p=0.003).
In conclusion, we assembled a vector useful for cardiac gene delivery, thus creating a platform for gene therapy studies in inherited heart diseases. In vivo viral delivery of CASQ2 cDNA attenuated ventricular arrythmia in mice with CPVT2.

3831 | BENCH
CnAbeta1 overexpression using adeno-associated vectors improves cardiac function and heart remodelling in both ischemic and non-ischemic heart failure

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Purpose: Heart failure is a major cause of death and disability worldwide. While conventional pharmacological treatment provides palliative care and delays death, the number of heart failure patients continues to rise especially among the elderly and new therapies are needed. Calcineurin promotes cardiac hypertrophy and failure by activating the transcription factor NFAT. In contrast, the calcineurin splicing variant CnAbeta1 has a unique C-terminal domain that activates the Akt pathway instead of NFAT. We recently showed that CnAbeta1 overexpression in mice improves cardiac function and remodelling post-infarction even when induced as late as 7 days post-surgery, suggesting that CnAbeta1 may be a good candidate for cardiac gene therapy.
Methods: To test this hypothesis, we developed an adeno-associated virus 9 (AAV9) vector in which CnAbeta1 expression is under the control of the cardiac-specific cTnT promoter. To induce myocardial infarction, mice underwent ligation of the coronary artery for 30 min followed by reperfusion and AAV9-CnAbeta1 or the negative control AAV9-GFP were systemically injected (3x10e10 Vp) seven

days later. Echocardiographic analysis was carried out 28 days post-infarction. To test the efficacy of AAV9-CnAbeta1 in non-ischemic heart disease, we induced aortic stenosis in a different group of animals by performing transaortic banding and injected the virus one week later. Echocardiographic analysis of the mice was carried out 21 days post-surgery.
Results: Animals that had undergone myocardial infarction and were treated with AAV9-CnAbeta1 showed significantly improved cardiac function 28 days post-infarction, compared with AAV9-GFP-treated mice. This was accompanied by reduced ventricular dilatation and improved remodelling. In the aortic stenosis model, treatment with AAV9-CnAbeta1 resulted in functional improvement, reduced myocardial mass and reduced heart remodelling 21 days post-surgery.
Conclusion: The positive results observed in the AAV9-CnAbeta1 treated groups in both ischemic and non-ischemic heart disease suggest that CnAbeta1 is a good candidate for the treatment of heart failure using gene therapy.

3832 | BENCH
Overexpression of microRNA-99a attenuates heart remodelling and improves cardiac performance after myocardial infarction

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MicroRNAs are involved in the regulation of various cellular processes, including cell apoptosis and autophagy. Expression of microRNA-99a (miR-99a) is reduced in apoptotic neonatal mice ventricular myocytes (NMVMs) subjected to hypoxia. We hypothesize that miR-99a might restore cardiac function after myocardial infarction (MI) by up-regulation of myocyte autophagy and apoptosis. We observed down-regulated miR-99a expression in NMVMs exposed to hypoxia using TaqMan quantitative reverse transcriptase-polymerase chain reaction analysis (RTPCR).We also observed that miR-99a overexpression decreased hypoxia-mediated apoptosis in cultured NMVMs. To investigate whether overexpression of miR-99a in vivo could improve cardiac function in ischaemic heart, adult C57/BL6 mice undergoing MI were randomized into two groups and were intra-myocardially injected with lenti-99a-green fluorescent protein (GFP) or lenti-GFP (control). Four weeks after MI, lenti-99a-GFP group showed significant improvement in both left ventricular (LV) function and survival ratio, as compared to the lenti-GFP group.Histological analysis, western blotting analysis and electron microscopy revealed decreased cellular apoptosis and increased autophagy in cardiomyocytes of lenti-99a-GFP group. Furthermore, western blotting analysis showed inhibited mammalian target of rapamycin (mTOR) expression in the border zones of hearts in miR-99a-treated group. Our results demonstrate that miR-99a overexpression improves both cardiac function and survival ratio in a murine model of MI by preventing cell apoptosis and increasing autophagy via an mTOR/P70/S6K signalling pathway. These findings suggest that miR-99a plays a cardioprotective role in post-infarction LV remodelling and increased expression of miR-99a may have a therapeutic potential in ischaemic heart disease.

3833 | BENCH
Long non-coding RNAs in the infarcted heart

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Purpose: Long non-coding RNAs (lncRNAs) constitute a novel class of non-coding RNAs. LncRNAs regulate gene expression, thus having the possibility to modulate disease progression. In this study, we investigated the expression of lncRNAs in the heart after myocardial infarction (MI).
Methods: Adult male C57/BL6 mice were subjected to coronary ligation or sham operation. Cardiac gene expression was investigated using whole-genome microarrays with an in-house analytical pipeline dedicated to lncRNAs. Cardiac function was evaluated by 18F-fluorodesoxyglucose positron emission tomography (18F-FDG PET).
Results: In a derivation group of 4 MI and 4 sham-operated mice sacrificed 24 hours after surgery, microarray analysis showed that MI significantly affected the cardiac transcriptome. 20 lncRNAs were up-regulated in the MI group, and 10 lncRNAs were down-regulated in the MI group (fold-change >2, false discovery rate $<5\%$). Among these, 2 lncRNAs (called lncRNA1 and lncRNA2) showed robust up-regulation in the MI group: lncRNA1 (5-fold) and lncRNA2 (13-fold). This was confirmed using quantitative PCR, in which lncRNA1 and lncRNA2 displayed 6- and 12-fold up-regulation in the MI group, respectively (both $P<0.05$). Up-regulation of these 2 lncRNAs after MI was further confirmed in an independent validation group of 8 MI and 8 sham-operated mice (9-fold and 16-fold for lncRNA1 and lncRNA2, $P<0.001$). In a time-course analysis involving 21 additional MI mice, the expression of both lncRNAs peaked 24 hours after induction of MI and returned to basal levels after 2 days. In situ hybridization revealed an increase of lncRNA1 expression in the left ventricle of MI mice. Both lncRNAs were robustly correlated with left ventricular ejection fraction determined 24 hours after MI by 18F-FDG PET ($r>0.8$). Bioinformatic analyses of microarray data revealed that lncRNA1 expression displayed strong association with genes coding for proteins involved in angiogenesis, fibrosis, hypertrophy, inflammation, and extracellular matrix remodeling, all pathways involved in the development of left ventricular remodeling and heart failure post MI. Among the genes most highly correlated with lncRNA1 ($r>0.80$), MMP9, TNFalpha, CXCR4, and BNP were all up-regulated in the heart of MI mice.
Conclusion: We show for the first time that expression of lncRNAs is regulated in the infarcted heart. This study provides the basis for future investigations of the role of lncRNAs in the diseased heart.

COMPUTED TOMOGRAPHY FOR ANATOMICAL EVALUATION OF CORONARY ARTERY DISEASE

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Gender-based warranty period of a coronary artery calcium score of zero: a 15-year follow-up study

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Background: Emerging evidence supports the absence of Coronary artery calcification (CAC) as a favorable cardiovascular risk factor. However, studies that have assessed the relationship between CAC=0 and adverse prognosis are somewhat varied, possibly owing to a limited duration of follow-up, and small numbers of events. Moreover, the relative prognostic impact of CAC=0 in men versus women is less well described.
Objective: The objective of this study was to lend further understanding towards the long-term risk of mortality according to CAC=0 in men versus women.
Methods: A total of 9,715 asymptomatic patients undergoing CAC Agatston scoring from a single center were enrolled and followed for a period of 15 years. Of these patients, 4,864 (mean age 52.1 ± 10.8 years; 42.2% women) were defined as having a baseline CAC score of 0. The prognostic utility of CAC=0 for all-cause mortality was assessed using Cox proportional hazard regression (HR) modeling.
Results: During a mean follow-up of 14.6 ± 1.1 years (range 13-17 years), 229 patients died, 127 (4.5%) and 102 (5.0%) events for men versus women, respectively ($p=0.45$). There was a substantial 14-year delayed onset of mortality among patients with a baseline CAC score of 0. The annualized death rate was non-linear: owing to an extremely low event rate (2.5-3.5 events per 1,000 person years) during the initial 12 years, accelerating substantially during the 13th (3.8 events per 1,000 person years) and 14th (4.2 events per 1,000 person years) years. The risk of all-cause mortality of women compared to men did not differ materially [unadjusted HR = 1.08, (95% Confidence Interval 0.83–1.40), $p=0.58$; risk-adjusted HR = 1.01, (95% Confidence Interval 0.78–1.32), $p=0.92$].
Conclusion: In asymptomatic patients, the CAC=0 portends a substantial 12-year warranty period against all-cause mortality, with no disparity between men and women.

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Epicardial adipose tissue promotes progression of coronary artery calcification in the early phase of atherosclerosis: results from the Heinz Nixdorf Recall study

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Purpose: Epicardial adipose tissue (EAT) predicts coronary events and is suggested to influence development of atherosclerosis. We aimed to determine, whether EAT volume predicts progression of coronary artery calcification (CAC) score.
Methods: For this analysis, participants were drawn from the population-based Heinz Nixdorf Recall study without known coronary artery disease. CAC was quantified from non-contrast cardiac electron beam computed tomography at baseline and after 5-years. EAT was defined as fat volume inside the pericardial sac. Association of EAT volume with CAC-progression (log(CAC[follow-up]+1) – log(CAC[baseline]+1)) was depicted as percent progression of CAC+1 per standard deviation (SD) of EAT with multivariable analysis adjusting for age, gender, body mass index (BMI), systolic blood pressure, anti-hypertensive medication, low- and high density cholesterol, lipid-lowering medication, diabetes, and present as well as former smoking.
Results: Overall, we included 3367 subjects (mean age59 ± 8, 47%male) in this analysis. Subjects with EAT above the gender-specific median showed higher progression in CAC then subjects with EAT volume below the median (median (Q1; Q3) CAC-progression 2.45 (0; 58.27) vs. 22.72 (0; 124.25), $p<0.0001$). In regression analysis, 6.3 (2.3-10.4%, $p=0.0019$) of progression of CAC+1 was attributable to 1SD of EAT, which persisted after adjustment for risk factors (6.3 (1.5-11.4)%, $p=0.024$). For subjects with CAC-score of >0-≤100, progression of CAC+1 by 20% (11-31%, $p<0.0001$) was attributable to 1SD of EAT. Effect sizes

were lower for higher CAC at baseline, with no relevant link for subjects with CAC-score ≥400 (0.2 (-3.5-4.2)%, p=0.9). Likewise, subjects aged<55 years at baseline showed strongest association of EAT with CAC-progression (20.6 (9.7-32.5)%, p<0.0001), while no relevant effect was found for subjects aged ≥65 (0.3 (-7.0-8.1)%, p=0.9). Interestingly, the effect of EAT on CAC-progression was more pronounced in subjects with low BMI and decreased with degree of adiposity (BMI≤25: 19.8 (9.2-31.4)%, p=0.0001, BMI>40: 0.8 (-26.7-38.9)%, p=0.96).
Conclusion: EAT is associated with the progression of coronary artery calcification, especially in young subjects and subjects with low CAC-score, suggesting that EAT may promote early atherosclerosis development.

3840 | BEDSIDE
Impact of napkin-ring sign by 320-slice coronary computed tomography and thin-cap Fibroatheroma by optical coherence tomography on slow flow phenomenon during PCI in non-ST elevation ACS

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Background: Coronary Computed Tomography (CCT) imaging enables the non-invasive visualization of coronary arteries. Napkin-ring sign (NRS) is one of the CCT characteristics defined as a low CT density attenuation plaque core surrounded by a rim-like area of higher CT attenuation values. In stable angina pectoris (SAP) patients, NRS has been reported to be associated with Thin-Cap Fibroatheroma (TCFA) by Optical Coherence Tomography (OCT), which is a precursor of vulnerable plaque and slow flow phenomenon (SF) during percutaneous coronary intervention (PCI) and a predictive factor of worse prognosis. We sought to identify if NRS by 320-slice CCT are associated with the presence of TCFA by OCT and SF during PCI in non-ST elevation acute coronary syndrome (NSTE-ACS) patients. We further sought to evaluate if CCT and OCT findings provide complimentary information to predict SF.
Methods and results: We investigated 109 NSTE-ACS patients who underwent 320-slice CCT before PCI. We excluded patients with cardiogenic shock, severe congestive heart failure, renal insufficiency, atrial fibrillation, and insufficient CT and/or OCT imagings. Transient or final Thrombolysis In Myocardial Infarction (TIMI) flow grade less than 2 was defined as SF in this study. Patients were divided into the two groups with or without napkin-ring sign (NRS: 53; 49%, non-NRS: 56; 51%), and clinical and angiographic findings were compared between these two groups. There were no significant differences in clinical presentation and angiographic findings between the two groups. SF was significantly more frequent in NRS group than in non-NRS group (NRS 14/53, non-NRS 4/56, P=0.0091). Of these 109 patients, OCT sub-analysis was performed in 53 patients (49%) and we compared OCT findings between lesions with (n=26, 49%) or without (n=27, 51%) NRS. TCFA was defined as lipid rich plaque with thinnest cap thickness less than 70μm. In OCT sub-analysis, TCFA was more frequently detected in NRS group (NRS 13/26, non-NRS 5/27, P=0.021). There were no significant differences in the frequency of plaque rupture NRS 8/26, non-NRS 8/27, P=1.00) and thrombus (NRS 13/26, non-NRS 10/27, P=0.42) between NRS and non-NRS groups. The presence of TCFA on OCT and NRS on CCT was both significantly associated with SF in OCT-sub group analysis.
Conclusion: NRS on CCT was associated with TCFA on OCT in patients with NSTE-ACS. CCT and OCT may provide complimentary information serving as predictors of SF during PCI, and help identify high risk NSTE-ACS patients for PCI.

3841 | BEDSIDE
Peri-ventricular epicardial adipose tissue accumulation is associated with impaired coronary microcirculation

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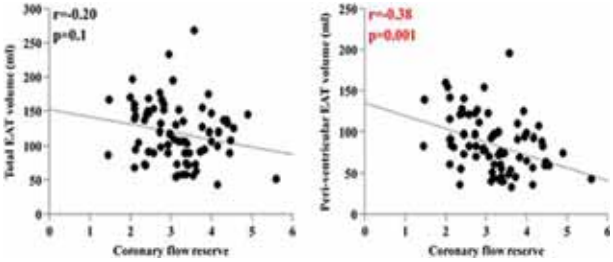
Purpose: Epicardial adipose tissue (EAT) is considered to play a crucial role in the pathogenesis of coronary atherosclerosis. Distribution of body fat varies in each patient and its extent of localization would be more important than its amount. The purpose of this study was to investigate the impact of ventricular-specific EAT volume on coronary microcirculatory vasodilator function.
Methods: Among patients who underwent multidetector computed tomography (MDCT) examination, 74 patients (48 men, mean age 68±10 years) with the absence of obstructive narrowing of left anterior descending coronary artery (LAD) were enrolled. EAT volume was calculated as the sum of EAT area and subsequently divided into peri-atrial and peri-ventricular EAT. All patients had transthoracic Doppler echocardiography (TTDE) examination for coronary flow reserve (CFR) measurement in the LAD. CFR lower than 2.5 was considered as impaired coronary microvascular function.
Results: Nineteen patients with impaired CFR had significantly increased peri-ventricular EAT volume than those with preserved CFR (104±35 vs 80±32 ml, p=0.006) whereas no significant differences were observed in total EAT volume (130±39 vs 115±45 ml, p=0.2) and in peri-atrial EAT volume (26±14 vs 35±18 ml, p=0.1). Significant correlation was observed between CFR and peri-ventricular EAT volume (r=-0.38, p=0.001) (Figure). Multivariate analysis revealed that peri-ventricular EAT volume was significantly associated with impaired CFR (p=0.01).



Conclusions: This is the first study demonstrating that ventricular-specific EAT volume accumulation (peri-ventricular EAT volume) estimated by MDCT was associated with impaired CFR.

3842 | BEDSIDE
Does increased soft plaque volume in coronary arteries by computed tomography coronary angiography predict adverse events?

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Purpose: Coronary computed tomography angiography (CCTA) has been rapidly adopted into clinical practice for the evaluation of patients with suspected coronary artery disease (CAD). In addition to the assessment for obstructive CAD, CCTA has the ability to detect, characterize and quantify coronary atherosclerosis. Pathological studies have shown that non-flow-limiting coronary plaques with greater lipid content are associated with increased risk of adverse events. The aim of our study was to evaluate the potential use of CCTA to characterize and quantify plaque volume for the prediction of adverse events.
Methods: Our Institute's Cardiac CT database was queried and 36 patients who experienced adverse events at follow-up (myocardial infarction and all cause death) were identified. An event-free, Morise score matched cohort was randomly identified. Using CCTA images, plaque volume in the major epicardial arteries were analyzed (Aquarius iNtuition, TeraRecon) using predetermined attenuation ranges in Hounsfield units (HU): -100 to 0 HU, 1 to 30 HU, 31 to 70 HU, 71 to 150 HU, and mean coronary lumen + 2SD to 1000 HU. Each epicardial artery, except the left main, was divided into proximal, mid, and distal segments, and plaque volumes were normalized for arterial segment length. Normalized volumes were analyzed separately for the entire length of the 3 major coronary arteries and for the proximal segments of the 3 coronaries along with the left main artery.
Results: There was no significant difference in the baseline characteristics of the 2 cohorts. Low attenuation plaque (1-30 HU) volumes were greater in the adverse event versus the control group (proximal segments 1.97 vs. 1.56 mm^2, p=0.004; entire length 1.17 vs. 1.01 mm^2, p=0.03). Similarly, intermediate attenuation plaque (31-70 HU) volumes were also greater in the adverse event versus the control group (proximal 2.63 vs. 2.09 mm^2, p=0.003; entire length 1.75 vs. 1.48 mm^2, p=0.03). There was no difference in the volume of high attenuation plaque.
Conclusion: This study demonstrated that adverse events appear to be associated with greater volumes of low and intermediate attenuation plaque which may be measures of lipid and fibrous atherosclerosis. The difference between the two groups is most apparent in the proximal epicardial arteries. These findings are consistent with the current understanding of vulnerable plaque. Further prospective studies are warranted to evaluate if CT quantification of coronary plaques has the potential to be used as a non-invasive prognostic tool to estimate risk of future cardiac events.

3843 | BEDSIDE
Impact of heterogeneous enhancement detected by multidetector computed tomography on microvascular obstruction and left ventricular remodeling in acute myocardial infarction

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Objectives: This study evaluated the clinical value of heterogeneous enhancement detected by myocardial contrast delayed enhancement (DE) with multidetector computed tomography (MDCT) for predicting microvascular obstruction (MVO) and left ventricular (LV) remodeling by delayed enhancement magnetic resonance imaging (DE-MRI) after acute myocardial infarction (AMI).
Methods: In 54 patients with first AMI, MDCT without iodine reinjection was performed immediately following successful percutaneous coronary intervention (PCI). DE-MRI performed within 7days and 6months after the onset was used to detect MVO and LV remodeling. LV remodeling was defined as any increase

in LV end-systolic volume at 6months after infarction compared with baseline in individual patients. Patients were divided into 2 groups according to the presence (Group I, n=19, Fig. 1A) or absence (Group II, n=35, Fig. 1B) of heterogeneous enhancement.

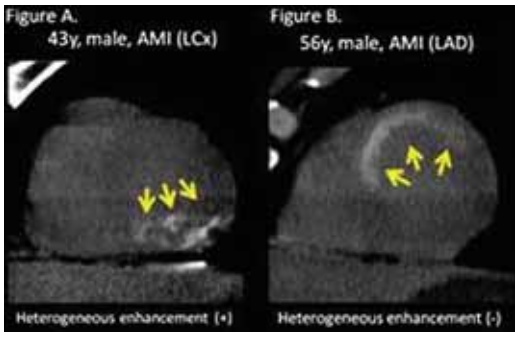

Figure 1. Heterogeneous enhancement.

Results: MVO and LV remodeling was detected in 28 (51%) and 17 (32%) patients, respectively. The presence of heterogeneous enhancement was related to higher rates of transmural infarction, higher peak CK-MB and lower LV ejection fraction (all P-values <0.05). The presence of heterogeneous enhancement showed high specificity of 100% and moderate sensitivity of 61% for the detection of MVO. In the multivariate analysis, heterogeneous enhancement was a significant independent predictor for LV remodeling (odds ratio 19.63; 95% confidence interval, 1.955-197.2, P=0.011).
Conclusions: Heterogeneous enhancement detected by MDCT immediately after primary PCI may provide promising information for predicting MVO and LV remodeling in patients with AMI.

ZOOMING ON DIFFICULT ISSUES IN AORTIC VALVE SURGERY

3884 | BEDSIDE
Pacemaker dependency after aortic valve replacement: do conduction disorders recover over time?

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Background: Conduction disturbances requiring permanent pacemaker (PM) implantation after aortic valve replacement (AVR) occur in 3-8% of patients.
Our aim was to evaluate long-term PM dependency and recovery of conduction disorders during follow-up in those patients.
Methods: We conducted a cross-sectional study of all consecutive patients submitted to permanent PM after AVR during seven years. Absence of rhythm recovery (sinus rhythm or atrial fibrillation with appropriate ventricular frequency) was defined as needing for pacemaker in the long-term. Patients who had a formal indication to pacemaker implantation before the surgery and those who had implanted the device 60 days or more after surgery were excluded.
Results: Ninety one patients (mean age 66±13 years old, 54% male) were submitted to permanent PM implantation (10.4±4.7 days after surgery), due to complete atrioventricular block (93.4%), slow atrial fibrillation (3.3%) and other atrioventricular conduction disturbances (3.3%). During 1026.6±732.0 days of follow-up 64% of the patients did not recover the rhythm. The risk of no rhythm recovery at long term seemed to be higher in patients submitted to aortic mechanic valve replacement compared to biological valve (77.8% vs 57.8%, p=0.056). The aetiology of valvular disease before surgery was another factor influencing recovery probability (p=0.03): endocarditis, prosthetic dysfunction and bicuspid valve were associated with lower rhythm recovery. Age, conduction disorders in preoperative ECG and medication with B-blocking, digoxin or antiarrhythmic drugs before surgery did not have any association with long-term PM dependency. Cardiopulmonary bypass and aortic cross-clamp times also did not influence the rhythm recovery. The time to PM implantation was similar between patients with rhythm recovery and those with no rhythm recovery (11.0±4.9 days after surgery vs 10.1±4.6 days after surgery, respectively; p=0.39). After multivariate analysis valvular disease aetiology (endocarditis, prosthetic dysfunction or bicuspid valve) was still associated with a lower probability of long-term rhythm recovery (p=0.01).
Conclusion: The majority of patients submitted to permanent PM implantation after AVR do not recover from conduction disorders during the follow-up. The aetiology of valvular disease before surgery was an independent predictor of late PM dependence.

3885 | SPOTLIGHT
Assessment of the aortic annulus with transesophageal echocardiography, CT-scan and magnetic resonance compared to direct surgical sizing: a prospective double-blinded study

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Purpose: To derive the most adequate procedures for measurements of the aortic annulus by multi-detector computed tomography (MDCT), magnetic resonance (MR) and transesophageal echocardiography (TEE) from comparisons with intraoperative sizing.
Methods: 45 patients, (48.9% males, age 78.9±3.7) underwent AVR for severe aortic stenosis after TEE, MDCT, and MR evaluation. In TEE, the annulus was measured at the base of leaflet insertion in the mid-esophageal long-axis view. In MDCT and MR, the diameter was derived after testing the accuracy of the left ventricle outflow tract measurement (basal ring) and of the basal attachment of the aortic commissures (virtual ring). Two double-blinded operators prospectively performed all assessments for each imaging technique. Intra-operative evaluation was performed after leaflet removal and decalfication by using Hegar (H) dilators. Statistical analysis are summarized in Table 1. The percentage of measurements falling within ± 2 mm from the H value constituted a further estimate of practical reliability.
Results: The most accurate results for MDCT and MR were obtained using for the former the average of the "basal ring" and "virtual ring", and for the latter the "basal ring" measurement. Inter-operator variability was verified with the paired t-test and the non-parametric Wilcoxon test. Table 1 summarizes the main statistical results obtained when comparing the three imaging procedures to the Hegar sizing H.

Table 1

	TEE	MDCT	RM
Data within ±2 mm	71%	80%	91%
Bland Altman plot width	7.6 mm (–3.3/+4.3)	4.9 mm (–2.8/+3.1)	5.7 mm (–2.1/+3.6)
Bland Altman plot (Delta)	0.5±0.2 mm	0.2±1.5 mm	0.7±1.5 mm
Regression line slope	0.65±0.10	0.80±0.10	0.90±0.10
Pearson's coefficient r	0.70±0.11	0.81±0.09	0.84±0.08
chi-square test	7.5	3.4	4.8

Conclusion: The proposed procedures for MDCT and MR allow an assessment of the aortic annulus superior to TEE. In particular the basal ring is the one able to warrant MR data as the highest accuracy and reliability. The ± 2mm "surgical allowance" highlights the real scenario in the non-invasive measurements and gives a valuable and trustworthy answer to the reliability of indirect measurements.

3886 | BEDSIDE
Peak oxygen consumption and functional capacity scores nine months after valve implantation for aortic stenosis

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Objective: To assess the peak oxygen consumption (pVO2) and NYHA classification after aortic valve implantation (AVI) for aortic stenosis (AS) and determine predictors of unfavourable outcomes for pVO2.
Methods: Nine months after AVI, cardiopulmonary exercise testing and NYHA classification were performed. The post-AVI pVO2 was compared to the predicted and pre-AVI values, the pVO2 in patients with unoperated asymptomatic/equivocal symptomatic (As/Es) AS, and with the NYHA classification. Predictors were sought by logistic regression.
Results: In 73 patients with mean age of 71.6±9.8 years, the mean pVO2 post-AVI was 89.2±20.2% of that predicted and lower (95% CI -17.4 to -2.1%; p=0.013) than that of 55 As/Es patients with mean gradient (MG) 52.6±11.8 mm Hg and age 69.5±9.8 years (Table 1). Post-AVI, 23/73 had pVO2 <83% of that predicted, and 11/37 had a decline in pVO2 >10%. MG <40 mm Hg [OR 4.1; 95% CI 1.3 to 3.1] and atrial fibrillation [OR 5.5; 95% CI 1.6 to 9.3] predicted pVO2 <83%. MG <40 mm Hg [OR 14.4; 95% CI 2.2 to 93.2] and pacemaker post-AVI [OR 6.4; 95% CI 1.2 to 4.6] predicted decline in pVO2 >10%. NYHA classification overestimated the functional capacity post-AVI. For patients classified NYHA I: post-AVI the reached of the predicted pVO2 was 94.1±18.2% compared to 102.4±20.6% in As/Es patients (95% CI -16.2 to -0.4%). Kappa for the NYHA class and pVO2 was a low 0.20.
Conclusions: Post-AVI pVO2 was lower than predicted and lack of improvement

Table 1. Results after AVI and in comparison with asymptomatic or equivocal symptomatic unoperated patients with severe aortic stenosis (As/Es-AS)

	All patients after AVI (n=73)	As/Es-AS with Vmax >4m/s (n=55)	P-value	95% CI
pVO2 (mL/kg·m^2)	18.0±5.2	21.0±6.6	0.004	1.0; 5.1
% of predicted pVO2 (%)	89.2±20.2	99.0±23.5	0.013	2.1; 17.4
pO2pulse (mL O2/beat)	11.7±3.1	12.8±3.2	0.057	–0.03; 2.2
% of predicted pO2pulse (%)	109.7±23.2	110.6±22.7	0.822	–7.2; 9.0
% of peak heart rate (%)	82.6±16.1	85.5±11.2	0.182	–1.6; 8.5
Age (years)	71.6±9.8	69.5±9.8	0.230	–1.4; 5.6
NYHA class (mean)	1.52±0.6	1.38±0.6	0.197	–0.35; 0.70

is not uncommon. Predictors of unfavourable outcomes for pVO2 were identified. NYHA classification overestimated the functional capacity post-AVI.

3887 | BEDSIDE
Serious limitations in the assessment of prosthesis-patient mismatch by using the effective orifice area index

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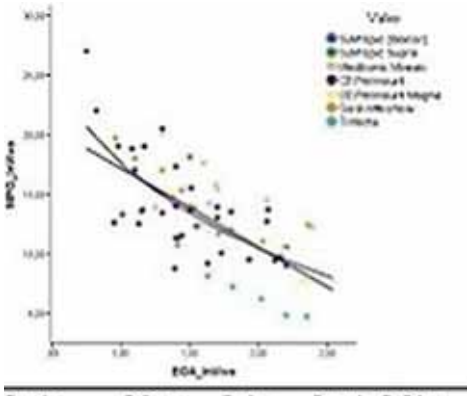
Prosthesis-patient-mismatch (PPM) is currently quantified by indexing the effective orifice area (EOA) with body surface area (BSA), but the relevance of PPM is highly controversial. EOA assessment requires flow velocities plus the area of the outflow tract (LVOTA) from echocardiograpy (continuity equation). Pressure gradient assessment requires only flow velocities (Bernoulli equation). Since the EOAindex relates flow velocity to patient-specific, anatomic parameters twice (i.e., LVOTA and BSA), we aimed to take a closer look at the way EOAindex is related to outcome.
Methods: We performed a meta-analysis-type search of the literature for studies that used EOA, EOAindex and pressure gradients in relation to outcome.
Results: PPM was addressed in 27 studies. Almost half suggested no impact of PPM on outcome (incl. survival). Despite EOA being patient-specific, 80% of studies used EOAs from other patient populations ("projected EOA"). This finding was unexpected and seriously questions the results. We then related patient-specific EOA values and the corresponding Bernoulli pressure gradients as reported in 29 separate studies (Figure). Expecting a logarithmic relationship, we found a "pseudo-linear" relationship. Considering this relationship, it is surprising that many studies related EOA to BSA, but none of them related pressure gradients to BSA.



Equation	R-Square	P-value	Regression Coefficient
Linear	0,499	<0,001	-6,657
Logarithmic	0,530	<0,001	-10,45

Conclusions: 1. Using EOAindex to assess the relevance of PPM may not be appropriate and may explain the PPM controversy. 2. EOA is patient-specific and cannot be transferred. This practice, however, represents a serious methodological limitation in the current literature. Other ways for PPM assessment are needed, possibly by relating prosthesis dimension to the LVOTA.

3888 | BEDSIDE
Isolated surgical aortic valve replacement in octogenarians before and after the introduction of transcatheter aortic valve implantation (TAVI)

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Purpose: Aortic valve stenosis is the most frequent valvular heart disease, with an incidence of 5% in the octogenarians. The reference treatment is the surgical aortic valve replacement. But, since few years, a new alternative treatment appeared, the transcatheter aortic valve implantation (TAVI). The aim of our study is to compare the preoperative characteristics and the perioperative data of octogenarian patients who undergo to an isolated surgical aortic valve replacement, before and after the coming of the TAVI.
Methods: We retrospectively included consecutive surgical isolated aortic valve replacements, performed in patients aged 80 years old and more, in our center, between the 1st of January 2006 and the 31st of December 2011. The first TAVI was performed in the beginning of 2009 in our center.
Results: We included 517 patients, divided into two groups, 229 patients in the "before TAVI" group (2006-2008), 288 patients in the "after TAVI" group (2009-2011). The mean (±SD) age was 83.2±2.0 in the "before TAVI" group and 83.5±2.1 in the "after TAVI" group (p=0.1). There were no significant differences for the preoperative characteristics: NYHA class (p=0.4), incidence of heart failure (p=0.4), left ventricular ejection fraction (59.8%±12.2 in the "before TAVI" group versus 59.9%±11.3 in the "after TAVI" group, p=0.9), coronary artery disease (p=0.2), peripheral vascular disease (p=0.1), chronic renal failure (p=0.3), chronic pulmonary disease (p=0.4), previous cardiac surgery (7 patients in the "before TAVI" group, 2 patients in the "after TAVI" group, p=0.08). The logistic EuroSCORE was 7.78%±4.60 in the "before TAVI" group and 7.33%±3.96 in the "after TAVI" group (p=0.2). The operative mortality (30 days) was comparable: 5.2% in the "before TAVI" group and 6.9% in the "after TAVI" group (p=0.4).
Conclusion: In our center, the coming of the TAVI did not impact the number of octogenarian patients who undergo the surgical isolated aortic valve replacement, their preoperative characteristics and the operative mortality.

3889 | BEDSIDE
Long-term results of freestyle stentless bioprosthesis in the aortic position: a single center cohort of 500 patients

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Background and aims: Stentless xenograft bioprostheses may be the future valve of choice for aortic valve replacement (AVR), according to their superior hemodynamics and mid-term clinical performances. The study aim was to investigate long-term clinical outcome after AVR with the Medtronic Freestyle xenograft bioprostheses
Methods: Between April 1997 and November 2004, a total of 500 patients (Mean age: 74.5±9.6 years; 52% male gender) underwent AVR with a Freestyle bioprosthesis, without population selection. The indications for AVR were aortic stenosis in 88%, severe aortic regurgitation in 7%, combined aortic disease in 3% and aortic endocarditis in 2% of the cases. The surgical procedure used modified subcoronary technique in n=479 cases and complete root replacement in n=21, conducted with mini-extracorporeal circulation. Concomitant procedures included coronary artery bypass grafting in 122 patients (24%) and mitral valve repair/replacement in 11.
Results: Mean cardiopulmonary bypass time was 98±26 min, and total aortic cross-clamp time 77±19 min. Operative mortality was 5.2%. The median follow-up time was 104.8±5.7 months. During this period, there were n=224 deaths (n=122 cardiovascular and n=102 non-cardiovascular deaths). The actuarial survivals for all-cause, cardiovascular and valve-related mortality were respectively 44±3%, 67±3% and 70±4% at 10 years and 31±5%, 50±7% and 58±7% at 12 years. Freedom from structural valve deterioration (SVD) at 10 years was 94±2%. The linearized SVD incidence was 0.6% per patient/year. Multivariate Cox regression analysis revealed that older age (1.15 [1.08-1.23], p<0.001), impaired renal function (1.72 [1.0-2.99], p=0.05)and concomitant coronary artery disease (2.0 [1.15-3.47], p=0.01) were independent predictors of cardiovascular death. The Freestyle bioprosthesis showed excellent performances and durability in the younger patients of the cohort (age<65 years at implantation, n=45). The 10-year actuarial survivals from all-cause, cardiovascular and valve-related mortality were respectively 69±9%, 83±7% and 87±6%.
Conclusion: The use of the Freestyle bioprosthesis for AVR resulted in good long-term cardiovascular survival and freedom from SVD in this cohort regardless of age at implantation

ISCHAEMIC HEART DISEASE AND COMORBIDITIES

3916 | BEDSIDE
The effect of beta-blockers on mortality in COPD patients after myocardial infarction: A Swedish nation-wide observational study

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Purpose: Investigate the effect of being prescribed a β-blocker at discharge on all-cause mortality in patients with chronic obstructive pulmonary disease (COPD) after a myocardial infarction (MI).
Background: Patients with MI and concomitant COPD is a high-risk group with increased short- and long-term mortality. β-blocker therapy has been shown to reduce mortality, prevent arrhythmias and heart failure development after an MI in a broad population. However, the effect of β-blockers in COPD patients specifically is less well established and they may also be under-prescribed.
Methods: Patients hospitalized for MI between 2005 and 2010 were identified from the nation-wide Swedish SWEDEHEART registry. Patients with MI and concurrent COPD who survived the hospital stay and got discharged were selected as the study population. In this cohort, patients who were discharged with a β-blocker were compared to patients not discharged with β-blockers. The primary endpoint was all-cause mortality.
Results: A total of 6119 patients were included, of which 5058 (82.7%) were discharged with a β-blocker while 1061 (17.3%) were not. After adjusting for potential confounders including baseline characteristics, comorbidities and in-hospital characteristics, patients discharged with a β-blocker had a lower all-cause mortality (HR 0.91, 95% CI 0.82-1.00, p=0.049) during the total follow-up time (maximum 7.2 years).
Conclusions: Patients with COPD who were discharged with β-blockers after

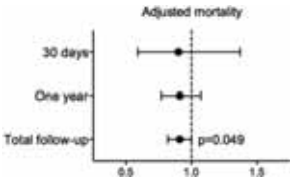

Figure 1

an MI had a survival benefit. Evidence based treatment strategies are needed to combat the increased mortality found in this patient population and our study contributes to the present available data on how to specifically manage COPD patients after an MI, with an increased assurance for β-blockers.

3917 | BEDSIDE
Role of renal dysfunction in drug prescription, adherence and long-term outcome in 73.005 Swedish myocardial infarction patients

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Purpose: Patients with acute coronary syndrome (ACS) and renal dysfunction have worse prognosis. This may be due to sub-optimal secondary preventive treatment, poorer treatment adherence, or ineffectiveness of current guidelines in these patients. We studied the prescription and adherence to secondary prevention guidelines in a nation-wide representative sample of ACS patients with known renal function. We also tested whether prescribing guideline-recommended therapies is associated with better outcome also in patients with reduced renal function.
Methods: We used the SWEDEHEART registry to prospectively study all patients admitted to Swedish coronary care units for an ACS during 2005-10, that survived at least one year (n=75.492). In 73.005 of these, creatinine levels were available to estimate glomerular filtration rate (eGFR) using the CKD-EPI formula. Data on vital status was extracted from the National Population registry, and drug use from the National Drug Prescription registry recording all dispensed drugs in Sweden. Patients were considered adherent 12 months after index event if they had collected a prescription during the previous 6 months.
Results: Compared with patients with eGFR ≥60 ml/min, patients with eGFR 30-59 ml/min (N=14361) were less likely to be prescribed aspirin (OR 0.51, CI 95% 0.48-0.55), statins (OR 0.35, CI 95% 0.34-0.37) and beta-blockers (0.77, CI 95% 0.73-0.81) but more likely to receive ACE/ARB (OR 1.12, CI 95% 1.07-1.16) at discharge. Patients with eGFR <30 ml/min were less likely to be prescribed each of these drugs. One year after index event, patients with eGFR 30-59 ml/min were less likely to be adherent to aspirin (OR 0.61, CI 95% 0.58-0.64), statin (OR 0.43, CI 95% 0.41-0.45), ACE/ARB (OR 0.99 CI 95% 0.95-1.03) and beta-blockade treatment (OR 0.79, CI 95% 0.76-0.83). Same pattern for adherence was found in patients with eGFR <30 ml/min. After adjustment for age, sex, diabetes, hypertension, previous heart failure, stroke and drugs on admission, performed PCI or CABG during hospitalization, receiving ≥3 guideline-recommended drugs at discharge was associated with an improved 4-year outcome (combined death or reinfarction) in patients with eGFR >60 ml/min (HR 0.67, CI 95% 0.62-0.72), eGFR 30-59 ml/min (HR 0.71, CI 95% 0.66-0.77), and eGFR <30 ml/min (HR 0.81, CI 95% 0.69-0.96).
Conclusions: Prescription of guideline-recommended therapies is associated with an improved prognosis also in patients with renal dysfunction. Despite this, these patients are less likely both to receive and adhere to such therapies.

3918 | BEDSIDE
Primary cancer risk and organ dose from medical radiation exposure in patients hospitalized for cardiovascular disease

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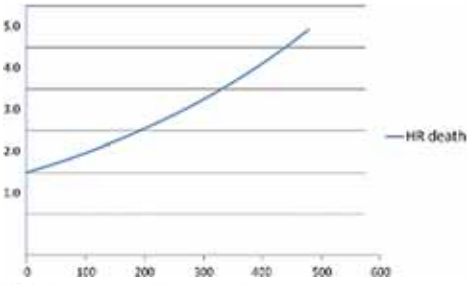
Background: Low-to-moderate (<200 milliSievert, mSv) radiation doses employed in cardiological procedures, such as coronary angiography and percutaneous coronary interventions, may increase cancer incidence in exposed patients after decades. The organ dose should be used when investigating the carcinogen effect of medical radiation.
Methods: To evaluate the association between radiological exposure and cancer, a retrospective cohort study was conducted in 16,311 patients with heart disease and no history of cancer consecutively admitted to the hospital between January 1970 and December 2009 and with a median follow-up of 10 years. The cumulative estimated effective dose (E) was calculated from electronic records of all hospital admissions, using the E values of the European Society of Cardiology 2014 position paper. Lung dose for the principal cardiac procedures was estimated starting from the lung dose conversion factor provided by the literature. Main causes of death and primary cancer onset were recorded during the follow-up. Analysis was performed by Cox regression model.
Results: We observed 6,174 deaths, including 873 cancer deaths (14%); E per patient was 20±19 mSv; estimated mean lung organ dose was 41±19 mSv. The E adjusted hazard ratio (HR) was 1.004 (95% CI 1.000 -1.009, p=0.045) for cancer death and 1.008 (95% CI 1.005-1.011, p<0.001) for (fatal and non-fatal) cancer onset. Lung organ dose was a significant predictor of primary lung cancer risk with adjusted HR of 1.003 (95% CI 1.001 -1.005, p=0.014).



HR for lung cancer and lung organ dose.

Conclusion: Cancer is the cause of death in 1 out of 7 patients admitted for cardiac disease and the radiological exposure from medical imaging is predictive of cancer risk and cancer death. Lung organ dose predicts subsequent lung cancer.

3919 | BEDSIDE
Chronic kidney disease is associated with worse outcomes in ACS patients: results from the TRACER trial

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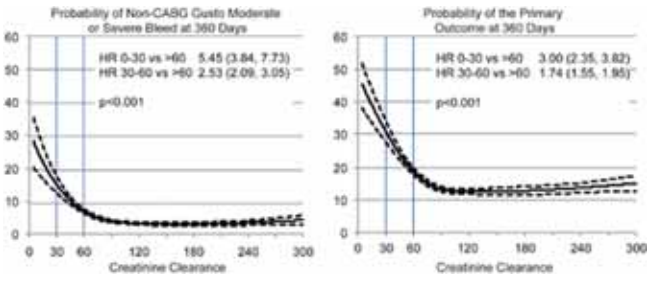
Purpose: We studied the relationship between renal function and clinical outcomes in the TRACER trial, which randomized 12,944 patients with non–ST-segment elevation acute coronary syndromes (NSTE ACS) to vorapaxar or placebo. Patients with renal dysfunction were not excluded.
Methods: Renal function was estimated using the Cockcroft-Gault formula. Patients were categorized as normal renal function (creatinine clearance [CrCl] >60 mL/min) or moderate (≥30 mL/min and ≤60 mL/min) or severe (<30 mL/min) renal impairment. The association between bleeding and ischemic outcomes and CrCl was also assessed using CrCl as a continuous variable with spline functions showing 95% confidence intervals.
Results: In total, 1477 (12.1%) patients had moderate and 190 (1.6%) had severe renal impairment. Patients with renal impairment were older, had lower body weight, and had more cardiac risk factors and prior cardiac events. As renal function declined, unadjusted rates at one year of GUSTO moderate or severe bleeding and the composite of cardiovascular death, myocardial infarction, stroke, recurrent ischemia requiring rehospitalization, or urgent coronary revascularization increased significantly (Figure). Within predefined clinical categories of renal function, the curves show steep slopes for the relationship between CrCl and outcomes.



Conclusions: Patients with impaired renal function are at significant increased risk of unadjusted one-year bleeding and ischemic outcomes. Importantly, the risk of adverse outcomes is not linear within typically used clinical categories of renal dysfunction.

3920 | BEDSIDE

Influence of glycated haemoglobin levels in a chronic ischaemic heart disease primary care cohort of diabetic patients. The BARIHD study

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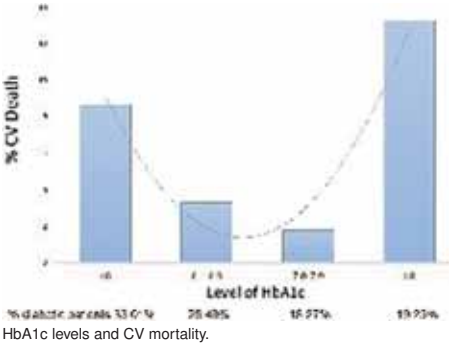
Purpose: There is scarce data about the influence of diabetes control measured by glycated haemoglobin (HbA1c) outside clinical trials in chronic ischaemic heart disease (CIHD). We assessed the influence of HbA1c levels in the outcomes during the follow up of CIHD cohort in a primary care physicians (PCP) setting

Methods: BARIHD was a cross-sectional multicentric study made with the collaboration of 69 PCP. The PCP included during February 2007,patients that fulfil the inclusion criteria: coronary artery disease (CAD) with at least 1 year of follow up since diagnosis, diagnosis clear established (stable angina, unstable angina or myocardial infarction-MI) in a discharge summary from cardiology department. Follow-up was done by clinical review or telephone contact and death or CV events were recorded, as well as the cause of death.

Results: 1108p were included, we found 318 diabetic patients (28.7%), they were older (71.1 vs 68.5 years old, p<0.001) with more female (33.9% vs 25.9%, p<0.001). Diabetic patients showed the same percentage of previous MI (54.3% vs 55.4%; p=ns), coronary angioplasty (73,9% vs. 75%; p=ns) or CABG (20.2% vs. 16.6; p=ns). Higher percentage of hypertension, atrial fibrillation, prior heart failure, peripheral artery disease was found in the diabetic group. The median of follow-up was 811 days, with 13p lost. CV death was higher in the diabetic group (6.5% vs 3.0%, p=0.008). In the figure we show the influence of HbA1c levels in the CV death during the follow-up (<6/8.7%;6.1-6.9/3.3%;7-7.9/1.8%;>8/13.3%;chi-square p-value=0,031).



HbA1c levels and CV mortality.

Conclusions: We found that HbA1c levels showed a U shape curve when we evaluated the CV death of the CIHD cohort, this finding highlights the importance of the new control levels proposed in the 2013 ESC diabetes guidelines.

3921 | BEDSIDE

Prognostic impact of vulnerable plaque on computed tomographic coronary angiography with normal myocardial perfusion image in patients with diabetes

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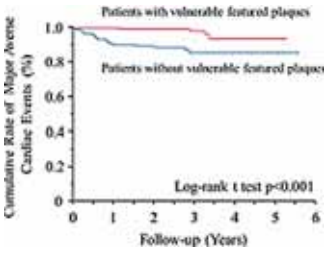
Purpose: Normal myocardial perfusion imaging (MPI) has a limited prognostic predictive value in patients with diabetes mellitus (DM). Computed tomographic coronary angiography (CTCA) is a reliable, noninvasive modality for assessing plaque composition as well as the severity of luminal narrowing. We evaluated the prognostic value of a vulnerable coronary plaque on CTCA for predicting long-term major adverse cardiac event (MACE) in patients with DM who had normal MPI.

Methods: A total of 334 consecutive patients with type 2 DM who had undergone CTCA and had normal findings on exercise-stress myocardial perfusion single-photon emission computed tomography was enrolled. CTCA analysis included the presence of more than 50% luminal stenosis, and vulnerable features including positive remodeling, low-attenuation plaque, and ring-like enhancement. The primary endpoint was a MACE including cardiac death, nonfatal myocardial infarction, unstable angina, and ischemia-driven revascularization.

Results: The 3-year cumulative event rate was 1.8% per year, and 80% of MACE occurred in patients with plaques exhibiting at least one of vulnerable features. Patients with ACS event had higher prevalence of more than 50% luminal stenosis (p<0.001), 2- or 3-vessel disease (p<0.001), and vulnerable featured plaques (p<0.0001) than those without MACE. In patient-based multivariate analysis, the presence of plaque with vulnerable features on CTCA was a significant predictor for MACE (p=0.003). Patients with vulnerable plaque had worse cardiovascular outcomes compared to those without vulnerable featured plaques (p<0.001) (Figure).



Kaplan-Meier analysis for MACE.

Conclusions: This study demonstrated that vulnerable coronary plaques were associated with long-term MACE in patients with type 2 DM, even with normal MPI.

CARDIO-METABOLIC DISTURBANCES- FROM BIRTH TO DEATH

3930 | BEDSIDE

Maternal obesity during pregnancy and premature cardiovascular mortality in later life

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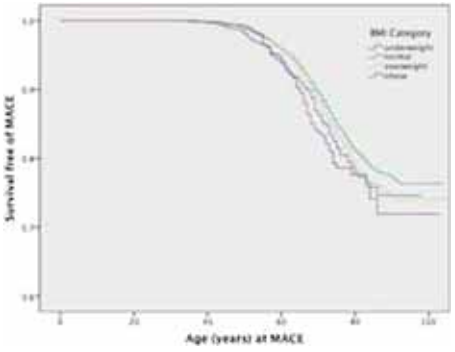
Purpose: We aimed to determine whether maternal obesity during pregnancy is associated with increased mortality from cardiovascular events in later life.

Methods: Maternity records of women who gave birth to their first child between 1950 and 1976 (n=18,912) from the Aberdeen Maternity and Neonatal databank were linked to the General Register of Deaths, Scotland and the Scottish Morbidity Record systems. Death and hospital admissions for cardiovascular events up to 1 January 2012 were recorded with median follow-up of 50 years. Maternal body mass index (BMI) was calculated from height and weight measured at the first antenatal visit. The effect of maternal obesity on outcomes was tested with time to event analysis with Cox proportional hazard regression to compare outcomes of mothers in underweight, overweight, or obese categories of BMI as recommended by WHO compared to mothers with normal BMI.

Results: All-cause mortality was increased in obese mothers (BMI>30kg/m^2) compared with mothers with normal BMI after adjustment for maternal age at delivery, socioeconomic status, smoking status, gestational age at BMI measurement, pre-eclampsia and low birth weight (hazard ratio 1.35, 95% confidence interval 1.02 to 1.78). In adjusted models, overweight and obese mothers have increased risk of major cardiovascular events, MACE (1.12, 1.01 to 1.24 and 1.37, 1.07 to 1.75 respectively) and hospital admission for a cardiovascular event (1.27, 1.16 to 1.39 and 1.49, 1.19 to 1.86) compared to mothers with normal BMI.



Conclusions: Maternal obesity is associated with an increased risk of premature death and cardiovascular disease in later life. Pregnancy is a key time when women are motivated to improve their health. This period could represent a window of opportunity for interventions to reduce obesity.

3931 | BEDSIDE

Incidence of reactive hypoglycemia after oral glucose load and significance of hypoglycemia on inflammation and blood coagulation

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Purpose: Hyperglycemia is known to induce hypoglycemia reactively after a big meal in patients with preserved insulin secretion. Since oral glucose tolerance test (OGTT) forces subjects to uptake 75g glucose within a few seconds, it is supposed that reactive hypoglycemia is induced in some subjects. That is, 75g OGTT is thought to be a splendid model to detect the reactive hypoglycemia after

acute hyperglycemia. Hereby, we planned to evaluate the incidence of reactive hypoglycemia in patients with coronary arterial disease, and the effect of hypoglycemia on inflammation and clot formation.
Methods: In this prospective study, 106 consecutive non DM patients (70±9 y.o., 73 male) with coronary arteriosclerosis from April 2012 to January 2014 were enrolled. Blood samples were collected until 4 hours after 75g OGTT. Hypoglycemia was defined that blood glucose level was less that 80 mg/dl after glucose load. We classified patients into 2 groups according to the onset of hypoglycemia: Hypo group (n=54) and Non-Hypo group (n=51).
Results: Hypoglycemia was seen in more than 50% of subjects and more frequently at 4 hours after glucose load than 2 hours (4hrs 50.9% vs. 2hrs 7.5%, P=0.004, Fig. 1A), although no patients felt any symptoms. Insulin level at 60minutes was greater in Hypo group than Non-Hypo group as shown in Fig. 1B. Increase ratio of white blood cell count and D-dimer between before and 4 hours after glucose load was greater in Hypo-group than Non-Hypo group (107.5±21.7% vs. 95.9±19.1%, p=0.034, and 120.6±47.4 vs. 101.9±20.4%, p=0.048, respectively).

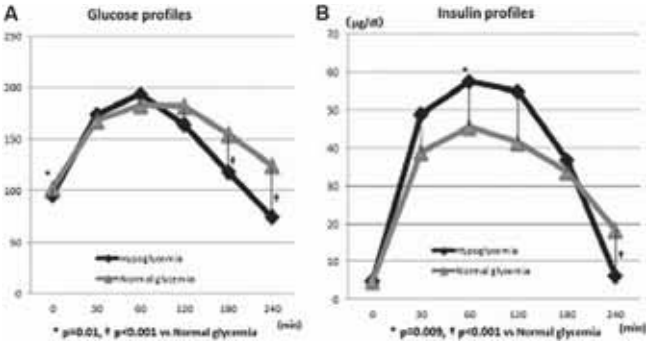

Figure 1. Glucose and insulin profiles of 4hrs OGTT.

Conclusion: More than 50% of patients were revealed to experience hypoglycemia when data were sampled until 4 hours after glucose load. Patients with hypoglycemia seemed to relate with inflammation and blood coagulation.

3932 | BEDSIDE
Postprandial hyperglycemia but not glycated hemoglobin predicts adverse epigenetic signatures and vascular dysfunction in type 2 diabetic patients with optimal glycemic control

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Purpose: Optimal glycemic control (OGC) failed to improve macrovascular complications in patients with type 2 diabetes (T2DM) but the underlying mechanisms remain largely unknown. The mitochondrial adaptor p66Shc is critically involved in oxidative stress and vascular damage. This study was designed to investigate whether epigenetic changes of p66Shc gene contribute to residual vascular risk in T2DM patients with OGC.
Methods: 40 T2DM patients and 20 age-matched controls (age 46±12 vs. 50±14, p=NS) were consecutively enrolled. T2DM patients were assigned to OGC strategy for 8 months. Glycated haemoglobin (HbA1c) and continuous blood glucose monitoring (CBGM) were assessed. Glycemic variability was measured as mean postprandial incremental area under the curve (AUCpp). Brachial artery flow-mediated dilation (FMD), oxidative stress marker 8-isoprostaglandin F2α (8-isoPGF2α) in 24-hour urine samples as well as p66Shc promoter methylation in peripheral blood monocytes were assessed at baseline and follow-up (FU). Data are expressed as mean ± SEM.
Results: Baseline and FU HbA1c values (9.4±2 vs. 6.4±1%, $p<0.01$) confirmed the achievement of OGC. T2DM patients showed endothelial dysfunction (FMD, 5.6±0.4 vs. 8.5±0.4%, $p<0.01$), increased oxidative stress (484±25 vs. 52±8 pg/ml/mg creatinine, $p<0.01$) and p66Shc upregulation (0.21±0.01 vs. 0.05±0.05 AU, $p<0.01$) as compared with controls. However, in T2DM patients OGC was not able to rescue endothelial dysfunction (FMD 5.7±0.3 vs. 5.6±0.4%, p=NS), 8-isoPGF2α levels (453±21 vs. 484±25 pg/ml/mg creatinine, p=NS) and p66Shc upregulation (0.22±0.02 vs. 0.21±0.01, p=NS) as compared with baseline values. DNA methylation of p66Shc promoter, an important repressor of p66Shc expression, was strongly decreased in T2DM patients and OGC did not revert such adverse epigenetic remodelling. Interestingly enough, this epigenetic modification was found in diabetics with relevant glycemic excursions despite OGC. Indeed, linear regression analysis adjusted for confounding factors showed that AUCpp (β=0.66, $p<0.01$) but not HbA1c (β=-0.17, p=0.43) was independently associated with persistent hypomethylation of p66Shc promoter.
Conclusions: In T2DM patients with OGC, glycemic excursions may drive persistent epigenetic changes of p66Shc promoter, oxidative stress and subsequent endothelial dysfunction. Targeting postprandial hyperglycemia rather than HbA1c may suppress chromatin changes responsible for the progression of vascular complications in T2DM.

3933 | BEDSIDE
Epigenetic signatures induced by chromatin modifying enzymes SUV39H1 and SRC-1 regulate vascular p66Shc expression and oxidative stress in obese individuals

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Purpose: Oxidative stress is an important mediator of vascular dysfunction in obese individuals. In this setting, environmental factors may induce epigenetic signatures leading to dysregulation of oxidant and inflammatory genes. The mitochondrial adaptor p66Shc is critically involved in the generation of reactive oxygen species, cellular apoptosis and vascular damage. The present study investigates epigenetic regulation of p66Shc in human obesity.
Methods: Small visceral fat arteries (VFA) were isolated from 10 obese and 10 age-matched healthy subjects. Organ chamber experiments were performed to assess endothelium-dependent relaxation to acetylcholine (Ach, 10^{-9} to 10^{-4} mol/L). Mitochondrial superoxide anion (O2-) was determined by ESR spectroscopy. Chromatin immunoprecipitation (ChIP) was performed to investigate epigenetic modifications on p66Shc promoter. Between-variable correlations were measured by Spearman's analysis. Probability values less than 0.05 were considered statistically significant.
Results: Maximal endothelium-dependent relaxations were impaired in VFA from obese subjects as compared with controls (64.9%±4.8 vs 93±2.9, $p<0.01$). In obese vessels p66Shc expression was increased (AU, 1.5±0.3 vs 0.7±0.2, $p<0.01$) and correlated with mitochondrial oxidative stress (r=0.76, $p<0.01$) as well as endothelial dysfunction (r= -0.47, $p<0.01$). Demethylation and increased acetylation at lysine 9 of histone 3 (H3K9) were the main epigenetic changes found on p66Shc promoter of obese subjects. Real-Time PCR array for chromatin modifying enzymes showed that H3K9 methyl-writing enzyme SUV39H1 was significantly downregulated (fold change vs. controls: -6.7, $p<0.01$) whereas acetyltransferase SRC-1 was increased (fold change vs. controls: 3.0, $p<0.01$) in VFA from obese subjects as compared with controls. To further investigate whether epigenetic changes are actively involved in the regulation of p66Shc expression, reprogramming of chromatin modifying enzymes SUV39H1 and SRC-1 was performed in vascular endothelial cells isolated from leptin-deficient obese mice (LepOb/Ob). Interestingly, overexpression of SUV39H1 and knockdown of SRC-1 suppressed p66Shc upregulation and endothelial ROS generation.
Conclusions: Reversible epigenetic signatures on p66Shc promoter may drive obesity-induced vascular disease. These novel findings suggest that reprogramming these modifications may restore vascular homeostasis in obese individuals.

3934 | BEDSIDE
Is long duration statin therapy associated with risk of diabetes in heterozygous familial hypercholesterolemia or familial combined hyperlipidemia?

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Purpose: Controversial findings exist regarding the potential diabetogenicity of statins. Aim of our study was to investigate the role of long duration statin treatment on glucose metabolism of heterozygous Familial Hypercholesterolemia (hFH) and familial combined hyperlipidemia (FCH) patients.
Methods: Study population consisted of 212 hFH patients and 147 FCH patients that visited our Lipid Outpatient Department (mean follow up of 11 and 10 years respectively). Several clinical data, such as history of diabetes mellitus (DM), cardiovascular disease, thyroid function, metabolic syndrome variables and lifestyle data were obtained whereas biochemical markers measured included glucose levels and lipid profile. Study endopoints were new onset DM and combined pre-diabetes/DM. In order to compare the effects of different doses of different kind of statins, a "statin treatment intensity product" was used.
Results: 14% of FCH and only 1% of hFH patients developed new DM during follow up. In the FCH group new onset DM was associated with metabolic syndrome, low HDL levels and central obesity but not with the kind or the intensity of statin treatment. In contrast, multivariate analysis revealed that high intensity statin treatment was associated with higher risk of developing pre-diabetes/DM compared with low intensity treatment (Exp(B)=4.169, 95% C.I.=1.089-15.95, p=0.037).
Conclusions: Long duration of high intensity statin therapy is not associated with diabetic risk in hFH patients. High intensity of statin treatment is associated with higher incidense of combined DM/pre-diabetes, but not with higher incidence of DM in the FCH population.

3935 | BEDSIDE
Insulin resistance and risk of cardiovascular disease in postmenopausal women

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Purpose: We sought to evaluate whether measures of insulin resistance would improve cardiovascular disease (CVD) risk prediction beyond traditional risk factors.
Methods: We identified 15,288 women from the prospective Women's Health Initiative Biomarkers studies who had data on fasting serum-insulin and serum-glucose, and no history of myocardial infarction, stroke, heart failure, coronary revascularization, atrial fibrillation, or diabetes at baseline (1993–1998). Follow-up was truncated at 10 years to identify CVD events (coronary heart disease death, non-fatal myocardial infarction or nonfatal and fatal ischemic stroke) within 10 years. We assessed the prognostic value of adding serum-insulin, HOMA-IR (homeostasis model assessment of insulin resistance), the serum-triglyceride/serum-high-density lipoprotein ratio (TG/HDL) or impaired glucose metabolism (glucose levels≥110 mg/dL) to traditional cardiovascular risk factors in separate Cox multivariable analyses, and assessed risk discrimination and reclassification.
Results: Over ten years 894 (5.8%) women had CVD events, an incidence rate of 6.4/1,000 person-years. Insulin resistance was significantly associated with CVD risk with age- and race/ethnicity-adjusted hazard ratios (HRs, 95% confidence interval [CI]) for a two-fold increase in baseline insulin levels of 1.21 (CI 1.12-1.31), in baseline HOMA-IR of 1.19 (CI 1.11-1.28), in baseline TG/HDL of 1.35 (CI 1.26-1.45), and 1.31 (CI 1.05-1.64) for women with impaired glucose metabolism at baseline. Insulin, HOMA-IR and TG/HDL were associated with increased CVD risk after adjustment for most traditional risk factors, but greatly attenuated after adjustment for HDL-cholesterol: After adjusting for age, race/ethnicity and HDL-cholesterol the HRs were 1.06 (CI 0.98-1.16) for insulin, 1.06 (CI 0.98-1.15) for HOMA-IR, 1.11 (CI 0.99-1.25) for TG/HDL and 1.20 (CI 0.96-1.50) for glucose. Adding measures of insulin resistance to traditional risk factors did not improve CVD risk discrimination and reclassification.
Conclusions: Insulin, HOMA-IR, TG/HDL and impaired glucose metabolism are significantly associated with CVD risk in postmenopausal women, but do not add significant prognostic information after adjustment for HDL-cholesterol.

COMPLICATIONS IN CARDIAC IMPLANTABLE ELECTRONIC DEVICES AND BEYOND

P3952 | BEDSIDE
Impact of early complications on outcomes among patients with implantable cardioverter defibrillator in primary prevention

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Background: The life-saving benefit of implantable cardioverter defibrillators (ICD) has been well demonstrated, and therefore their utilization has considerably grown in the last 10 years. At the same time, complications have become an increasingly important concern.
Objectives: This study aimed to assess the prevalence and impact on outcomes (late complications and overall mortality) of early complications after ICD implantation for primary prevention in a large French population.
Methods: From a mutlicentric French registry (DAI-PP registry, 2002-2012), 5547 consecutive patients, with coronary artery disease or dilated cardiomyopathy, were implanted with an ICD in the setting of primary prevention. From 5338 (96%) patients with full information, we determined prevalence, independent associated factors and prognosis of the occurence of early (within 30 days post implantation) complications.
Results: Early complications occurred in 709 patients (13.5%), mainly related to lead dysfunction or hematoma (56%). Independent factors associated to early complications were renal impairment (clearance <30ml/min, OR=1.69, 95%CI 1.19-2.41, P<0.001), cardiac resynchronization therapy (OR=1.61, 95%CI 1.17-2.21, P=0.004), anticoagulant therapy (OR=1.30, 95%CI 1.04-1.63, P=0.02) and older age (OR=1.02, 95%CI 1.01-1.02, P=0.03). During a mean follow-up of 3.1±2 years, 834 patients experienced ≥1 complication (15.6%), mainly inappropriate therapies and/or lead dysfunction (75%). After consideration of potential confounding factors, early complications were significantly associated with the occurrence of late complications (OR=2.15, 95%CI 1.73-2.66, P<0.0001) and a higher risk of mortality during follow-up (HR=1.48, 95%CI 1.17-1.88, P=0.001).
Conclusions: Early complication is a frequent event after ICD implantation occurring in one out of six patients. These events are associated with a significant increase of late complications and overall mortality.

P3953 | BEDSIDE
Chronic venous obstruction during cardiac device revision: safety and efficacy of percutaneous techniques

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Purpose: Over past decade widening of indications and technological advances resulted in a dramatic increase in pacemaker and cardioverter defibrillator (ICD) implantations and therefore upgrading and revision procedures. 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 the incidence of venous obstruction after chronic transvenous system implantation, to determine its predictors and to evaluate feasibility of percutaneous transluminal vein angioplasty to overcome venous occlusion.
Methods: 170 consecutive patients admitted for system revision due to device upgrading (78,4%), lead malfunction (20,5%) or infection (1,1%) between January 2004 and January 2013 were included. All patients underwent ipsilateral contrast venography. Venous obstruction was classified as significant stenosis (>75%), near occlusion or total occlusion.
Results: All procedures were successful. Venous obstruction was found in 28 (16,5%) patients: 48,2% as complete occlusion, 28,6% as near occlusion and 28,6% as significant (>75%) stenosis. Incidence of venous obstruction was significantly increased in patients with 3 (p=0,05) and 4 (p=0,03) existing leads and with a previous cardiac resynchronization therapy with defibrillator (CRT-D) system (p=0,004). Different techniques were performed to obtain venous access: 8 percutaneous transluminal vein angioplasty and 15 distal venous puncture, far from the stenosis. In 5 cases there weren't any difficulties to advance cardiac leads according to standard methods. Transluminal vein angioplasty was performed with a 6x40 mm balloon, inflated at 8-10 atm for 5-10 minutes; no complications occurred and electrical parametres of existing leads remained stable after procedure and at follow up.
Conclusions: Venous obstruction is a relatively frequent finding during cardiac device revision which seems to be related to number of existing leads and devices complexity. Transluminal vein angioplasty and distal venous puncture are safe and effective approach, allowing ipsilateral transvenous lead placement.

P3954 | BEDSIDE
Riata silicone defibrillation leads failure: increase in prevalence after 5 years of follow-up

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Introduction: Riata silicon implantable cardioverter defibrillator (ICD) leads (St. Jude Medical, Sylmar, CA) show an increased incidence of insulation defects, particularly "inside-out" lead fracture where inner, separately insulated cables penetrate through the surrounding silicone of the lead body. The exact incidence of Riata lead problems is not clear and seems to range between 2-4% per year in the first 5 years after implantation according to registry data. Long-term follow-up of Riata lead after 5 years is not very clear.
Methods: The aim of this study was to analyze incidence of Riata leads failure on a long-term follow-up. A retrospective analysis was performed in 198 consecutive patients, who were implanted with transvenous Riata ICD-leads from January 2003 to December 2010 in our center. 35 pts were followed in other centres and were considered lost of follow-up. 163 patients are under regular follow-up with device control and chest X-ray every 3 months.
Results: During a mean follow-up of 6.5±3.8 years, 23 of 163 patients died of severe heart failure or other causes, no one confirmed being died of lead failure. 3 patients underwent heart transplantation. Considering diagnosis of lead failure including perforation, dislogement and malfunction due to specific insulation defect: 2 pts (3.26%) had perforation in less then 3 months after implantation; 13 pts (8%) had lead failure or fracture with insulation defect. Comparison of leads parameters before and afetr 5 years of follow-up showed that the fracture rate obviously increased after 5 years. On the 13/163 patients with lead failure necessitating intervention, 5 lead fracture occurred before 5 years and 8 supplementary cases happened after 5 years of follow-up.
Conclusion: Riata leads had high rate of malfunction in different period after implantation. Insulation defects of lead is especially higher after 5 years that implies a very careful and strict follow-up on the long run.

P3955 | BEDSIDE
Clinical course of high-risk (...) leads after generator replacement with an ICD equiped with a noise-identifying algorithm

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Purpose: The problem of premature insulation failure of (...) ICD leads is well documented. Lead replacement is currently redommended only when evidence of electric failure is present, even when battery replacement is scheduled. The purpose of this analysis was to investigate the clicinal course of these leads after battery replacement with a ICD equiped with a noise-identifying algorithm
Methods: Between 03/2002 and 11/2010 673 silicon-insulated Riata leads were implanted in our hospital, 192 of which are still active. Between 02/2012 and 12/2013 51 patients with such a lead underwent routine battery replacement and received an ICD equiped with the Secure Sense algorithm. Prior to surgery, all lead measurements were within normal range and the original Riata leads were not scheduled to be replaced, according to current recommendations. Fluoroscopic or radiologic evidence of externalization was present in 20% of the cases. All patients underwent intraoperative lead testing twice: first with the old battery (a 25 Joule cardioversion shock) and second after induction of ventricular fibrillation with the new battery.
Results: Within a median time of 91 days, 12 patients (23,5%) had to undergo lead replacement due to lead malfunction: Three leads had to be replaced right after the first intraoperative shock because of severe noise sensing. Eight patients presented with Secure Sense alarm (vibration) for noise sensing, with a first occurence in the morning after surgery. The algorithm failed to identify noise sensing in one patient; the patient's device was programmed according to MADIT-RIT redommendations and delivered no inappropriate therapies. None of the patients received an inappropriate therapy.
Conclusions: One quarter of the Riata leads which appeared to be intact at the time of surgery scheduling had to be exchanged within 3 months following battery replacement. The combination of the Secure-Sense algorithm with a more conservative programming according to MADIT-RIT resulted in none of the patients receiving inappropriate therapies.

P3956 | BEDSIDE
Effects of pacemaker electrodes on tricuspid regurgitation and right sided heart functions

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Purpose: The aim of this study was to assess the effect of trans-tricuspid placement of permanent pacemaker (PPM), implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) leads on tricuspid valve and right sided heart function by two-dimensional echocardiography prospectively.
Method: Initial echocardiography was performed before PPM/ICD and CRT implantation and re-evaluation by echocardiography was performed immediately after procedure, in the 1th, 6th and 12th month after implant. A total of 41 patients (31 male, 10 female; mean age: 63.6±12.2 years) were included in the study prospectively.
Results: Patients with baseline absent TR of 8 (19.5%) developed abnormal TR (9.8% mild, 9.8% moderate) after implant. Patients with baseline mild TR of 23 (56.1%) developed abnormal TR (41.5% moderate, 7.3% severe) after implant. Patients with baseline moderate TR of 10 (24.4%) developed abnormal TR (19.5% severe) after implant. TR worsened by 1 grade in 70.8% and 2 grade in 17.1% after implant. Worsening of TR is generally observed following first month. Vena contracta and PISA values of TR is increased during the study period especially after 1st month visit. In overall, there is no significant difference in the TR worsening between PPMs/ICDs and CRTs groups. During follow-up right ventricular dimensions (RV1, RV2, RV3) are increased but longitudinal right ventricular systolic/ diastolic functions and right ventricular TAPSE values are not worsened. Right atrial systolic and diastolic volumes are progresively increased and right atrial systolic functions are progressively decreased. There is no difference between pacemaker groups in terms of right atrial and right ventricular function changes.
Conclusions: Implantation of permanent transvenous right ventricular electrodes is associated with worsening of tricuspid regurgitation. The right atrium and right ventricle is also affected in some extent from the pacemaker implantation. There is no significant difference in the TR worsening and right ventricular and right atrial functions between PPMs/ICDs and CRTs sub-groups.
Better understanding of lead-induced tricuspid regurgitation and right sided heart dysfunction will be essential to the development of preventive strategies, which can then be tested in future clinical trials.

P3957 | BENCH
Differences in encapsulating tissue of polyurethane and silicone leads severely damaged in the intracardiac part

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Purpose: Endocardial lead may undergo in vivo insulation damage in the intracardiac part (ICP): silicone (SIL) insulated lead mainly due to abrasion, and polyurethane (PTU) mostly in the mechanism of environmental stress cracking. Tissue reaction to different lead insulation and lead damage is poorly understand. The aim of our study was to determine the differences in clinical and histopathomorphological features in patients (pts) with severely damaged insulation of polyurethane and silicone leads.
Methods: 116 consecutive pts. underwent lead removal. 36 pts. presented severe degree of insulation lead damage in ICP. Leads were analysed with optical microscope and scanning electron microscope to determine abrasion with conductor exposure in SIL and environmental stress cracking in PTU leads. Tissue fragments were processed and analysed according to standard protocols. Both hematoxylin-eosin and immunostainig were used to identify tissue and cells.
Results: In the analyzed population there were 18 pts. with SIL and 18 pts. with PTU insulated leads. In PTU group when comparing with SIL more pts. underwent lead removal due to non-infective indications (83,3% vs 55,5%), in all pts. with PTU leads cardioverter-defibrillator system were implanted. None significant differences in co-morbidities were observed between SIL and PTU groups. In SIL group there were more implanted leads per pt (mean number 2,2 vs 1,4), with longer mean dwell time (133,3 vs 55 months), and with longer mean transvenous lead removal procedure time (129,2 vs 100,3 minutes) $P<0,05$. Histopathological analyse of encapsulating tissue revealed that in pts. with SIL insulated leads cell poor tissue (16-94% vs 10-55%; p=0,009), hyalinization (14-82% vs 9-50%; P=0,04), macrophages presence (11-64,7% vs 5-27,7%; P=0,03), and calcifications (5-29,4% vs 1-5,5%; P=0,06) were more often observed. No statistically significant differences were seen in vasculogenesis, hemosiderine deposits, and foreign body giant cells presence in encapsulating lead tissue between groups. In the heart muscle fragments comparing SIL vs PTU group interstitial fibrosis (18,7% vs 28,6%), vacuolar degeneration (11,1 vs13,3%), adipose tissue (0 vs 5,9%), cardyomyocytes hypertrophy (11,1% vs 6,6%) were observed.
Conclusions: Encapsulating SIL lead tissue is mainly cell poor, with hyalinization, and calcifications. Encapsulating tissue structure may influence on procedure time and difficulty. Macrophages were more often seen in neighborhood of SIL leads with abrasions where may take part in the process of phagocytosis of small detached in abrasion process silicone fragments.

P3958 | BEDSIDE
Transvenous lead extraction: to reimplant or not to reimplant?

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Purpose: Advanced indications for primary preventive implantable cardioverter-defibrillator (ICD) therapy and cardiac resynchronization therapy (CRT) bear steadily increasing numbers of cardiovascular implantable electronic device (CIED) recipients worldwide. The higher burden of CIED interventions is associated with local and systemic CIED infections and lead-related complications requiring complex transvenous lead extraction (TLE) procedures and careful reassessment of the indication to reimplant a new CIED system. The purpose of the study was to investigate the need and indications for reimplantation in explanted patients (pts).
Methods: Prospectively collected data on 150 consecutive CIED pts [123 male (82%), median age 67 years (56-76)] undergoing total TLE at our center between January 2012 and October 2013 were reviewed for indication and type of reimplanted device.
Results: TLE was indicated for pocket infection in 48 pts (32.0%), device-related systemic infection in 44 pts (29.3%), and lead-related complications in 58 pts (38.7%). Eight patients (5.3%) died during hospitalization and were excluded from analysis. Thirty-two of the 142 included pts (22.5%) did not receive a new CIED system due to lack of a proper indication according to the current ESC guidelines. Among the 110 reimplanted pts (77.5%), 77 pts (70%) received the same CIED system, whereas 33 pts (30%) underwent either an upgrade (n=16), downgrade (n=15), or change to a subcutaneous ICD (n=2). In this group 14 pts received a cardiac resynchronization device.
Conclusion: Reimplantation of a CIED was not indicated in 22.5% of our TLE study population. Patients with an indication for CIED following TLE need to be reassessed carefully with regard to upgrade or downgrade of the previous system. Almost half of these patients had an indication for CRT therapy. Furthermore novel therapy strategies such as subcutaneous ICD or wireless pacing are gaining in importance in this patient population.

NEW THERAPIES IN HEART FAILURE

P3959 | BENCH
Intravenous infusion of purified poloxamer 188 (MST-188), improves left ventricular systolic and diastolic function in dogs with advanced heart failure

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Background: Calcium overload occurs in heart failure (HF) leading to cardiomyocyte dysfunction and death. MST-188 (purified poloxamer 188) is a rheologic agent that has been shown to improve left ventricular (LV) function in experimental myocardial infarction. Its activity results from improved microvascular blood flow and/or repair of damaged cell membranes. Microscopic cardiomyocyte sarcolemmal disruption can occur in the failing heart and possibly lead to unregulated calcium entry into the cell resulting in calcium overload. We examined the effects of acute i.v. infusion of MST-188 on LV function in dogs with microembolization-induced HF (LV ejection fraction, EF∼30%).
Methods: 21 HF dogs were randomized to 2 hours infusion of low dose (LD) MST-188 (225 mg/kg, n=7), high dose (HD) MST-188 (450 mg/kg, n=7) or v/v normal saline (control, n=7). LV end-diastolic (EDV) and end-systolic (ESV) volumes, EF and Ei/Ai and deceleration time (DT) of mitral inflow velocity, the latter two indexes of LV diastolic function, were measured at baseline, at end of infusion, and at 24 hours, 1 week and 2 weeks post-infusion. The change between baseline and all other time points (treatment effect, Δ) was calculated.
Results: Data are shown in the table. Saline in control dogs had no effect on any measures. Compared to control, LD and HD MST-188 reduced ESV, increased EF, Ei/Ai and DT and tended to decrease EDV without affecting heart rate or aortic pressure. The benefits tended to last for at least 1 week and in some instances 2 weeks after end of infusion (2 weeks data not shown).
Conclusions: Intravenous MST-188 elicits improvements in LV systolic and diastolic function that last for at least 1 week after end of infusion. The results support continued development of MST-188 for the treatment of acute HF.

P3960 | BEDSIDE
Endothelin receptor blockade in heart failure with diastolic dysfunction and pulmonary hypertension

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Purpose: About 70-83% of patients with heart failure and preserved ejection fraction develop pulmonary hypertension, which is associated with worse prognosis. Up to date, there are no treatment recommendations regarding the pulmonary hypertension in this patients.
Methods: In this multicentric, randomised placebo-controlled pilot trial we investigated clinical and hemodynamic effects of the endothelin-receptor blocker bosentan versus placebo during a 6 months follow up period. Eligible probands received either 12 weeks bosentan (4 weeks 62,5mg b.i.d., followed by 8 weeks 125mg b.i.d.) or placebo. Right heart catheterization was performed at screening to verify pulmonary hypertension. At study entrance, week 12 and week 24 six minute walking tests, echocardiographic measurements and quality of life tests were performed.
Results: None of the 20 probands experienced worsening of heart failure. Six minute walking distance (6MWD) did not change in the bosentan group, but trend wise increased in the placebo group (from 302.29.9±86.66 m at study entrance to 383.95±74.91m at week 24; p=0.097); Fig.1. Echocardiographically estimated PAP significantly decreased in the placebo group (66.18±16.98 mmHg at study entrance to 48.57±9.93 mmHg at week 24; p=0.003), but did not change in the bosentan group (57.67±22.78.1 mmHg to 55,2±25.2 mmHg). Whereas estimated atrial pressure over the study period continuously decreased in the placebo group (11.09±4.91 to 10.00±3.78 to 9.29±3.45; p=0.034) a periodical increase was found in the bosentan group (Fig.2). In comparison to study entrance, after 24 weeks there was a trend of a better Minnesota Living with Heart Failure Questionnaire (61.00±17.50 vs. 49.38±16.41; p=0,06) in the placebo group.
Conclusions: In this pivotal trial we could demonstrate that bosentan in patients with HF-PEF and pulmonary hypertension did not improve exercise capacity, quality of life or hemodynamic measures assessed by echocardiography. In contrast, bosentan may be disadvantageous in comparison to placebo.

P3961 | BENCH
Long-term therapy with Bendavia (MTP-131) augments mitochondrial ATP-sensitive potassium channel opening in left ventricular myocardium of dogs with advanced heart failure

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Background: The level of the reduced form of nicotinamide adenine dinucleotide phosphate namely, NADPH, is increased in the failing heart and can lead to reduced opening of the mitochondria ATP-dependent potassium channels (mKATP). This abnormality can lead to ionic dysregulation in the mitochondrial environment with subsequent matrix contraction and reduced ATP production. Increased opening of mKATP improves oxidative phosphorylation by maintaining architecture of the inner mitochondrial membrane, preserving the low permeability of the outer membrane to ADP and permitting "efficient" energy transfer between mitochondrial and myofibrillar ATPases. Bendavia (MTP-131) is a novel mitochondria-targeting peptide that was previously shown to improve left ventricular (LV) function in dogs with chronic heart failure (HF) and to improve rate of ATP synthesis by mitochondria. The present study tested the hypothesis that chronic therapy with Bendavia augments mKATP opening in LV myocardium of dogs with chronic HF (LV ejection fraction ∼30%).
Methods: Ten dogs with coronary microembolization-induced chronic HF were randomized to 3 months therapy with subcutaneous injections of Bendavia (0.5 mg/kg once daily, n=5) or to subcutaneous daily injections of saline (Control, n=5). Fresh LV tissue at the end of 3 months of therapy was used to isolate mitochondria. mKATP was measured using the thallium-sensitive fluorophore assay kit and expressed in relative fluorescence units (RFU) per mg protein. Mitochondria ATP to ADP ratio was measured using the bioluminescent ApoSENSORTM assay kit.
Results: Compared to HF Controls, therapy with Bendavia resulted in a significant increase in opening of mKATP (1372±112 vs. 2775±254 RFU/mg protein, $p<0.05$). Further, Bendavia therapy significantly increased ATP/ADP ratio (0.46±0.04 vs. 0.94±0.07, $p<0.05$).
Conclusions: Long-term therapy with Bendavia augments opening of mKATP and increases ATP/ADP ratio in dogs with chronic advanced HF. These findings are consistent with the observed improvement of LV function in dogs with advanced HF following long-term therapy with Bendavia.

P3962 | BENCH
Long-term therapy with capadenoson, a partial adenosine A1-receptor agonist, reverses abnormalities of myocardial energy metabolism in left ventricular myocardium of dogs with chronic heart failure

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Background: Fatty acid (FA) and glucose oxidation are abnormal in heart failure (HF) and contribute to LV dysfunction. FA translocase (FAT/CD36), a protein involved in transmembrane transport of FA, carnitine palmitoyl transferase1b (CPT1b), a protein involved in transport of FA across the outer mitochondria (MITO) membrane, and citrate synthase (CS), a rate-limiting enzyme in the citric acid cycle, act to regulate FA utilization by MITO. Expression of all 3 proteins is abnormal in the failing LV. In addition, MITO biogenesis and function are also abnormal in HF as evidenced by downregulation of peroxisome proliferator-activated receptor coactivator-1α (PGC-1α) a transcriptional factor that regulates MITO biogenesis. We tested the hypothesis that capadenoson (CAP), a partial adenosine A1-receptor agonist shown to improve LV function in HF dogs, normalizes protein levels of CD36, CPT1b, CS and PGC-1α in LV myocardium of HF dogs (LV ejection fraction ∼30%).
Methods: LV tissue from 12 HF dogs randomized to 3 months therapy with CAP (7.5 mg twice daily, n=6) or to no therapy (Control, n=6) and tissue from 6 normal (NL) dogs was used. Protein level of CD36 was normalized to GAPDH and levels of CPT1b and CS were normalized to porin, a MITO protein unchanged in HF. The aforementioned proteins as well as phosphorylated (p-) and total (t-) protein levels of PGC-1α were measured in LV homogenate by Western blotting.
Results: Protein levels of CD36, CPT1b, and CS were reduced in HF-Controls compared to NL. CAP therapy partly restored levels of all 3 proteins (Table). Com-

Table 1

	NL	HF-Control	HF-CAP
CD36/GAPDH	1.13±0.12	0.43±0.09*	0.66±0.09†
CPT1b/Porin	2.40±0.28	0.94±0.12*	1.28±0.01†
CS/Porin	1.04±0.10	0.52±0.06*	0.97±0.12†
p-PGC-1α/t-PGC-1α	2.09±0.14	0.88±0.08*	2.01±0.20†

*$p<0.05$ vs. NL; †$p<0.05$ vs. HF-Control.

Abstract P3959 – Table 1

	Control			LD MST-188			HD MST-188		
	Δ 2 hrs	Δ 24 hrs	Δ 1 wk	Δ 2 hrs	Δ 24 hrs	Δ 1 wk	Δ 2 hrs	Δ 24 hrs	Δ 1 wk
EDV (ml)	0.1±0.5	2.0±0.7	2.0±0.8	–4.0±1.7	–1.0±1.6	–3.0±1.0	–3.0±1.0	–4.0±1.2	–1.0±0.7
ESV (ml)	–0.1±0.3	1.0±0.3	2.0±0.5	–9.0±1.2*	–5.0±2.1*	–6.0±2.3*	–10±1.4*	–8.0±1.3*	–7.0±1.3*
EF (%)	0.1±0.4	0.1±0.5	–0.9±0.3	10.0±0.6*	7.0±0.8*	9.0±2.4*	11.0±0.9*	8.0±2.0*	8.0±2.1*
Ei/Ai	–0.4±0.3	–0.3±0.4	–0.3±0.5	1.2±0.2*	0.9±0.2*	0.7±0.3	1.0±0.2*	0.8±0.2*	0.2±0.3
DT (msec)	1.0±0.8	0.6±1.7	0.7±1.7	7.4±1.7*	6.1±2.5*	5.3±2.8	8.3±1.4*	6.4±0.7	2.4±1.5

hrs, hours; wk, week; *$p<0.05$ vs. Control.

pared to NL, levels of p-PGC-1α and t-PGC-1α and the ratio of p- PGC-1α /t-PGC-1α were significantly reduced in HF-Controls but were all normalized after therapy with CAP (Table 1).
Conclusions: In HF dogs, chronic therapy with CAP normalizes expression of proteins involved in myocardial FA oxidation by MITO and in biogenesis of MITO. Improved myocardial energy metabolism in HF can contribute to the reported improvement of global LV function with CAP therapy.

P3963 | BEDSIDE
Low-dose Tolvaptan as furosemide alternative preserves renal function and renin-angiotensin system during intensive treatment in patients with congestive heart failure

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Background: Although loop diuretics are broadly used for congestive heart failure (HF), there frequently appear serious adverse effects such as worsening of renal function and activations of the sympathetic and renin-angiotensin system via arterial underfilling. On the other hand, the effects of sodium channel independent diuretic Tolvaptan on those complications in acute phase of HF patients are still unclear.
Methods and results: Fifty-five consecutive patients hospitalized due to worsening of congestive HF were randomly assigned to receive either daily 40 mg of intravenous furosemide or 7.5 mg of oral Tolvaptan, in addition to intravenous 0.025γ of carperitide and 200 mg of canrenoate potassium. Renal functions and neurohumoral factors were evaluated for 5 days after the admission. As results, patient characteristics were similar between Furosemide (n=27) and Tolvaptan group (n=28). Total of 5-day urine volume or fluid balance was not significantly different (9772 vs. 9240 mL, -4265 vs. -3500 mL, respectively), and similar degrees of improvement in BNP were achieved in both groups (-186±517 vs. -283±581 pg/mL). However, the value of serum creatinine (Cr) significantly deteriorated in Furosemide group (21±52 vs. -2.1±15%, p=0.031), and worsening of renal function that was defined as increase of creatinine more than 0.3 mg/dL occurred more frequently in Furosemide group (26 vs. 3.6%, p=0.019). Consequently, increase of Cr to earn 1000 mL of urine was 2.5-fold higher in Furosemide group (0.044±0.065 vs. 0.016±0.026 mg/dL/1000mL, p=0.043). On the contrary, increase in the ratio of BUN/Cr was significantly higher in Furosemide group (16±37 vs. -10±48%, p=0.027), suggesting arterial underfilling via forced dehydration. In terms of neurohumoral factors, although decreases of catecholamines were not significantly different (adrenaline: 57±87 vs. 61±69%, noradrenaline: 44±55 vs. 67±23%, dopamine: 14±234 vs. 55±60%), the value of plasma renin activity was enhanced only in Furosemide group (229±446 vs. 7.9±89%, p=0.013).
Conclusion: Low-dose Tolvaptan preserved renal function and renin-angiotensin system during intensive treatment in patients with congestive HF. This novel therapy may release HF patients from adverse effects with furosemide.

P3964 | BEDSIDE
Ivabradine adding on beta blocker based strategy provides better heart rate lowering than beta blocker alone based strategy in real life clinical practice: an analysis from REALITY HF study

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Purpose: Resting heart rate (HR) has emerged as a target of therapy and important determinant of prognosis in chronic heart failure (HF) and therapeutic interventions for HR reduction have been proven to be associated with improved outcomes. Although, beta-blocker (BB) therapy has been known to be very effective in lowering HR, recent analysis reported that majority of patients receiving BB therapy still have elevated resting HR. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study data were analyzed to evaluate the effects of ivabradine added to BB therapy versus BB monotherapy on achieving lower resting HR in real life clinical practice in patients with chronic HF.
Methods: REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients' clinical characteristics and the effects of current treatment modalities on resting HR and enrolled 1054 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF and LVEF <40%. 531 patients in sinus rhythm who were receiving or newly initiated BB therapy and 106 patients who were receiving or newly initiated ivabradine treatment as an add-on therapy to BB were included in this analysis. Adjustment, modification or up titration of HF medication was left to physician discretion during follow-up (FU) period. Resting HR and medications were obtained at baseline (V0) and reevaluated at 1-month (V1) and 4-month (V2) FU visits.
Results: In patients receiving ivabradine added to BB therapy, mean resting HR significantly reduced from 80.9±15 bpm at V0 to 74.0±10 bpm at V1 ($p<0.005$) and further decreased to 66.9±9 bpm at V2 ($p<0.001$). Initially, resting HR slightly increased from 74.4±13 bpm at V0 to 74.5±12 bpm at V1 ($p<0.001$) and then slightly but significantly decreased to 73.8±12 bpm at V2 (p=0.001) in patients receiving BB alone. In patients receiving ivabradine and BB combination therapy, proportion of patients with a resting HR <70 bpm increased from 21.7% at V0 to 27% at V1 and further increased 65% at V2. In patients receiving BB therapy alone, proportion of patients achieving a resting HR <70 bpm was 38.2% at V0, 30.9% at V1 and 39% at V2.
Conclusions: In patients with systolic HF in real life clinical practice, ivabradine adding on BB strategy provides better HR lowering as compared to BB alone strategy and almost two-third of patients achieves a resting HR <70 bpm with ivabradine regimen while only one-third reaches this level of HR with BB therapy alone.

P3965 | BEDSIDE
The effect of ivabradine on aortic stiffness in patients with heart failure

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Purpose: The aim of the current study is to evaluate the effect of using ivabradine treatment on aortic stiffness by by transthoracic echocardiography (ECHO) in heart failure patients who were administered ivabradine treatment.
Methods: The study included clinic patients who were diagnosed with heart failure, in sinus rhythm and who had still symptoms despite the medical treatment. Patients who were not receiving β-blockers or patients with a heart rate >70 bpm despite the treatment with β-blockers at a maximum tolerable dose were selected as the study group.For the control group, heart failure patients with a heart rate <70 bpm were determined. ECHO were performed and the aortic elastic properties were calculated
Results: A total of 182 patients were included in the study. By the end of the twelve month, a decrease in left ventricular end diastolic volume and left ventricular end systolic volume were observed, while ejection fraction (EF) increased (p=0.03). When aortic elastic parameters were evaluated between the two groups, there was no significant difference in aortic strain, aortic distensibility, and aortic stiffness index at the time of enrolment and at the three month visits. At the twelve month visit, it was found that aortic strain ($P<0.01$) and distensibility ($P<0.01$) significantly increased, while there was a significant decrease in the aortic stiffness index ($P<0.01$).The correlation analysis assessed the correlation between heart rate, EF and aortic elastic properties and revealed that there was a correlation between aortic elastic properties heart rate and EF (Fig. 1)

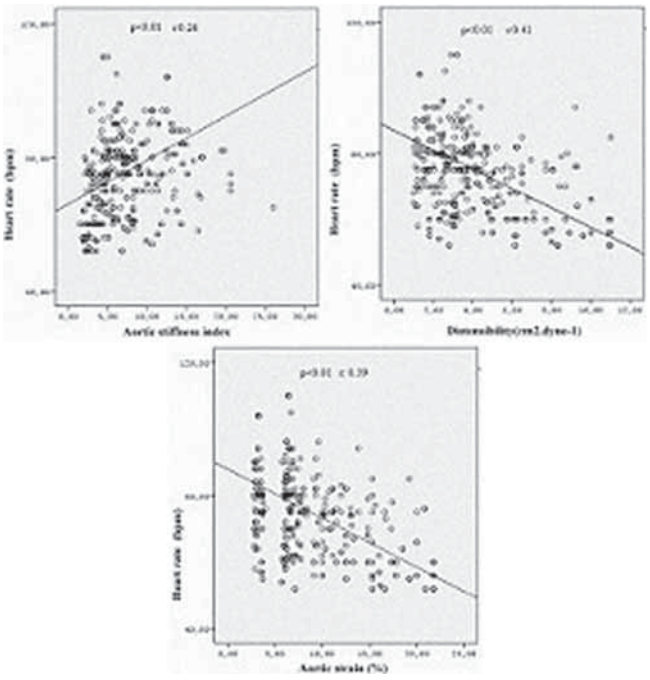

Figure 1

Conclusion: At the 12-month follow-up of the heart failure patients who were administered ivabradine treatment, significant improvements were achieved in aortic stiffness with ivabradine treatment.

PERCUTANEOUS EDGE-TO-EDGE MITRAL REPAIR

P3966 | BEDSIDE
Percutaneous mitral valve repair: mitra clip in functional versus degenerative disease - initial results in a prospective cohort of the German transcatheter mitral valve interventions (TRAMI) registry

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Aims: A substantial percentage of patients with mitral regurgitation (MR) in need of mitral valve repair are currently considered at high risk or prohibitive risk for conventional surgery. In Germany, the largest prospective cohort of patients studied has been treated using a percutaneous transcatheter approach. We report differences in patients with degenerative or primary (PMR) versus functional or secondary MR (SMR) enrolled in the investigator-initiated German transcatheter mitral valve interventions (TRAMI) registry.
Methods and results: Between January 2009 and July 2013, 734 patients [mean age 78 years in PMR and 75 years in SMR; the cohort included 42.9% women in PMR and 38.1% in SMR] were enrolled in the prospective arm of the registry with all patients with (100%) having undergone a percutaneous edge-to-edge therapy for MR using the mitra clip. At baseline, 91.7% in PMR and 93% in SMR of patients were in New York Heart Association (NYHA) functional class III or IV+. Mean logEuroScore was 22% in PMR and 20% in SMR patients. According to etiology in PMR 20% of patients had a left ventricular ejection fraction (LVEF) $\leq$30% compared to 38.2% in SMR ($p<0.0001$%). 70% of patients presented with functional MR (SMR). Mean number of clips was not different with 1.5 and 1.6 (PMR/SMR). According to a significant learning curve total procedure time was reduced to 98.4/104.1 min with low fluoro times of 23.3/32.1 min in PMR/SMR in TRAMI compared to previous EVEREST data. Procedural success was achieved in 95/97.1% of patients, with residual grade III in only 4.1 and 2.1% post-intervention, a significant decline to previous reports. The periprocedural complication rate was low, peri- and postprocedural transcatheter re-intervention or conversion to surgery in 30 days was only 1.4 and 2.2% in PMR and SMR respectively.
Conclusions: This is the first report on prospective study data from the German TRAMI registry comparing degenerative and functional etiology suggesting that mitra clip therapy is a reliable treatment option in daily clinical routine for patients with significant MR and high risk for surgery.

P3967 | BEDSIDE
MitraClip implantation in patients with end-stage systolic heart failure

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Purpose: The aim of the present study was to investigate the predictors of mortality of percutaneous mitral valve repair (PMVR) using the MitraClip System in patients affected by severe MR (mitral regurgitation) with end-stage heart failure and severely reduced left ventricular ejection fraction (LV-EF).
Methods: Between October 2008 and October 2013, 304 consecutive patients undergoing PMVR at 4 Italian centers were prospectively enrolled in a registry. To the purpose of our study, we analyzed the 88 patients with functional MR and LV-EF$<$30% who reached 1 year follow-up.
Results: Mean age was 70$\pm$10 years, 71.6% were male, with a mean EuroSCORE II of 9.8$\pm$4.5%. Patients with MR grade $\geq$3+ were 5.7% and 11.4% at discharge and 1 year, respectively, versus 100% at baseline ($p<0.0001$), with a marked clinical benefit (NYHA class $\geq$3 at 1 year 9.0%, vs. 86.3% at baseline; $p<0.0001$). One year all-cause mortality was 21.6%. Baseline factors associated with 1 year mortality at univariate analysis were lower haemoglobin values (12.2$\pm$1.6 vs 11.4$\pm$1.6 g/dl; p=0.04), higher creatinine values (1.35$\pm$0.95 vs 1.67$\pm$0.67 mg/dl; p=0.01), lower glomerular filtration rate values (65.1$\pm$29.2 vs 54.3$\pm$33.1 ml/min/1.73m^2; p=0.03), presence of chronic renal failure (8.9 vs 36.6%; p=0.002), higher EuroSCORE II and STS score values (8.0$\pm$6.3 vs 12.9$\pm$10.2%; p=0.02 and 6.2$\pm$5.8 vs 9.9$\pm$8.4%; p=0.05; respectively), lack of implantable cardiac defibrillator with resichronization therapy (ICD-CRT) (27.6 vs 10%; p=0.05) and NYHA class 4 (41.2 vs 16.9%; p=0.03). At Cox proportional hazards analysis, chronic renal failure (p=0.029; OR 4.0; 95%CI 1.2-14.2), lack of CRT-ICD (p=0.021; OR 0.22; 95%CI 0.06-0.80), and NYHA class 4 (p=0.047; OR 9.3; 95%CI 1.03-83.4) were independent predictors of 1 year mortality. Lower haemoglobin values almost reached statistical significance (p=0.06; OR 0.72; 95%CI 0.0.51-1.01)
Conclusion: MitraClip procedure reduces functional MR and improves NYHA class even in end-stage heart failure patients. However, among these critically ill patients, the 1-year mortality is still prohibitive in case of renal failure, NYHA class IV, or anaemia, while the presence of ICD-CRT appears protective.

P3968 | BEDSIDE
Anatomic predictors of procedural success in patients undergoing transcatheter mitral valve repair with the MitraClip system

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Objectives: We sought to assess anatomic predictors of acute and midterm procedural success in patients with severe symptomatic mitral regurgitation (MR) at high surgical risk undergoing transcatheter mitral valve repair (TMVR) with the MitraClip (MC) system.
Background: MC procedure has been proven to reduce heart failure related symptoms and to improve quality of life in surgical high risk patients with symptomatic MR. Anatomical predictors for procedural success are not well defined.
Methods: 123 consecutive patients (age 77.5$\pm$8.0years) at high surgical risk (EuroScore 29.8$\pm$21.5%) underwent TMVR with the MC system and completed 6 months follow- up (FU).
Structural parameters of the mitral valve (MV) were assessed with 3D echocardiography using a dedicated MV analysis software.
MC failure was defined as: MR grade $>$2+ after the procedure, inability to reduce MR, re-clip or MV surgery, aborted procedure, partial clip detachment.
Results: MC failure was observed in 21 patients (16.8%). Reasons for acute procedural failure were the occurrence pericardial tamponade (n=3, 2.4%), or relevant MV stenosis (n=3, 2.4%). In 8 patients (6.5%) MR could not be reduced relevantly after clip deployment. During FU 7 patients (5.6%) needed re-intervention, including 6 patients (4.8%) with relapse of more than moderate MR. Multivariable logistic regression identified coaptation length (CL) (OR 0.56, 95% CI 0.3-1.04, p=0.02), coaptation depth (CD) (OR 2.22, 95% CI 0.87-5.7, p=0.01) and distance between the papillary muscles (DPM) (OR 1.07, 95% CI 1.0-1.1, p=0.02) as independent predictors of MC failure. Receiver operating characteristic (ROC) curve analysis identified an optimal cut-off for CL $<$2.7mm, for CD $>$6.3mm and for DPM $>$32mm for the identification of MC failure. A combined variable including these cut-off values had a specificity of 95.05%, a sensitivity of 10%, a positive predictive value of 28.6% and a negative predictive value of 84.2% for MC failure.
Conclusion: Using 3D echocardiography MV anatomy can be assessed prior to TMVR with determination of anatomic landmarks. Awareness of MV anatomy characteristics is important for planning of the procedure. In our study, we found patients undergoing TMVR with the MC having a CD $>$6.3mm, CL $<$2.7mm and DPM $>$32mm to be at increased risk for procedural failure. Incorporation of these cut-off values for the prediction of procedural success had an specificity of 95.05%, a sensitivity of 10%.

P3969 | BEDSIDE
Influence of mitral valve tethering on results after MitraClip implantation for patients with functional mitral regurgitation and high surgical risk

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Purpose: MitraClip (MC) is a new technology for treatment of functional mitral regurgitation (MR) in patients with high surgical risk. We assessed the mitral valve tethering accurately and looked at its prediction power for MC implantation success and remaining MR after the procedure.
Methods: This study included consecutive 121 patients with severe functional mitral regurgitation and high surgical risk, who underwent MC implantation between March 2009 and August 2013 in our heart center. We measured left ventricular (LV) geometries and following parameters as assessments of tethering by transthoracic echocardiography before implantation procedure; tenting area, coaptation distance, annular diameter, basal anterior mitral leaflet angle (ALAbase), middle mitral anterior leaflet angle (ALAmid), distal mitral anterior leaflet angle (ALAtip), posterior leaflet angle (PLA), interpapillary muscle distance, LV sphericity index.
Results: 52 patients had small remaining MR$\leq$1+ grade, 69 patients had larger remaining MR $>$1+ grade at discharge. Baseline characteristics of age, sex, severity of initial MR were similar between the two groups. Patients with larger remaining MR had larger left ventricular end-diastolic diameter (67.0$\pm$9.8 vs 63.0$\pm$8.8mm, p=0.0267), greater tenting area (3.1$\pm$0.8 vs 2.7$\pm$0.8cm^2, p=0.0207) and coaptation distance (12.3$\pm$2.6 vs 10.8$\pm$2.4mm, p=0.0048) but similar ALAbase, ALAmid, ALAtip, PLA, interpapillary muscle distance and LV sphericity index. Multivariate analysis identified tenting area $\geq$3.0cm^2 (odds ratio 2.83, 95% confidence interval 1.04 to 7.70, p=0.042) and LV end-diastolic diameter $\geq$61mm (odds ratio 2.67, 95% confidence interval 1.12 to 6.37, p=0.027) as independent predictors of larger remaining MR $>$1+.
Conclusions: Tenting area and LVEDD are easy and reliable echocardiographic parameters for identifying leaflet tethering prior MC implantation. Severe leaflet tethering predicts larger remaining MR and deteriorates patient outcome. Therefore these parameters may influence patient selection criteria.

P3970 | BEDSIDE
Echocardiographic assessment of left and right ventricle reverse remodeling after MitraClip implantation

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Purpose: MitraClip implantation is a new therapeutic option in symptomatic patients with severe mitral regurgitation who are at high risk for surgery. The object of this echocardiographic study was to investigate 6 and 12 months left ventricular and right ventricular remodeling after MitraClip implantation.
Method: This study included consecutive 123 patients (72±10 years, ♂ 62%, 77±15kg,30% Diabetes mellitus, CKI 18%, NTproBNP 7054 [180-35000] pg/ml, LVEF 38±15%, CRT 30%, logEURO-Score 26±17%, 100% NYHA III/IV), who had MC implantation between March 2009 and August 2013 in our heart center. Patients were regularly followed up at our outpatient clinic and underwent transthoracic echocardiography at baseline, 6-month and 12-month follow-up.
Result: At 6–month follow-up, 91 percent of patients had 2+ or less mitral regurgitation and 92% at 12-month follow up. During the follow up, significant and continuous improvement of left and right ventricular dimension and function were observed. The left ventricular end-diastolic volume (LVEDV) was 156±74, 140±70 and 134±64ml ($P<0.0001$) at baseline, 6 months and 12 months, respectively. The left ventricular end-systolic volume (LVESV) was 102±70, 90±65 and 83±57ml ($P<0.0001$), the left ventricular ejection fraction (LVEF) was 39.1±17.0, 41.2±16.3 and 43.5±16.1% (P=0.01), the right ventricular end-diastolic diameter (RVEDD) which was assessed by 4-chamber view was 43.4±6.7, 41.7±6.5 and 41.0±5.4mm (P=0.0007), the tricuspid annulus plane systolic excursion (TAPSE) was 16.6±4.5, 18.7±4.5 and 19.2±4.4mm ($P<0.0001$) and the tricuspid regurgitation pressure gradient (TRPG) was 43.8±13.7, 39.3±12.5 and 36.1±10.0mmHg at baseline, 6 months and 12 months, respectively.
Conclusion: Significant reverse remodeling of both left and right ventricle was observed with decrease of LV and RV-size. Concurrent functional recovery decrease of neurohumoral activation (NTproBNP-level) was concomitant recognized. MitraClip implantation may give favorable effects on both morphology and function of left and right ventricle in patients, who have no different therapeutic Options.

P3971 | SPOTLIGHT
Cost-effectiveness of percutaneous edge-to-edge mitral valve repair in patients with high surgical risk

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Purpose: Percutaneous edge-to-edge mitral valve repair (pMVR) was shown to be effective and well tolerated in patients with severe mitral regurgitation (MR) and at high surgical risk (HSR). However, very little is known about its medico-economic impact. Our aim was to assess cost-effectiveness of pMVR compared to conventional treatment in this population.
Methods: A decision-tree model was constructed to simulate clinical outcomes and economic impact of both strategies (pMVR strategy versus conventional strategy) over a one-year time horizon in the perspective of the French sickness fund. Probabilities of events were extracted from literature search involving HSR patients (on the basis of predicted operative mortality scores) treated with pMVR, and from the French hospital information system (PMSI) for medically managed patients (conventional strategy). Cost analysis was restricted to direct medical costs, using rates from year 2013, and assuming a reimbursement of the pMVR device in addition to Diagnosis-Related Groups's tariffs. Associated costs and specific survival after cardiovascular event were assessed in order to calculate the incremental cost-effectiveness ratio (ICER). Uncertainty was analysed using one way and probabilistic sensitivity analyses (second order Monte Carlo simulation).
Results: Specific survivals at 12 months in pMVR strategy and in conventional strategy were 91±2% and 84±4% respectively, this difference being explained by an expected decrease of rates of hospitalizations for congestive heart failure (CHF). Mean cost of the pMVR strategy was estimated at 28852±4298€ per patient, mainly represented by the cost of the device (73%) and the hospital stay for its implantation (18%). Mean cost of conventional strategy was estimated at 5597±796€ per patient, 99% being associated with the cost of unplanned hospitalizations for CHF. Based on Monte Carlo simulation (1000 samples), the ICER was 360292±206539€ per death avoided. Variables with the highest impact on ICER were: the survival after hospitalization for CHF, the probability of hospitalizations for CHF in medically managed patients, and the cost of pMVR device.
Conclusions: Based on this model, pMVR is expected to slightly improve specific survival at 12 months in HSR patients with severe MR, while inducing major incremental costs in comparison to conventional strategy. A lower price of the device would lead to a more acceptable ICER. Further investigations based on prospective, comparative clinical trials are needed to more accurately determine the cost-effectiveness of this innovation.

P3972 | BEDSIDE
Impact of tricuspid regurgitation on clinical and echocardiographic outcomes after percutaneous edge-to-edge mitral valve repair: Insight from the GRASP registry

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Purpose: To evaluate the impact of baseline tricuspid regurgitation (TR) on the outcomes after percutaneous edge-to-edge mitral valve repair.
Methods: In a retrospective analysis of the prospectively maintained Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation (GRASP) registry, 171 consecutive patients were obtained. Two different groups, dichotomized according to the degree of pre-procedural TR (moderate/severe [MSTR, N=58] and none/mild [NMTR, N=113]), had their clinical and echocardiographic outcomes through 12-month compared. The primary safety end point was the incidence of major adverse events and the primary efficacy end point was freedom from death, surgery for mitral valve dysfunction, or grade ≥3+ MR.
Results: At 30-day, the primary safety and efficacy endpoints were equivalent (8.6% vs. 2.7%, p=0.089; and 93.1% vs. 96.5%, p=0.267; respectively for MSTR and NMTR). Marked reduction in MR grades observed post-procedure were maintained through 12-month. The reduction in TR magnitude occurred early and was sustained over time. At 30-day and 12-month follow-up, respectively 66% and 60% of the surviving patients initially included in the MSTR group had their TR grades reduced to ≤2+, while the patients of NMTR group revealed stable TR grades during follow-up; nonetheless, the between-group differences identified at baseline were consistently observed through 12-month.
While NYHA functional class significantly improved in both groups compared with baseline, it was impaired in the MSTR compared with the NMTR group (NYHA > II at 30-day: 41.1% vs. 15.2%, $p<0.001$; at 1-year: 34.3% vs. 12.0%, respectively, p=0.008). Left ventricle reverse remodeling and ejection fraction improvement were revealed in NMTR group, following the same trend in MSTR group. The primary efficacy endpoint at 12-month determined by Kaplan-Meier freedom from death, surgery for mitral valve dysfunction, or grade ≥3+ MR was comparable between groups, but combined death and re-hospitalization for heart failure rates were higher in the MSTR group. Multivariate analysis demonstrated that MSTR (HR: 2.28; 95% CI: 1.01 to 5.19; p=0.049) and baseline renal failure (HR: 2.51; 95% CI: 1.02 to 6.20; p=0.046) were independent predictors of this combined endpoint.
Conclusions: Percutaneous edge-to-edge mitral valve repair led to improvement in MR, TR, and NYHA functional class in patients with baseline MSTR. Despite similar safety and efficacy compared with NMTR group through 12-month, MSTR independently predicted death and re-hospitalization for heart failure.

TOPICS IN ACUTE CORONARY SYNDROMES

P3973 | BEDSIDE
Diagnostic and prognostic value of the admission ECG in acute chest pain patients in the context of the new universal definition of myocardial infarction and the high sensitive troponins

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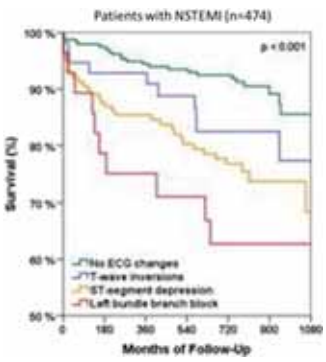
Background: The new Universal Definition of acute myocardial infarction (AMI) and the high-sensitive troponin (hs-cTn) assays have changed the incidence of AMI. The consequences on the diagnostic and prognostic value of changes in the admission ECG in acute chest pain patients are unknown.
Methods: In a prospective multicenter study, we enrolled 2880 patients with symptoms suggestive of AMI. They were stratified according to left bundle branch block (LBBB), ST-segment elevation, ST-segment depression, T-wave inversion or no changes in the admission ECG. Final diagnoses were adjudicated by two independent cardiologists according to the universal definition of AMI and hs-cTnT levels. The primary endpoint was all-cause mortality.
Results: AMI was the final diagnosis in 20% of patients, with 4% having STEMI and 16% NSTEMI. The sensitivity and specificity of presence of any ischemic



changes on the admission ECG was 57% and 83%, with positive and negative predictive values of 45% and 88%. The presence of ST-segment elevations on the admission ECG had a specificity and positive predictive value for STEMI of 98% and 60%. In patients with NSTEMI (n=474), the presence of left bundle branch block (LBBB), ST-segment depression, T-wave inversion or no changes on the admission ECG was associated with 3 year survival rates of 63%, 68%, 77% and 86% ($p<0.001$, Figure). After adjustment for age, LBBB, ST-segment depression and T-wave inversion remained associated with outcome in patients with NSTEMI (HR 2.3, 2.3 and 2.1, p all <0.05).
Conclusion: Sensitivity and specificity of changes in the admission ECG have further decreased to 57% and 83% with the new Universal Definition of AMI and the introduction of hs-cTn assays. When present, ECG changes remain independent predictors of a worse outcome.

P3974 | BEDSIDE
Simplifying the GRACE score: external validation of the Canada Acute Coronary Syndrome risk score in a national registry

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Purpose: Patients admitted for acute coronary syndromes may have their risk stratified by risk scores. Amongst them, the GRACE risk score is considered the best to estimate in-hospital mortality. However, its calculation involves multiple continuous variables and requires appropriate software. The Canada Acute Coronary Syndrome risk score (C-ACS) stratifies individual risk, graded from 0 to 4, using four categorical variables: heart rate >100 beats/min, systolic blood pressure <100 mmHg, age ≥75 years, Killip >1. The primary objective of this study is to assess correlation between C-ACS and in-hospital mortality.
Methods: We performed a retrospective analysis of patients admitted for myocardial infarction included in a National Acute Coronary Syndrome Registry between October 1st 2010 and October 1st 2013. Each patient's C-ACS and GRACE scores were calculated. We registered in-hospital mortality in the groups defined by the risk scores. We evaluated how C-ACS and GRACE scores were able to predict in-hospital mortality, using Odds ratio, Chi-square test and ROC analysis.
Results: From 8186 patients included in the Registry, it was possible to calculate both the C-ACS and the GRACE scores in 7496. Patients were categorized in four groups: C-ACS = 0 in 54.2% of the patients, C-ACS=1 in 29.4%, C-ACS=2 in 12.3% and C-ACS>2 in 4.1%. In-hospital mortality in patients with C-ACS=0 was 1.1%, with C-ACS= 1 was 3.9% (OR 3.71,IC95% 2.57-5.36, $p<0.001$), with C-ACS=2 was 10.3% (OR 10.51, IC95% 7.30-15.14, $p<0.001$) and with C-ACS>2 was 27% (OR 33.76, IC95% 22.85-49.89, $p<0.001$).
Patients were also categorized using the GRACE score: 38.5% of the patients were low risk (in-hospital mortality of 0.6%), 28.9% were intermediate risk (in-hospital mortality of 2%) and 32.6% were high risk (in-hospital of 9.8%).
Comparative analysis of both risk scores using ROC curves revealed areas under the curves of 0.78 for the A-ACS and 0.77 for the GRACE.
Conclusions: The C-ACS has a good predictive value for in-hospital mortality in patients admitted with myocardial infarction, which is comparable to the GRACE score. Because this risk score is simple and easy to memorize, it has the potential for widespread clinical use.

P3975 | BEDSIDE
Incremental value of copeptin to high-sensitivity cardiac troponin t alone in the early risk stratification of acute chest pain

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Purpose: Recently, two novel approaches have shown to improve the early diagnosis and risk stratification of acute myocardial infarction (AMI): high-sensitivity cardiac troponin (hs-cTn) and copeptin, a sensitive marker of endogenous stress. It is unknown, whether the combination of hs-cTn and copeptin would further increase prognostic accuracy.
Methods: In a prospective, international multicenter study, copeptin and high-sensitivity cardiac troponin T (hs-cTnT) were determined at baseline in 2049 patients presenting to the emergency department with acute chest pain. Patients were followed up 2 years regarding all-cause mortality.
Results: During follow-up, 155 (8%) patients died. Overall, the 2-year prognostic accuracy, as quantified by the area under the receiver operating characteristic curve, did not differ significantly for the combination of copeptin and hs-cTnT (AUC 0.78 (95% 0.76-0.79) as compared to hs-cTnT alone (AUC 0.79 (95%CI 0.77-0.81); p=0.386 for comparison). However, patients tested positive for both investigational biomarkers at admission (copeptin ≥9pmol/l AND hs-cTnT ≥14ng/l, n=478 (23%)) showed in average a six-fold risk of death within 2 years (mortality rate 21.1%) as compared to patients tested positive for none (mortaltity rate 1.8%) or only one of the two investigational biomarkers (mortality rates 7.8% for hs-cTnT positive only, 3.9% for copeptin positive only; $p<0.001$ for all comparisons).
Conclusions: Using copeptin additionally to hs-cTnT seems to substantially improve the early risk prediction in unselected chest pain patients, as this dual marker strategy has the potential to detect patients with a sixfold risk of death during 2 year FU already at presentation.
Trial registration: ClinicalTrials.gov number, NCT00470587

P3976 | BEDSIDE
Comparison of enoxaparin versus fondaparinux in non-ST-elevation myocardial infarction - a real world analysis of 44.813 patients in the SWEDEHEART registry

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Background: In the OASIS-5 trial, fondaparinux reduced major bleeding and improved survival compared with enoxaparin in patients with non-ST-elevation myocardial infarction (NSTEMI). Large scale real-world comparisons are lacking.
Methods: All 2006-2010 patients (n=44.813) in the SWEDEHEART registry with a NSTEMI treated with either enoxaparin or fondaparinux were included. The two treatments were compared with regard to in-hospital major bleeding or death; 30 day death, myocardial infarction (MI), stroke or bleeding. Adjustments were made for calendar time and admitting hospital, baseline characteristics (model 1) and invasive coronary interventions (PCI/CABG; model 2).
Results: Overall, 58.7% (n=26.292) received enoxaparin and 41.3% (n=18.521) received fondaparinux. Fondaparinux use increased gradually from 0.7% in 2006 to 86.8% in 2010. Baseline characteristics were similar regarding age, sex, diabetes, previous cardiac history and prior major bleeding events. In-hospital PCI was more frequently utilized in the fondaparinux treated group (47.1% vs. 39.2%). The odds ratio (OR) of in-hospital severe bleeding was reduced by 48% and death by 28% in the fondaparinux treated group (Table). At 30 days the OR of MI or stroke was similar, but the OR of bleeding and death remained significantly lower.
Conclusion: In this nationwide real world analysis, the change from enoxaparin to fondaparinux was associated with a substantially reduced risk of bleeding, and improved survival.

P3977 | BEDSIDE
The clinical impact of early invasive strategy on non-ST-segment elevation myocardial infarction according to the time-varying patterns of cardiac biomarker

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Background: The clinical benefit of early invasive strategy in patients with non-ST-segment elevation myocardial infarction (NSTEMI) is still left uncertain. We sought to evaluate the clinical impact of early invasive strategy on NSTEMI patients according to the time-varying patterns of cardiac biomarker.
Methods: This trial included 465 consecutive NSTEMI patients received percutaneous coronary intervention (PCI), and they were classified into two groups according to the changing pattern of cardiac biomarkers at first follow-up assessment: group I: rising pattern of both creatine kinase muscle-brain fraction (CK-MB) and troponin I (n=241), group II: falling pattern of CK-MB and/or troponin I (n=224). The primary endpoint was 12-month major cardiac and cerebrovascular events (MACCE), which was comprised of cardiovascular death, acute MI, ischemic stroke and repeated revascularization. We compared incidence of MACCE between early (<12 hours after arrival) and delayed (≥12 hours) PCI in each group.
Results: There were no statistically significant differences of baseline characteristics between group I and II. The rates of 12-month MACCE were not different between early and delayed PCI group (6.5% vs. 11.7%, p=0.152) in all study subjects. In group II, early PCI had similar rates of MACCE compared with delayed PCI (13.9% vs. 11.7%, p=0.780). But, patients treated with early PCI had signif-

Abstract P3976 – Table 1. In-hospital and 30 day events

	Enoxaparin	Fondaparinux	Crude OR	Model 1 OR	Model 1 + PCI/CABG OR
In-hospital events					
Bleeding	1.8% (477/26292)	1.1% (208/18521)	0.61 (0.52–0.72)	0.52 (0.41–0.66)	0.52 (0.41–0.67)
Death	4.0% (1054/26292)	2.7% (501/18521)	0.67 (0.60–0.74)	0.71 (0.60–0.84)	0.72 (0.61–0.85)
30 day event					
Bleeding	2.2% (566/26292)	1.4% (254/18521)	0.63 (0.54–0.73)	0.53 (0.43–0.66)	0.54 (0.43–0.66)
Death	5.9% (1549/17244)	4.2% (783/14154)	0.71 (0.65–0.77)	0.78 (0.68–0.90)	0.79 (0.69–0.91)
MI, stroke, death or bleeding	16.8% (4420/26292)	14.1% (2603/18521)	0.81 (0.77–0.85)	0.83 (0.76–0.91)	0.84 (0.77–0.91)

icantly lower rates of 12-month MACCE in group I (2.8% vs. 11.8%, p=0.028). Also, the MACE-free survival rates were significantly lower in early PCI compared with delayed PCI in group I (97.2% vs. 88.2%, log rank p=0.03) (Fig. 1).

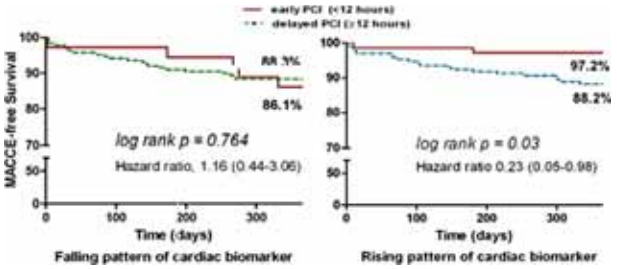

Figure 1

Conclusions: Early invasive strategy was associated with better clinical outcomes at 12-month follow-up in NSTEMI patients with rising pattern of cardiac biomarker.

P3978 | BEDSIDE

Thrombectomy in non-ST-elevation myocardial infarction - more than mechanical reduction of distal embolisation: a substudy of the TATORT-NSTEMI trial

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Purpose: Aim of thrombus aspiration in acute myocardial infarction is to reduce reperfusion injury. Further, distal embolisation of thrombotic material induces an inflammatory response contributing to the no-reflow phenomenon. Thus, one might speculate that thrombectomy influences the cascade of thrombosis and inflammation. Aim of the current study was therefore to analyse the impact of thrombus aspiration on markers of inflammation and reperfusion injury such as interleukin 6 (IL-6), asymmetric dimethylarginine (ADMA) and B-cell surface antigen CD40 (CD40).
Methods: This study is a prespecified subanalysis of the Thrombus Aspiration in ThrOmbus containing culpRiT lesions in Non-ST-Elevation Myocardial Infarction (TATORT-NSTEMI) trial investigating the impact of thrombectomy on microvascular obstruction (MO)/no-reflow. In brief, patients with non-ST-elevation myocardial infarction (NSTEMI, n=440) with relevant thrombus burden were randomised to undergo standard percutaneous coronary intervention (PCI) alone (group 1) versus thrombectomy before PCI (group 2). MO was assessed by cardiac magnetic resonance imaging (CMR). The main finding was that thrombectomy did not reduce MO in comparison to standard PCI. In 71 patients of group 1 and 69 patients of group 2 blood samples were collected immediately following primary PCI. Levels of ADMA, IL-6 and CD40 were measured by ELISA. The occurrence of mortality, reinfarction, target vessel revascularisation and congestive heart failure (MACE) was assessed at 6-month follow-up.
Results: Patients were well balanced with respect to baseline characteristics such as age, gender or left ventricular ejection fraction (all $p>0.05$).
Thrombus aspiration did not lead to a reduction of IL-6, ADMA and CD40 as the levels of these biomarkers did not differ significantly between the thrombectomy group versus the standard PCI group (IL-6: 13.8±29.5 vs. 12.0±25.6 pg/ml, p=0.49; ADMA: 50.0±12.6 vs. 48.1±15.9 ng/ml, p=0.25; CD40: 111.8±270.4 vs. 127.5±393.4 pg/ml, p=0.81). Levels of IL-6, ADMA and CD40 did not differ significantly between patients with and without MO (p=0.47, p=0.68 and p=0.20, respectively).
In contrast to IL-6 and ADMA (p=0.34 and p=0.68), high levels of CD40 were significantly associated with the occurrence of MACE (CD40≥median: HR 4.75, 95%CI 1.03-22.0, p=0.046).
Conclusion: Thrombus aspiration does not lead to reduced levels of IL-6, ADMA or CD40. These findings reflect the main results of the TATORT-NSTEMI trial and recent large scale clinical trials failing to demonstrate a beneficial effect of thrombectomy on reperfusion success and clinical outcome.

P3979 | BEDSIDE

Kidney failure and non-ST-segment elevation acute coronary syndromes: three formulas... one problem

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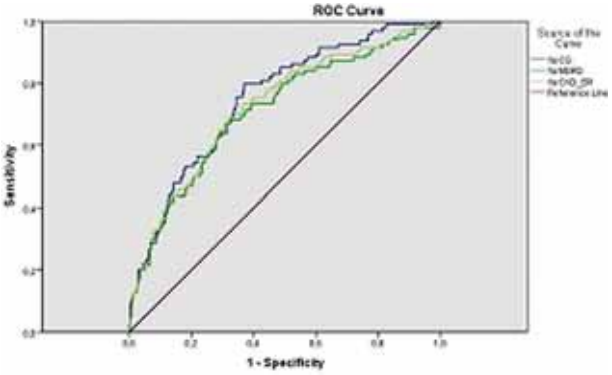
Purpose: Chronic Kidney Disease (CKD) and acute kidney lesion are a frequent morbidity in patients admitted for non-ST-segment elevation acute coronary syndromes (NSTE-ACS) and are associated with worse outcomes. Several equations to correctly identify patients with CKD through glomerular filtration rate (GFR) exist, but it is still not consensual which one is the most appropriate in the setting of NSTE-ACS. We aimed to compare which of the 3 more commonly used formulas - Cockcroft-Gault [CG]; Modification of Diet in Renal Disease [MDRD] and Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] – is more effective in predicting worse outcomes at 1-year follow up.
Methods: Prospective study of 493 consecutive patients [age 66.64±12.88; 66.7% men; 31.8% diabetics; 74.1% hypertensive; 10.7% known CKD] admitted to our, tertiary hospital, intensive care unit for NSTE-ACS between October 2009 and October 2012. GFR estimates from CG, MDRD and CKD-EPI were compared in terms of mortality risk prediction and of a composite primary endpoint (re-infarction, stroke and mortality) at 1-year follow up.
Results: Prevalence of GFR <60 ml/min/1.73m^2 was 46.6% using CG, 46.9% with MDRD and 43.2% with CKD-EPI. All formulas had a good discriminatory power in predicting 1-year composite primary endpoint with CG proving to be the best formula by ROC curve analysis [AUC (CG): 0.750 vs AUC (MDRD): 0.711 vs AUC (CKD-EPI): 0.725]. All formulas were also good in predicting total mortality at 1-year follow-up with CG showing the best results [AUC (CG): 0.773 vs AUC (MDRD): 0.719 vs AUC (CKD-EPI): 0.738]



Composite primary endpoint at 1 year.

Conclusions: In our, almost exclusively white, population all formulas proved value in predicting adverse outcomes at 1-year follow up. The CG formula was significantly more accurate than MDRD and CKD-EPI.

OPTICAL COHERENCE TOMOGRAPHY: FINDING THE CAUSE

P3980 | BEDSIDE

Additive value of integrated backscatter intravascular ultrasound in detection of vulnerable plaque by optical frequency domain imaging: An ex vivo autopsy study of human coronary arteries

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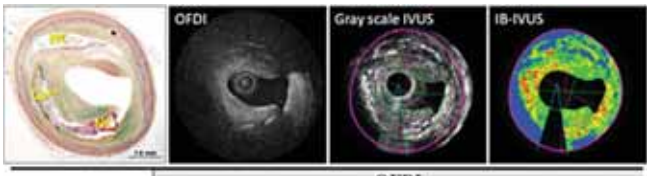
Background: Detection of coronary lesions susceptive to plaque rupture and thrombosis by intravascular imaging devices may serve to stratify the risk of future adverse events in patients.
Methods: We interrogated a total of 30 coronary arteries from 14 human autopsy hearts by ex vivo optical frequency domain imaging (OFDI) and integrated backscatter intravascular ultrasound (IB-IVUS). Coronary segments were sectioned at 3-mm intervals and assessed histologically. A total of 360 pairs of cross-sectional images co-registered to histology were investigated to evaluate diagnostic ability of the intra-coronary imaging devices in the assessment of lesion morphologies.
Results:. Overall, OFDI showed a good utility in the recognition of various coronary plaque compositions such as calcification, necrotic core, cholesterol crystals,



		OFDI			
		Fibrous	Lipid rich	TCFA	Fibrocalc
Histology	AIT/Fib	85	0	0	2
	PIT	66	39	3	17
	Th FA	4	60	5	2
	TCFA	1	2	14	1
	Fibrocalc	0	11	1	47

Figure 1. Comparison of histology and imaging.

and fibrous tissue (Figure). However, OFDI mis-diagnosed 9 non-TCFA lesions as TCFA (pseudo-TCFA), with the result corresponding to positive predictive value (PPV) = 60.9%. The main cause was signal interference from macrophages which cause signal attenuation.
Then, utilizing a recursive partitioning analysis, we defined IB-IVUS-derived TCFA as (i) %area lipid >65.1%; (ii) 32.3< %area lipid <65.1% and plaque area >10.5mm^2. PPV of TCFA identification by IB-IVUS alone was 50.3%. With combination of OFDI and IB-IVUS data, PPV of TCFA detections was improved to 100.0%.
Conclusions: OFDI was capable of accurately recognizing most of coronary morphologies. However, the signal interference from macrophages dampen the diagnostic accuracy of OFDI, especially for the recognition of vulnerable plaque. Additive use of gray scale and IB-IVUS may be useful to compensate for the limitation of OFDI.

P3981 | BEDSIDE
Prognostic value of culprit plaque morphology assessed by optical coherence tomography in patients with acute coronary syndrome

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Purpose: Patients presenting with acute coronary syndrome (ACS) may have different plaque morphologies at the culprit lesion. In particular, plaque rupture (PR) has been shown as the more frequent culprit plaque morphology in ACS. However, its prognostic value is still unknown. In this study, we evaluated the prognostic value of PR compared with non-PR in patients presenting with ACS.
Methods: We enrolled consecutive patients admitted to our coronary care unit for ACS and undergoing coronary angiography. Optical coherence tomography analysis of the culprit lesion was performed. Culprit lesion was classified as PR (evidence of a ruptured fibrous cap that connect the lumen with the lipid pool) and non-PR. Prognosis was assessed according to culprit plaque morphology. Major adverse cardiac events (MACE) were defined as the composite of cardiac death, non-fatal myocardial infarction, unstable angina and target lesion revascularization (median follow up 31.1±13.4 months).
Results: We enrolled 139 consecutive ACS patients (mean age 64.3±12.0 years, male 73.4%, 92 patients with Non-ST elevation ACS and 47 with ST-elevation ACS). PR was detected in 82/139 (59%) patients. There were no differences in clinical presentation, stent type, median stent length and stent diameter between patients with PR compared with patients without PR. Of importance, MACE occurred more frequently in patients with PR as compared with patients without PR (31.7% vs 15.8%, p=0.03) and was mainly driven by unstable angina and non-fatal myocardial infarction.
Conclusions: Patients with ACS presenting with PR as culprit lesion have a worse prognosis compared with patients without PR. This finding should be taken into account in risk stratification and management of patients with ACS.

P3982 | BEDSIDE
Clinical and morphological features of coronary thrombosis caused by plaques with intact fibrous cap in comparison with plaque rupture: optical coherence tomography and intravascular ultrasound study

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Background: Although plaque rupture (PR) and subsequent thrombus formation is known as the primary cause of acute coronary syndrome (ACS), other pathogeneses can also induce coronary thrombosis with intact fibrous cap (IFC). We sought to assess the clinical and morphological features of the ACS culprit lesions with IFC in vivo using optical coherence tomography (OCT) and intravascular ultrasound (IVUS).
Methods: A total of 287 culprit lesions of 286 ACS patients who underwent both OCT and IVUS imaging at the time of primary coronary intervention were investigated. Intraluminal thrombus was identified by OCT, and the culprit lesions with thrombus was categorized into those with PR (PR group) and those with IFC (IFC group) according to the OCT findings. Patients' clinical characteristics and IVUS findings were compared between PR and IFC group.
Results: Intraluminal thrombus was observed in 196 lesions (68.3%), of which 100 lesions were categorized into PR group and 52 lesions were into IFC group by OCT. Forty-four lesions with massive thrombus interfering with plaque visualization were excluded from the analysis. Female gender was less frequent in PR group as compared to IFC group (15.0% vs 34.6%, p=0.010). Peak creatine kinase (CK) and CK-MB values were significantly greater in PR than in IFC (2304±2184 vs 1399±1947 IU/L, p=0.015 and 247±244 vs 140±180 IU/L, p=0.007, respectively), whereas no significant difference was observed in CK and CK-MB levels at the baseline. In IVUS analysis, percent plaque area (%PA) and remodeling index (RI) were significantly larger in PR than in IFC (%PA: 87.2±4.7% vs 85.5±5.2%, p=0.043; RI: 1.13±0.18 vs 1.02±0.19, p=0.001). Echo-attenuated plaque was more frequent in PR than in IFC (41.0% vs 17.3%, p=0.006).
Conclusions: Intraluminal thrombosis in lesions with IFC observed by OCT showed differentiated clinical and morphological characteristics from those with PR. OCT may enable to identify the different pathogenesis of coronary thrombosis in ACS setting, which may further lead to specific therapeutic strategy according to the pathogenesis.

P3983 | BEDSIDE
Serial change of thin fibrous cap distribution on the luminal surface after lipid lowering therapy assessed by three-dimensional-optical coherence tomography

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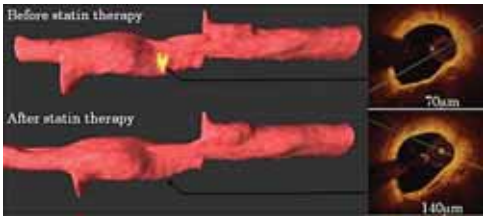
Purpose: Recently reports showed that statin therapy significantly increased fibrous-cap thickness in patients with dyslipidemia. We speculated that a distribution of thin-fibrous cap on the luminal surface could affect the vulnerability of plaque. Therefore, we evaluated the luminal surface distribution of thin-fbrous cap by OCT.
Method: 18 consecutive patients with TCFA on non-target lesion detected by OCT were enrolled in this study. They were administered statin to improve low density lipoprotein (LDL) cholesterol level and underwent OCT examination at follow up. We selected frames which have a thin-fibrous cap less than 100 maicrons and analyzed the frame each 0.2mm interval (150 frame). We compared the thickness and angle of fibrous cap between baseline and follow up. Moreover, fibrous cap which was less than 100 microns detected automatically and then 3D-OCT images were reconstructed to assess a change of surface area of thin-fibrous cap visually.
Result: LDL choresterol level was decreased 132±45 mg/dl at baseline to 83±17 mg/dl at follow up. Minimum thickness of thin-fibrous cap in the lesion was significantly increased (baseline:66±19 follow up: 115±40, p=0.001). and maximaum angle was significantly decreased (baseline: 37.6±19.8 follow: 7.9±14.6, p=0.002) 3D-OCT demonstrated that the distribution of thin-fibrous cap visually decreased from BL to FU (figure).



3D-OCT with color mapping image of TCFA.

Conclusion: 3D-OCT with color mapping might be useful to understand the distribution of thin-cap fibroatheroma (TCFA). Lipid lowering therapy could stabilize vulnerable plaque due to not only increasing the fibrous cap thickness but also decreasing surface area of TCFA.

P3984 | BEDSIDE
Increased rate of cardiovascular events in patients with high carotid plaque temperature. Insights from a new noninvasive method

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Purpose: Controversy exists regarding the prognostic role of inflammation in coronary artery disease (CAD). Microwave radiometry (MWR) is a new noninvasive method, which allows the in vivo measurement of the internal temperature of tissues reflecting local inflammation. The aim of the present study was to evaluate in patients with CAD the prognostic value of carotid atherosclerotic plaque inflammation, as assessed by MWR, in cardiovascular events.
Methods: Consecutive patients with significant CAD documented by coronary angiography were evaluated by 1) ultrasound echo-color Doppler (US-ECD) study of both carotid arteries, and 2) microwave radiometry (MWR). During the ultrasound study, carotid plaque thickness was evaluated in all carotids. 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.
Results: We included 74 consecutive patients with significant CAD. Eight patients (10.8%) had high ΔT temperatures bilaterally. The mean follow-up period for all patients was 12.12±7.9 months. MACE was 37.5% in the group with bilateral high ΔT and 13.6% in non-high ΔT group (p=0.08). 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 carotid plaque thickness (OR: 8.55, 95% CI 1.09-67.00, p=0.04). In Kaplan-Meier plots patients with bilateral high ΔT showed higher event rates, compared with patients in non-high ΔT group (log-rank p=0.02).

Conclusions: Evaluation of functional characteristics of carotid plaques through Microwave Radiometry may have incremental prognostic impact on risk assessment of CAD patients.

P3985 | BEDSIDE
Impact of nonculprit plaque characteristics on slow flow phenomenon during percutaneous coronary intervention

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Background: The slow flow (SF) phenomenon is more prevalent in patients with acute coronary syndrome (ACS), who frequently exhibit vulnerable plaques in remote coronary arteries. We aimed to clarify the impact of nonculprit plaque characteristics on the occurrence of SF using multidetector computed tomography (MDCT).
Methods: The study population comprised 180 consecutive patients with suspected unstable angina who underwent MDCT before intervention. The characteristics of culprit and nonculprit lesions were compared between patients with and without SF.
Results: SF was observed in 43 (23.8%) of the 180 patients. The prevalence of positive remodeling (PR), low-attenuation plaque (LAP), and napkin-ring sign (NRS) in culprit lesion was significantly higher in the SF group than in the non-SF group (86.1% vs. 39.4%; $p<0.001$, 81.4% vs. 18.3%; $p<0.001$, and 65.1% vs. 16.1%; $p<0.001$, respectively). The same result was observed for nonculprit lesions (58.1% vs. 14.6%; $p<0.001$, 45.2% vs. 6.6%; $p<0.001$, and 14.3% vs. 4.9%; $p<0.04$, respectively). Multivariate analysis revealed LAP [odds ratio (OR), 12.8; 95% confidence interval (CI), 3.7–54.7; $p<0.001$] and NRS (OR, 5.1; 95% CI, 1.3–25.3; p=0.03) in culprit lesions and PR (OR, 4.7; 95% CI, 1.1–22.2; p=0.04) in nonculprit lesion were independent predictors of SF.

Independent Predictors for Slow Flow

	Odds ratio (95% CI)	P Value
Culprit lesion		
Positive remodeling	1.5 (0.5–4.7)	0.48
Low-attenuation plaque	12.8 (3.7–54.7)	<0.001
Napkin-ring sign	5.1 (1.3–25.3)	0.03
Nonculprit lesion		
Positive remodeling	4.7 (1.1–22.1)	0.04
Low-attenuation plaque	2.4 (0.5–11.8)	0.26
Napkin-ring sign	0.5 (0.1–4.1)	0.50

Conclusions: The plaque characteristics of nonculprit lesions are strongly associated with SF occurrence during percutaneous coronary intervention. Assessment of plaque characteristics of both culprit and nonculprit lesions using MDCT may be useful for the prediction of SF.

P3986 | BEDSIDE
Features of plaque vulnerability at non-culprit plaques containing cholesterol crystal: frequency-domain optical coherence tomography analysis

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Purpose: Cholesterol crystals are often seen within atheromatous plaques, particularly at sites of plaque disruption. While crystallization of cholesterol has been considered to penetrate fibrous caps via volume expansion, crystals can also induce inflammation potentially destabilizing plaques. However, it remains to be elucidated whether cholesterol crystals contribute to plaque vulnerability. As frequency-domain optical coherence tomography (FD-OCT) enables the visualization of cholesterol crystals in vivo, we sought to evaluate the characteristics of plaques containing cholesterol crystal by using FD-OCT.
Methods: 263 non-culprit lipid plaques in 250 consecutive patients with stable coronary artery disease were analyzed by FD-OCT imaging in a target vessel that underwent percutaneous coronary intervention. Cholesterol crystals were identified as a thin, linear region with high signal intensity and backscattering. Characteristics of plaques with and without cholesterol crystals were compared.
Results: 39.6% of study population had at least one cholesterol crystals within non-culprit lipid plaques. Plaques with cholesterol crystal were predominantly located in the proximal segment of left anterior descending artery and right coronary artery. Plaques containing cholesterol crystals exhibited a smaller fibrous cap thickness (84.1±27.9 vs. 106.9±40.1 um, p=0.003), larger lipid index (2357.4±1742.7 vs. 914.2±1151.7 mm°, $p<0.0001$), greater prevalence of thin-cap fibroatheroma (26.9 vs. 5.5%, p=0.005) and microchannel (46.1 vs. 19.4%, $p<0.0001$). In addition, a significant association was observed between the maximum number of cholesterol crystal within plaques and fibrous cap thickness (r=-0.26, p=0.008). Lowering LDL-C level below 1.8 mmol/l associated with greater fibrous cap thickness at plaques without cholesterol crystal (138.4±47.3 vs. 98.0±31.9 um, p=0.001) but not at plaques containing cholesterol crystal (85.2±26.9 vs. 77.1±21.6 um, p=0.31).
Conclusions: Lesions containing cholesterol crystal exhibited distinct FD-OCT features associated with plaque instability. The current findings suggest an important association between cholesterol crystal and plaque vulnerability in vivo.

PHYSICAL ACTIVITY: A POTENT BUT UNDESIRED THERAPEUTIC OPTION

P3987 | BEDSIDE
Athletic CardioClub, the Romanian original way in promoting primary cardiovascular diseases prevention

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Background: A healthy life style based on physical exercise is one of the most efficacious ways for prevention of the cardiovascular diseases.
Objective: To present the results obtained by the Romanian Athletic CardioClub (RO-ACC) after the first two year of activity. The RO-ACC's slogan is: "Let's run for your heart !".
Methods: The Romanian Athletic CardioClub (RO-ACC) is an association founded in April 2012 by the Romanian Society of Cardiology, Romanian Heart Foundation and 17 cardiologists in order to promote physical activity for cardiovascular diseases prevention in large groups of people on the physicians self-example basis. RO-ACC promotes its objective in 4 ways: 1.Promoting the exercise benefits of on its website. 2. Testing the cardiovascular health of its members by its experts.3. An on-line data-base where the RO-ACC members can introduce the kilometers performed every day by walking, running, swimming, cycling or skiing in order to accumulate at least 600 km/year (the "Ojective 600" program, opened at 01.02.2013). This limit was based on the recommendation of at least 30 min. of moderate exercise /day, 5 days a week (that means 3 km walking/day, 60 km/month and 720 km/year. The 600 km threshold was established for the first two years as a reasonable motivation). Awards and diplomas are delivered for the first three places for each sort of activity and for the members with good results in sport competitions. 4. Encouraging participation to the RO-ACCs members to formal competitions (middle/long distance running, triathlons, swimming) in mixed teams physicians-non-physicians.
Results: A 11.8 times increase (from 32 to 379) of the RO-ACC members was seen after 22 months. The non-physicians members increased from 3.12% to 33% and 126 members participated at the "Objective 600 km" program in 2013. Participants to formal competitions increased from 8 to 64 (16.88%). One gold, one silver and two bronze medals have been won at the 2013 edition of the World Health and Medical Games (Zagreb, Croatia).
Conclusions: An original system organized by cardiologists as a sport association based on: 1. education in the benefits of exercise; 2.the physicians self-example in mixed physician-non-physician sport teams and 3. a virtual competition motivated by awards, proved to be a good solution for implementation of the physical activity in large groups of people as a way for cardiovascular diseases prevention.

P3988 | BEDSIDE
Subclinical atherosclerosis, inflammatory markers and physical activity level in middle-aged men. Results of longitudinal over 25 years prospective observation

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Purpose: The purpose of the study was to investigate the influence of lifetime physical activity (PA) patterns on selected indices of low-grade inflammation and atherosclerosis in longitudinal observation of middle-aged men.
Methods: The subject of the study was a cohort of 101 men (mean age at follow up 59,7±9,0 years), free of cardiovascular symptoms and treatment, participating in regular follow-up examinations in the years 1980/90-2011/12. Self-report PA was assessed by interviewer-administered Seven-Day PA Recall and Historical PA questionnaire. Serum inflammatory markers (high-sensitivity C-reactive protein, oxidized LDL, homocysteine, interleukine 6, TNF alpha, adiponectine, adhesion molecules, leptin and resistine) were determined using Elisa kit. Subclinical atherosclerosis was measured by assessing the coronary artery calcification (CAC) using multi-slice computed tomography; the carotid intima-media thickness (CIMT) using high-resolution B-mode ultrasound; and the reactive hyperemia index (RHI) using peripheral arterial tonometry (EndoPAT2000). The participants were divided according to tertiles of exercise-related energy expenditure (EE) in kcal/week at baseline, i.e. <2050 (moderate; n=33), 2050-3840 (high; n=34), >3840 (very high; n=34).

Results: The moderate, high and very high PA groups were comparable in terms of age, education, family history and atherosclerosis risk factors at baseline. The most pronounced association between PA and inflammatory markers was found for hsCRP, oxLDL and leptin with the significantly lower concentrations among men with maintained high PA. The mean hsCRP was 2.65, 2.40 and 2.82 mg/L; the mean oxLDL was 106.4; 89.19 and 161.11 ng/ml; the mean leptin was 9.09±7.92; 5.43±4.00; 7.79±7.95 in the moderate, high and very high PA group, respectively ($p<0.05$). The group with stable high PA level (EE 2050-3840 kcal/week) had also the most favorable profile of the indices of atherosclerosis (mean CAC of 10.7±28.9 Agatston units; CIMT of 0.64±0.15 mm and RHI of 2.15±0.4) with no cases of CAC >400, CIMT ≥0.9 mm and RHI <1.67.
Conclusions: Maintaining regular PA level with EE 2050-3840 kcal/week through young and middle adulthood is associated with the most favorable inflammatory status and may protect against atherosclerosis in men. Higher PA level is associated with increased low-grade inflammation and less beneficial atherosclerosis indices, as measured by hs-CRP, ox-LDL, leptin, CAC, IMT and RHI.

P3989 | BEDSIDE
Intensity of exercise predicts cardiovascular complications in type 1 diabetic patients

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Purpose: Cardiovascular disease (CVD) is the most common cause of death and disability among patients with type 1 diabetes (T1D) and it has been shown that diabetic nephropathy accounts for the increased cardiovascular morbidity and mortality in these patients. Physical activity improves the risk profile of patients with T1D. We recently showed in a prospective setting that the intensity of exercise predicts the incidence and progression of diabetic nephropathy in T1D. Little is known about the causal relationship between physical activity and CVD. Therefore, the aim of this study was to assess how physical activity affects the development of incident CVD in patients with T1D.
Methods: This is a longitudinal study including 1513 T1D patients participating in the nationwide multicenter Finnish Diabetic Nephropathy Study (FinnDiane). The median follow up time was of 9.0±2.4 years, 47.6% were men, the mean age was 36.9±12.1 years, and the duration of diabetes was 20.1±12.2. Leisure time physical activity (LTPA) was assessed with a previously validated self-report questionnaire. CVD, at baseline and follow-up, was defined based on medical records as follows: clinically verified myocardial infarction, ischemic limb amputation or a peripheral artery procedure. Patients with major CVD events, end-stage renal disease (ESRD) and patients with unknown renal status were excluded from the study.
Results: During the follow-up period, 86 patients out of 1513 developed a new CVD event. The intensity of LTPA was associated with incident CVD. Lower intensity of LTPA was associated with incident CVD 10.2 vs. 5.0 vs. 1.0% ($P<0.001$) in patients with low vs. moderate vs. high intensity of LTPA, respectively. To explore the possible bias regarding existing renal disease and physical inactivity we analyzed incident CVD in patients with normal AER separately and intensity was still associated with incident CVD ($p<0.001$). The absorbed assiocation betweeen intensity and incident CVD survied a Cox Regression analysis when adjusted for sex, duration and smoking. In addition, the duration of exercise was associated with incident CVD (p=0.041). Neither the total amount nor the frequency of LTPA were associated with incident CVD.
Conclusions: This study suggests that exercise, in particular, high intensity exercise, may reduce the incidence of CVD events in patients with T1D.

P3990 | BEDSIDE
Cardiovascular fitness and the risk of subsequent cardiovascular events among middle-aged asymptomatic men and women

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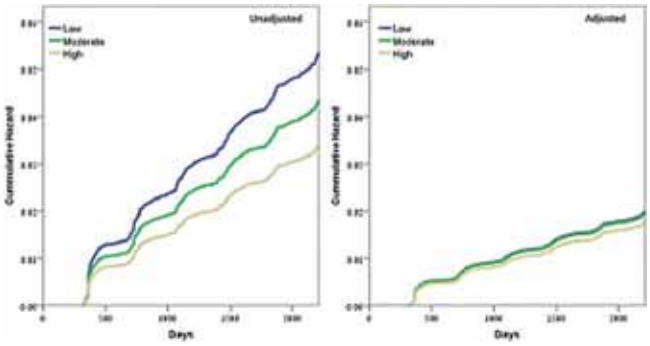
Purpose: Our aim was to examine whether reduced cardiovascular fitness is an independent predictor of the development of cardiovascular events in apparently healthy middle-aged adults or merely a marker of associated comorbidities and risk factors.
Methods: We investigated 15,595 men and women who were annually screened. All subjects were free of ischemic heart disease, and had completed maximal exercise stress test (EST) according to the Bruce protocol at their first visit. Subjects were categorized into age- and sex-specific quintiles (Q) according to Bruce protocol treadmill time. With fitness defined as low (Q1), moderate (Q2-4), or good (Q5). The primary endpoint was a composite of symptoms-driven percutaneous coronary intervention and acute coronary syndrome.
Results: Mean age of study patients was 48±10 years and 73% were men. A total of 679 events occurred during 92,092 person-years of follow up. Kaplan Meier survival analysis showed that the cumulative probability of cardiovascular events at 7 years was significantly lower among subjects with good fitness (unadjusted $P<0.001$ [Figure: left panel]). However, after multivariate adjustment for other known cardiovascular risk factors, including obesity, hypercholesteremia, low high density lipoprotein-cholesterol, and diabetes mellitus, good fitness was no longer significantly associated with reduced risk for cardiovascular events (HR = 0.87 [95% CI 0.67-1.14], adjusted p=0.87 [Figure: right panel])).



Cumulative hazard rate.

Conclusions: Our findings suggest that the association between cardiovascular fitness and the risk of subsequent cardiovascular events in asymptomatic middle-aged men and women may be related to the co-existance of multiple known cardiovascular risk factors.

P3991 | BEDSIDE
Exercise intensity and disease expression in carriers of sarcomeric hcm causing mutations

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Purpose: Physical exercise is supposed to enhance the degree of left ventricular hypertrophy in Hypertrophic Cardiomyopathy (HCM). Moreover, intense exercise is accepted as a trigger of ventricular arrhythmias in HCM. We aimed to study the contribution of physical activity on the age of diagnosis and severity of the disease in a population of HCM-mutation carriers.
Methods: 224 HCM-mutation carriers from 69 families (aged 41±16, 56% males) were studied. 161 individuals (66.3%) met HCM criteria. 79% were carriers of a mutation in MYBPC3 and 21% in MYH7. Patients were classified in 3 groups: (1) 191 (86%) sedentary or mild, (2) 23 (10%) moderate and (3) 10 (4%) intense competitive exercise. 128 (67%) of the sedentary, 15 (65%) of the moderate exercise and 7 (70%) of the intense exercise carriers were affected. Clinical, ECG, echocardiographic variables and outcomes were analyzed.
Results: Males performed more frequently moderate or intense exercise (group 2+3) than females (27, (20%) vs 6, (7%), p=0.001). Despite the penetrance of the disease was similar regardless the intensity of the exercise (65-70%), HCM patients who performed exercise (group 2+3) had an earlier diagnosis compared to sedentary (group 1) (mean age 34±12 vs 42±17 years old, binary p=0.04, long rank p=0.04). Mean maximal wall thickness was similar in patients who performed exercise compared to sedentary patients 19.0±5.2 mm vs 20.5±6.1 mm (ns). A similar proportion of HCM-patients who performed exercise (5, 23%) compared to sedentary patients (45, 34%) had obstruction (ns). HCM-patients who performed exercise had more syncope (32% vs 13%, p=0.02). There were no other differences in symptoms. Atrial fibrillation and NSVT on Holter was similar in exercise-HCM and sedentary-HCM patients. Proportion of cardiac events was similar between groups (17, 13% vs 3, 14%, ns) during 5.5±3.3 years FU. On multivariate, adjusting for age and sex, intensity of exercise was not predictor of maximal wall thickness.
Conclusions: Moderate or intense exercise is associated with an early diagnosis of HCM in carriers of sarcomeric mutations. HCM-patients who perform significant exercise have similar maximal left ventricular wall thickness than sedentary patients. Atrial and ventricular arrhythmias were not associated with exercise intensity in our population of HCM patients with sarcomeric mutations. The magnitude of the effect of exercise in phenotypic expression of HCM seems to be moderated.

P3992 | BEDSIDE
Physical activity, obesity status and 10-year cardiovascular disease incidence; a follow-up (2001-2011) of the Attica study

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Objective: To evaluate physical activity behaviours among adults within a 5-year period, and its relationship to 10-year risk for cardiovascular disease events.
Methods: From May 2001 to December 2002, 1514 men and 1528 women (>18 y) living in greater Athens area, Greece, were enrolled. In 2011-12, 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. Weekly energy expenditure was assessed using the validated IPAQ tool. Physical activity behaviours during the first 5-years of follow-up were classified as (a) physically inactive throughout study course, (b) sedentary at baseline, but active at 5-year, (c) active at baseline, but sedentary at 5-year and (d) physically active during the first 5-years of follow-up.
Results: 587 (61%) men and 673 (68%) women were classified as physically inactive at baseline examination, whereas 661 (69%) men and 728 (73%) women were classified as physically inactive at 5-year follow-up. Prevalence of obesity was 20.8% in men and 15.9% in women at baseline examination, while another 14.5% of men and 14.2% of women became obese during the follow-up period. Multivariable analysis, after adjusting for age, sex, smoking, eating habits, history of hypertension, diabetes and hypercholesterolemia, and education level, revealed that only participants who remained physically active during the first 5-years of the follow-up were protected against CVD (relative risk= 0.55, 95%CI 0.30, 0.99), whereas, the other two physical activity categories did not show any significant associations with CVD risk ($p>0.16$). Moreover, body mass index at baseline examination was highly associated with 10-year CVD risk (relative risk per 1 kg/m^2 = 1.04, 95%CI 1.01-1.07); whereas, obese participants experienced 29% higher CVD risk, as compared with normal/overweight. Then the analysis was stratified by obesity and physical activity status. It was found that only among normal weight participants, physical activity offered a protection against CVD (i.e., 32% and 34% lower risk among sedentary and physically active but normal weight participants, as compared with obese and sedentary); whereas, among obese individuals, physical activity was not associated with CVD risk reduction (p=0.17).
Conclusions: Obesity seems to play a detrimental role in CVD risk reduction, shaking down the "slogan" better active and obese than non-active and lean. Actions towards the epidemic of obesity are urgently needed in order to further prevent CVD in the studied population.

P3993 | BEDSIDE
Pre-hospital activity of daily living determines length of hospitalization in super-elderly patients with acute decompensated heart failure

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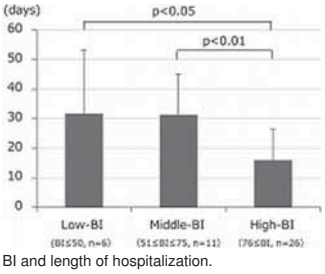
Background: The economic burden of hospitalization for heart failure is staggering in developed countries. Especially in Japan, the unprecedentedly rapid aging of society and universal health insurance system provoke long-term hospitalization in super-elderly patients that became seriously growing medical problem.
Aims: We hypothesized that the length of hospitalization (LOH) may be associated with pre-hospital activity of daily living (ADL) in super-elderly patients (over 85 years) with acute decompensated heart failure.
Methods: Forty-three patients (27 males, mean age 87.2 years) were enrolled. Pre-hospital ADL was evaluated by Barthel index (BI) and the patients were allocated into 3 groups based on BI; the High-BI group (76≤BI), the Middle-BI group (51≤BI≤75), and the Low-BI group (BI≤50). In addition, all patients were also divided into 2 groups based on the median of LOH; the Short-LOH group (≤17 days) and the Long-LOH group (18 day≤).
Results: The mean body mass index, left ventricular ejection fraction, and plasma brain natriuretic peptide level on admission were 21.4 kg/m^2, 49.8%, and 994 pg/mL. The LOH in the Low-BI group and the Middle-BI group were significantly longer than in the High-BI group (Figure). The percentage of BI≤75 patients was lower in the Long-LOH group than in the Short-LOH group (p=0.04). Except for BI, there were no significant differences in baseline characteristics between the 2 groups. Logistic regression analysis revealed that BI≤75 (p=0.01, Odds Ratio=7.37) and body mass index (p=0.01, Odds Ratio=0.73) were independent predictors of long LOH.



BI and length of hospitalization.

Conclusions: Pre-hospital ADL is associated with the LOH in super-elderly patients with acute decompensated heart failure. Continuous maintenance of ADL at higher level could be essential for the reduction of LOH.

RENAL DENERVATION THERAPY

P3994 | BEDSIDE
Low efficacy of renal denervation as a result of anatomically inadequate operative technique

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Inefficacy of renal denervation (RD) in Symplicity HTN-3 study may be caused by inadequate operative technique rather than reflect true limitations of the technology. The technique - to perform 4-6 point ablations equally distributed along the length of renal artery (RA) - may only be effective if the renal nerves likewise follow the whole course of the artery from aortal origin to segmental division. However, surgical studies show that renal nerves form a fan-shaped triangle plexus converging toward hilum, i.e. proximally the nerves go at a distance from RA obliquely to it and join it in the middle and distal portion so that number of fibers available for endovascular RF ablation is minimal in proximal part and maximal in distal part of RA. Then anatomically adequate technique would be to perform ablations mainly in distal portion of RA instead of their equal distribution along the artery.
Objective: To evaluate whether ablation of sympathetic nerves in distal part of RA is more effective than standard RD.
Methods: We initiated randomized controlled study in which we compare the modified operative technique (ablations performed in distal part and major branches of RA) with standard RD in patients with resistant hypertension using Symplicity device.
Results: At the time of this analysis 24 patients (12 treated by modified technique and 12 – by standard RD) completed 1 months follow up. No significant damage of RA was detected. The only complication was small pseudoaneurysm at a punction site.
Ambulatory BP decreased powerfully in the group of modified technique: -16.9/-7,2 (SD 20.6/9,9) mmHg (mean 24-hr BP, systolic/diastolic respectively), p=0,015 and only slightly in the group of standard RD: -2,9/-2.2 (SD 17,2/8,6) p=0,56. The difference in the effects was statistically significant for mean 24-h systolic BP (p=0,04) and close to significance for 24-h diastolic BP (p=0,09). Office BP lowering was also greater with modified technique, however, the difference was not significant: -28,2/-11,8 vs -20,2/-10,7 respectively.
Conclusion: Radiofrequency ablation of sympathetic nerves in distal part and segmental branches of renal artery seems to be equally safe but significantly more effective than standard RD.

P3995 | BEDSIDE
Prognostic ability of MR-proadrenomedullin in patients undergoing renal denervation

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Background and methods: Renal denervation (RD) is a new therapeutic option in patients with resistant hypertension. Midregional proadrenomedullin (MR-proADM) exerts various effects on the cardiovascular system and showed to be a prognostic marker for various cardiovascular diseases, especially in patients with heart failure and probably hypertension. Therefore, the aim of our study was to evaluate the prognostic effect of MR-proADM in patients undergoing RD. We measured MR-proADM using a flouroimmunoassay (BRAHMS MR-proADM Kryptor) in 110 patients before, 1 and 6 months after RD in a multicenter setting. In addition brain natriuretic peptide (BNP), atrial natriuretic peptide (MR-proANP), c-reactive protein (CRP) and Cystatin C were measured. All patients were followed up by office and ambulatory blood pressure (ABP) measurements. For statistical analyses linear effect models were used to determine the association of biomarkers and BP.
Results: 6 months after RD the mean systolic ABP was reduced by 8mmHg, the responder-rate (drop in ABP systolic BP ≥5mmHg) was 59%. MR-proADM and BNP were significantly associated with blood pressure reduction after 6 month (coefficient MR-proADM -0.0019, p=0.047; BNP 0.0059, p=0.036; Table 1). In responders, MR-proADM concentrations showed a higher increase after 6 months compared to non-responders, but did not reach statistical significance (Figure 1). Biomarkers at baseline were not able to predict for therapy-responder (Table 2).

Association of biomarkers and BP

MR-proADM	MR-proADM	MR-proANP	Cystatin C	BNP	CRP
Coefficient	–0.0019	0.0035	0.0006	0.0059	0.0070
p-value	0.047	0.18	0.73	0.036	0.086

Linear mixed effect models for biomarkers and blood pressure. Table summarizing the results for the linear mixed effect models for biomarkers and systolic mean ABP are given. All biomarkers are log-transformed. The covariates in the model are: systolic BP (mean, overall), age (baseline), female, BMI, smoker, diabetes, hyperlipidemia, CHD.

Conclusions: In patients undergoing RD MR-proADM and BNP showed a sig-

nificant association with BP reduction after 6 month, but baseline measurements had no prognostic use for therapy success in this short time follow-up period.

P3996 | BEDSIDE
Renal denervation: a real-world prospective multi-centre registry

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Purpose: To assess efficacy and safety of renal denervation (RDN) in a real world population of patients with resistant hypertension (HTN).
Methods: Prospective multi-centre French registry of consecutive patients referred to our institution for RDN. All patients were screened for secondary HTN. Blood pressure (BP) measurements as well as medication intake were compared pre and post-procedural at 1, 6, 12 and 24 months.
Results: Between November 2010 and December 2013, 69 patients were included. They were 63.0±12.0 years old, 62% male, 40% diabetic, 18% eGFR <45 mL/min/1.73m^2. The mean number of antihypertensive drugs per patient at baseline was 5.12±1.1, with 56% taking 5 or more different therapeutic classes (Diuretics 85%, Calcium channel blockers 76%, Beta-blockers74%, ACE-inhibitors 61%, ARA-II 56%, aldosterone antagonists 27%. A polar artery was present in 8/69 patients. Three different denervation systems (Simplicity in 63 patients, EnligHTN in 3, and OneShot in 3) were used. There were no procedure-related complications. As shown in figure 1, available 24h ambulatory blood pressure measurements (ABPM) as well as office BP have shown a significant reduction in systolic BP values over the two-year period. Systolic ABPM decreased from 165.1±19.7 mmHg to 136.1±9.3 mmHg (p<0.01 at two years in paired t-test compared with baseline), while office systolic BP decreased from 181.4±19.4 mmHg to 141.5±16.3 mmHg (p<0.001). Medication intake also decreased from 5.1±1.1 to 4.5±1.3 drugs/patient in the same period. Follow-up imaging tests have not shown any late complication or renal stenosis so far.

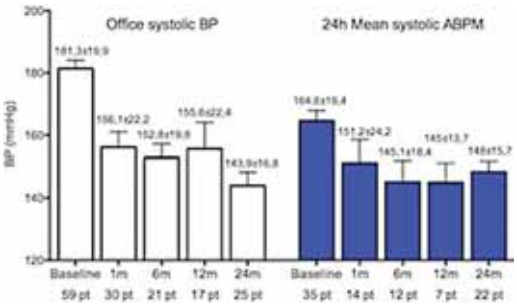

Figure 1

Conclusion: In our series, renal denervation has proved to be an efficient and safe tool for BP lowering in a real world population of resistant hypertensive patients.

P3997 | BENCH
Renal denervation attenuates progression of kidney and heart injury in obese spontaneously hypertensive rats

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Background: Metabolic syndrome is associated with increased sympathetic drive possibly contributing to the progression of cardiac and renal dysfunction. Renal sympathetic denervation (RDN) decreases sympathetic renal efferent and afferent nerve activity.
Methods: Obese spontaneously hypertensive rats with RDN at the age of 34 weeks (SHR-ob RDN) were compared to sham operated SHR-ob (SHR-ob) and their normotensive lean controls (Ctr.). Blood pressure was measured by telemetry. Kidney and heart function was determined by magnetic resonance imaging (MRI) and invasive pressure measurements. Renal and cardiac remodeling were scored by immunohistochemical analysis. Animals were sacrificed at the age of 48 weeks.
Results: In SHR-ob, RDN attenuated the progressive increase in blood pressure and preserved a systolic blood pressure of 156±7 mmHg compared to 220±8 mmHg in sham operated SHR-ob at 100 days after RDN. In SHR-ob, heart rate, increased body weight, dyslipidemia and hyperinsulinemia were not modulated by RDN. The significant increase in plasma renin activity as well as the reduction in urinary sodium excretion in SHR-ob were inhibited by RDN. Renal catecholamine levels and tyrosin hydroxylase staining were significantly increased in SHR-ob compared to Ctr. and pronouncedly reduced by RDN (- 80%) suggesting effective denervation of the kidney. Progression of renal dysfunction as characterized by increased urinary albumin/creatinine ratio and reduction in glomerulary filtration rate were significantly attenuated by RDN in SHR-ob. Attenuation of renal injury by RDN in SHR-ob was confirmed by renal desmin staining, a marker for glomerular podocyte damage. RDN prevented the progression of glomerulosclerosis, as scored by semiquantitative morphometric evaluation. In SHR-ob, renal perfusion was reduced by 30% compared to Ctr. and normalized by RDN. Increased left ventricular enddiastolic pressure in SHR-ob was reduced by RDN from 16±4.1 mmHg to 10±3.7 mmHg (p<0.01), while left ventricular enddiastolic volume was not changed, suggesting an attenuation of impairment of left ventricular compliance by RDN. This was associated with reduced left ventricular interstitial fibrosis formation in SHR-ob RDN. The progression of left ventricular hypertrophy was not significantly influenced by RDN.
Conclusion: In SHR-ob, RDN attenuated the progressive increase in blood pressure and preserved better cardiac and renal function independent of changes in metabolic conditions. RDN may therefore provide cardiac and renal protection in obese and hypertensive patients with renal dysfunction.

P3998 | BENCH
Short-term safety and efficiency of cryoablation for renal sympathetic denervation in a swine model

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Purpose: Catheter-based renal sympathetic denervation treatment (RDN) has been shown in several studies to be an effective therapy for medically-refractory hypertension by lowering sympathetic tone. However, Medtronic has announced that the SYMPLICITY HTN-3 trial has failed to meet its primary efficacy endpoint of changing in office systolic BP from baseline to six months. Different from radiofrequency ablation, we used cryoenergy for sympathetic denervation of the renal arterial,with cryoablation (CR) balloon to perform circumferential denervation.
Methods: Sixteen swine (32 renal arteries), randomly assigned to four groups: control group (n=10), CR-7d group (n=8), CR-14d group (n=8), CR-28d group (n=6). Eleven swine in three CR groups underwent cryoablation of the renal sympathetic nerves. After renal angiogram, the 7.5F cryocatheter with a balloon of a certain diameter (4mm, 5mm, 6mm and 7mm) was introduced into the renal artery via femoral access using 8F guiding sheath and 0.018" guiding wire. The balloon was then inflated using contrast material to the desired size, and the flood flow was blocked. Complete circumferential denervation were created in both renal arteries by achieving the temperature of the balloon surface lower to average minus 95℃ (various between minus 80℃ to minus 110℃) for 3 min each. Thawing was done by warming the balloon immediately after cryoablation and then the catheter was retracted. The control group underwent the same procedure except ablation. Renal angiogram of the femoral arteries were performed after denervation and before the sacrifice in order to get the diameter of renal arteries and the pressure of aorta abdominalis. Euthanasia of the swine were then performed on the 7th, 14th and 28th day to get NE changes of renal cortex.
Results: (1) Renal angiogram all indicated that cryoablation did not induce hemadostenosis, endovascular thrombi, vascular injury or other severe complications. (2) Compared with control group, in CR-7d, CR-14d and CR-28d groups, NE of renal cortex were significantly decreased (457.93±23.16ng/g VS 92.28±107.39ng/g, 46.87±54.65ng/g, 9.58±11.54ng/g; P≤0.05). (3) SP and DP of aorta abdominalis at any time are similar (P>0.05).
Conclusions: Percutaneous catheter-based cryoablation of the renal artery is safe. CR could effectively reduce NE storing in the renal cortex, even better than RF ablation, and the efficiency could maintain 28d at least. Whether this alternative innovative device are superior to predecessor RDN technologies, the long–term follow up safety and efficiency are undergoing.

P3999 | BEDSIDE
Renal denervation reduces sympathetic tone of renal artery vasculature without detrimental effects: a non-invasive cardiovascular magnetic resonance follow-up study

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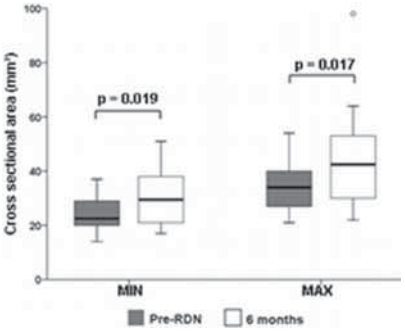
Purpose: To study non-invasively the effects of renal denervation (RDN) on renal artery wall anatomy and function using magnetic resonance imaging (MRI).
Methods: We prospectively included 26 patients undergoing RDN. A 3.0T MRI of the renal arteries was performed before RDN and at 6-month follow-up. We quantified the vessel sharpness of both renal arteries at baseline and follow-up using a quantitative analysis tool. In a subgroup of 17 patients, we additionally assessed the maximal (MAX) and minimal (MIN) cross-sectional area at the proximal part of both renal arteries, and we quantified renal artery distensibility as (MAX - MIN)/(pulse pressure × MIN), pulse pressure being the difference between systolic and diastolic brachial blood pressure.
Results: Neither renal artery sharpness (48.95±7.17 vs. 47.33±7.64, p=0.26) nor renal artery distensibility (6.87±2.83 vs. 7.01±2.98 mmHg^{-1} × 10^3, p=0.59) were significantly different before RDN vs. at 6-month follow-up. Both MIN and MAX cross sectional areas increased significantly after RDN (23.48±6.87 vs. 27.33±9.51 mm^2, p=0.019, and 33.76±8.52 vs. 38.80±11.78 mm^2, p=0.017, respectively) (figure).



Renal artery cross sectional area change.

Conclusions: RDN is not associated with significant changes in renal artery sharpness or distensibility, indicating no adverse effect of RDN on renal artery anatomy and function. The effect of RDN on the sympathetic tone of the vasculature might explain the enlargement of the renal arteries post RDN.

P4000 | **BEDSIDE**
Effects of renal sympathetic denervation on exercise blood pressure, heart rate and capacity in patients with resistant hypertension

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Renal denervation reduces office blood pressure in patients with resistant hypertension. This study investigated the effects of renal denervation on blood pressure, heart rate, and chronotropic index at rest, during exercise and recovery in 60 patients (renal denervation group=50, control group=10) with resistant hypertension, using a standardized bicycle exercise test protocol performed 6- and 12-months after renal denervation. After renal denervation, exercise blood pressure at rest was reduced from 158±3/90±2mmHg to 141±3/84±4mmHg ($p<0.001$ for systolic blood pressure/p=0.007 for diastolic blood pressure) after 6-months and 139±3/83±4mmHg ($p<0.001$/p=0.022) after 12-months. Exercise blood pressure tended to be lower at all stages of exercise at 6- and 12-month follow-up in patients undergoing renal denervation, although reaching statistical significance only at mild-to-moderate exercise levels (75-100 Watt). At recovery after 1min, blood pressure decreased from 201±4/95±2mmHg to 177±4/88±2mmHg ($p<0.001$/p=0.066) and 188±6/86±2mmHg (p=0.059/p=0.01) after 6- and 12-months, respectively. Heart rate was reduced after renal denervation from 71±3bpm at rest, 128±5bpm at maximum workload, and 96±5bpm at recovery after 1min to 66±2bpm ($p<0.001$), 115±5bpm (p=0.107), and 89±3bpm (p=0.008) after 6-months and to 69±3bpm (p=0.092), 122±7bpm (p=0.01), and 93±4bpm (p=0.032) after 12-months. Mean exercise time increased from 6.59±0.33min to 8.4±0.32min ($p<0.001$) and 9.0±0.41min (p=0.008) and mean workload increased from 93±2W to 100±2W ($p<0.001$) and 101±3W (p=0.007) at 6- and 12-month follow-up, respectively. No changes were observed in the control group. In conclusion, renal denervation reduced blood pressure and heart rate during exercise, improved mean workload and increased exercise time without impairing chronotropic competence.

ATHEROSCLEROSIS

P4001 | **BENCH**
Antibodies to periodontal pathogens in relation to coronary plaque characteristics on intravascular ultrasound and to cardiovascular outcome

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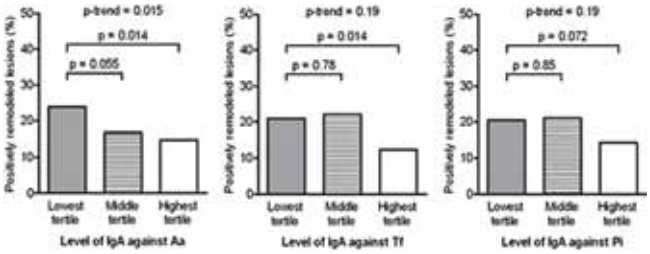
Purpose: Positive associations between clinically established periodontitis and cardiovascular disease have been proposed, but remain controversial. This study aims to investigate the associations of circulating antibodies to periodontal pathogens with 1-year cardiovascular outcome, as well as the extent of coronary atherosclerosis, plaque vulnerability and lesion remodeling on intravascular ultrasound (IVUS) imaging.
Methods: Grayscale and virtual histology (VH) IVUS imaging of a non-culprit coronary artery was performed in 581 patients who underwent coronary angiography. IgG and IgA to P. gingivalis, A. actinomycetemcomitans, T. forsythia and P. intermedia were measured in blood samples.
Results: Antibodies to the above mentioned bacteria were not associated with coronary plaque burden, VH-IVUS-derived thin-cap fibroatheroma lesion morphology or 1-year incidence of major adverse cardiac events (MACE), which included all-cause mortality, acute coronary syndrome or unplanned coronary revascularization. IgA to A. actinomycetemcomitans, T. forsythia and P. intermedia



(borderline) were associated with lower extent of positive lesion remodelling (Figure). In diabetic patients specifically, IgG to P. gingivalis tended to be associated with coronary plaque burden (p-trend=0.080), while IgA to P. gingivalis tended to be associated with incident MACE (p-trend=0.060).
Conclusions: Plasma IgG and IgA to major periodontal pathogens were not associated with the extent of coronary atherosclerosis (with the exception of a trend in diabetics) nor with coronary plaque vulnerability. High levels of IgA to periodontal pathogens were associated with lower extent of coronary remodeling. Altogether, these results do not add evidence for a substantial role of periodontal infection in coronary artery disease.

P4002 | **BEDSIDE**
Association between histological findings in epicardial adipose tissue and MDCT parameters in patients with coronary artery disease

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Purpose: Epicardial adipose tissue (EAT) is a source of inflammatory mediators and is associated with coronary artery disease (CAD) risk factors. In addition, lower CT attenuation of visceral adipose tissue and subcutaneous adipose tissue (SAT) is associated with adverse cardio-metabolic risk. However, whether lower CT attenuation of EAT is associated with CAD risk factors or histological findings is uncertain. We evaluated infiltration of macrophages and adipose cell area in EAT of CAD and non-CAD groups and also investigated the relationships between the histological findings and MDCT parameters or CAD risk factors.
Methods: Samples were obtained from EAT, SAT, and paracardial adipose tissue (PAT) during cardiac surgery (CAD group (bypass), n=30; non-CAD group, n=49). Infiltration of macrophages was investigated by immunohistochemical staining (CD68, CD11c, and CD206). Each adipose cell area was measured and the average value was computed. MDCT was performed before surgery and Agatston score was evaluated. Mean CT value was assessed using a dedicated workstation
Results: In EAT, there were many CD11c (M1)-positive macrophages in the CAD group compared with those in the non-CAD group ($P<0.001$). In contrast, the numbers of M1 macrophages in SAT and PAT were not significantly different between the two groups (P=0.379 and P=0.479, respectively). In EAT, the ratio of CD11c/CD206 (M1/M2)-positive macrophages in the CAD group was higher than that in the non-CAD group (P=0.005). Additionally, adipose cell area in EAT was significantly larger in the CAD group than in the non-CAD group ($P<0.001$). This difference was not found between the 2 groups in SAT or PAT. Furthermore, the number of M1 macrophages in EAT was positively correlated with Agatston score and Gensini score (r=0.302, P=0.017 and r=0.410, P=0.001, respectively). Also, mean CT value in EAT was significantly lower in the CAD group than in the non-CAD group (-72±16HU vs -65±18HU, P=0.004) and was negatively correlated with Agatston score and Gensini score (r= -0.235, P=0.049 and r=-0.255, P=0.028, respectively). Mean CT value in EAT was significantly correlated with adipose cell area in EAT (r=-0.303, P=0.009) but was not correlated with M1 macrophages in EAT (r=-0.107, P=0.385).
Conclusions: The number of M1 macrophages in EAT is increased and CT value in EAT is lower and is correlated with arteriosclerosis parameters of MDCT. Infiltration of M1 macrophages in EAT is a precipitating factor of coronary arteriosclerosis. Lower CT attenuation in EAT has the potential to become a CAD risk factor and may be caused by hypertrophy of adipose cells.

P4003 | **BEDSIDE**
ADAMTS7 as a novel genetic locus for coronary atherosclerosis and cardiovascular prognosis

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Overexpression of ADAMS7 gene accelerates migration of vascular smooth muscle cells (VSMCs) in vitro and exacerbates neointimal thickening and progression of atherosclerosis. Recent GWAS have showed that this gene contains a SNP rs3825807 A>G leading to a Ser-to-Pro substitution in the prodomain of the protease, and that the GG genotype is associated with protection from atherosclerosis and coronary artery disease (CAD).

Aim: To investigate whether the SNP rs3825807 A>G is associated to a better survival in CAD patients.
Methods: A prospective study was performed with a cohort of 1128 patients with angiographically proven CAD who underwent a mean follow-up period of 63 (6-182) months. Genotyping of ADAMTS7 rs3825807 A>G was performed using oligonucleotides probes marked with specific fluorescence for each one of the alleles (combination of PCR technique and TaqMan). Survival analysis through Cox regression model was applied to data to examine the effect of rs3825807 A>G (AA, AG and GG) on survival. Hazard ratios (HRs) and 95% CIs are reported. A p-value less than 0.05 was considered significant.
Results: After Cox regression, using the mutated rs3825807 GG as a reference, AA genotype remained in the equation as an independent risk factor for CAD mortality (HR=2.8; CI: 1.17-6.5; p=0.020). Survival function for the Cox regression showed that at the end of the follow-up, the estimate survival probability was 89.8% for GG genotype, 82.2% for AG and 72.3% for AA (p=0.047).

Survival function (ADAMTS7 GG, AG, AA.)

Conclusion: Our results showed that CAD patients with GG genotype and, consequently, reduction of the ADAMTS7 function had a better survival than AA genotype. Translation of GWAS discoveries for coronary patients can have implications into prognostic and therapeutic of these patients.

P4004 | BENCH
FHL-2 inhibition leads to decreased atherogenesis in ApoE-/- mice: role of immune cells

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Background: Four-and-a-half LIM domain protein-2 (FHL2) is expressed in endothelial and vascular smooth muscle cells. FHL2 negatively regulates endothelial cell and early outgrowth cell survival and migration, but its role in atherogenesis is unknown.
Methods and results: To investigate the role of FHL2 in atherosclerosis, we crossed FHL2 knockout (FHL2–/–) with apolipoprotein E-deficient (ApoE–/–) mice, and fed them a high-cholesterol, high-fat diet for 7 weeks. FHL2–/–ApoE–/– mice displayed significantly less atherosclerotic plaque formation, as assessed by oil red O staining, in the aortic sinus and aorta, compared with ApoE–/– mice. This was associated with significantly enhanced collagen and smooth muscle cell contents within the atherosclerotic plaques of FHL2–/–ApoE–/– mice, as determined by Sirius red and alpha-actin staining, respectively, compared with ApoE–/– mice. These results suggest that absence of FHL2 promotes smaller and more stable plaques. Decreased plaque formation in FHL2–/–ApoE–/– mice was associated with significantly reduced aortic ICAM-1 mRNA and VCAM-1 expression levels in the atherosclerotic plaques. Relative monocyte/macrophage content within the atherosclerotic plaques, as determined by MOMA-2 immunostaining, and in spleens, as determined by FACS analysis, was equivalent in both animals groups. FACS analysis of T cells in spleens showed a significant increase in CD4+CD25+Foxp3+ regulatory T cell numbers in FHL2–/–ApoE–/– compared with ApoE–/– mice. CD3+ T cell number was significantly higher within the atherosclerotic plaques of FHL2–/–ApoE–/– mice. Moreover, analysis of cells recruited into the peritoneal cavity showed higher numbers of active regulatory T cells and lower numbers of pro-inflammatory Ly6c(hi) monocytes in FHL2–/–ApoE–/– mice. In addition, the effect of bone marrow (BM)-specific and vascular deficiency of FHL2 on atherosclerosis was studied. ApoE–/– or FHL2–/–ApoE–/– mice were lethally irradiated and transplanted with BM of ApoE–/– or FHL2–/–ApoE–/– mice. After 7 weeks of high-cholesterol, high-fat diet, both chimeric mice groups showed an intermediate phenotype in terms of atherosclerotic plaque formation in the aortic sinus and aorta compared with ApoE–/– or FHL2–/–ApoE–/– mice. These results suggest that FHL2 deficiency both in the BM and in vascular cells is involved in the observed effects on atherogenesis.
Conclusion: Our findings suggest that FHL2 in BM-derived and vascular cells may play an important role in atherogenesis by promoting plaque formation, involving upregulation of adhesion molecules and modulation of immune cells.

P4005 | BENCH
Differential expression of Notch pathway components in atheroprotected vs atherosusceptible regions of endothelium of mouse aorta

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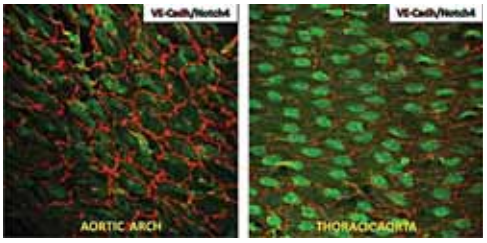
Purpose: Atherosclerotic lesions occur in the arterial tree at sites characterized by disturbed flow; the latter interferes with the expression of pro-survival and anti-inflammatory genes involved in the protection of endothelium. The Notch pathway is involved in protecting endothelial cells from inflammation-induced apoptosis. Whether differences in hemodynamic forces affect the status of Notch, predisposing endothelial cells to apoptosis and thus promoting the onset of atherosclerosis is not known.
Methods: We evaluated by immunofluorescence protein levels of Notch receptors (Notch1 and Notch4), Delta-like ligand 4 (Dll4) and Notch target genes (Hey1 and Hey2) in the endothelium of whole mount preparations of aortic arch (turbulent flow) and thoracic aorta (laminar flow) of C57BL/6J mice (n=14). We also measured their mRNA levels in endothelium-enriched RNA isolated from those regions.
Results: Protein levels of Hey2, Notch4 and Dll4 were lower in the aortic arch compared to the thoracic aorta. Similarly, quantitative RT-PCR showed a significant reduction in Dll4 (0.65-fold), Hey2 (0.74-fold) and Notch4 (0.78-fold) mRNAs in the aortic arch. There were no clear differences between aortic arch and thoracic aorta in Hey1 and Notch1 protein levels and the increase of their corresponding mRNAs in the aortic arch wasn't statistically significant.



Notch4 in endothelium of mouse aorta.

Conclusions: Our data provide the first in vivo evidence of differences in expression levels of Notch signalling components between regions of mouse aorta predisposed to atherosclerotic plaques formation as compared with atheroprotected regions. More studies are needed to establish whether these topographical differences are also associated with a dysregulation of the Notch pathway that could play a role in atherosclerosis onset and progression.

P4006 | BENCH
Validation of intravascular optical coherence tomography by analyzing in vivo vulnerable plaques in atherosclerosis Watanabe rabbits during one year: correlation with histological finding

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Background: Rupture of an atherosclerotic plaque is the primary underlying cause of most acute coronary events and strokes. Atherosclerosis Watanabe rabbit model is a unique animal model with spontaneous rupture of plaque without external intervention. The aim of this study is to establish a correlation between histological and intravascular optical coherence tomography (OCT) analysis of vulnerable plaque (VP).
Methods: After approval by ethics committee (N° CEE A.2012.189), 34 heritable hyperlipidemic male Watanabe rabbits were studied between January 2013 and January 2014. Two groups were studied: group 1 treated by atorvastatin from the age of 3 months and a control group without atorvastatin. OCT and histology

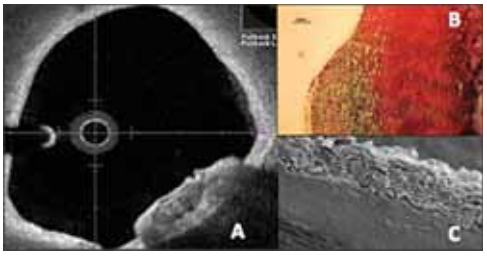

Figure 1. A: OCT; B: Histology; C: SEM.

were performed at the age of 3 (n=6), 6 (n=8), 9 (n=10), 12 (n=10) months in both groups. The aorta was totally imaged by OCT. Parts of aorta were fixed in Bouin's solution and embedded in paraffin. Slides were stained with Hematoxylin-eosin. Scanning Electron Microscopy (SEM) was performed on these regions of interest.
Results: OCT was feasible in all animals. A mean of 20 plaques by rabbit were analyzed. We obtained excellent correlation between OCT and histopathology (Fig. 1). The number of VP and the mean plaque thickness were more important in the control Group. We observed spontaneous rupture of vulnerable plaque by OCT confirmed by histological analysis.
Conclusion: This study establishes the first correlation between OCT and histology in a model of spontaneous VP rupture. The results of this study are unique as we followed directly the evolution of a high number of plaques as well as the effect of statins and showed the benefit of this treatment on these plaques.

CARDIOVASCULAR MAGNETIC RESONANCE IN ELECTROPHYSIOLOGY

P4007 | BEDSIDE
The utility of Cardiac Magnetic Resonance Imaging (CMR) in the diagnosis of cardiac sarcoidosis

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Background: Autopsy reports suggest that cardiac sarcoidosis occurs in up to 30% of patients with pulmonary sarcoidosis, yet the clinical diagnosis is made in only 5% of cases. Current diagnostic algorithms are complex and lack sensitivity and specificity. Cardiac MRI (CMR) provides a unique opportunity to diagnose myocardial inflammation/scar with high resolution and no ionizing radiation. We investigated the prevalence of Late Gadolinium Enhancement (LGE) on CMR in patients with sarcoidosis and the relationship between LGE and cardiac arrhythmias and left ventricular (LV) function.
Aim: To determine the prevalence of LV inflammation/scar diagnosed with LGE detected on CMR at 1.5T in patients with biopsy proven sarcoidosis and to determine the diagnostic utility and clinical significance of LGE on CMR.
Methods: Consecutive patients with biopsy proven sarcoidosis referred for CMR to evaluate for cardiac sarcoidosis were retrospectively reviewed. Independent review of medical records, electrocardiograms, holters and echocardiograms was conducted and correlated with CMR findings. The prevalence of LGE and the relationship with cardiac arrhythmias and LV function was assessed.
Results: We evaluated 34 patients (51±10 years; 17 Male) with biopsy proven sarcoidosis who underwent CMR. A mid-wall pattern of LGE, consistent with LV inflammation/scar, was detected in eight (24%) patients. Of those who had LGE on CMR, 88% had corresponding hyper-intense myocardial signal on T2 weighted imaging indicating active inflammation.
LGE was associated with the presence of clinically significant arrhythmia (p=0.04); however, there was a non significant association between LGE and LV dysfunction (EF≤55%; p=0.07). The mean LV Ejection Fraction (EF) in the LGE positive group was 59% compared with 65% in the LGE negative group. The mean right ventricular EF was 60% in the LGE positive group compared with 58% in the LGE negative group. There was no association with pulmonary stage and LGE on CMR (p=0.21).
Conclusion: LGE identified on CMR in patients with sarcoidosis was associated with clinically significant arrhythmias and may represent a more sensitive diagnostic tool for cardiac sarcoidosis. As cardiac manifestations of sarcoidosis have important prognostic implications, further prospective evaluation of CMR is warranted.

P4008 | BENCH
T2 mapping and cardiac fatty acid binding protein both detect myocardial injury after transthoracic shocks

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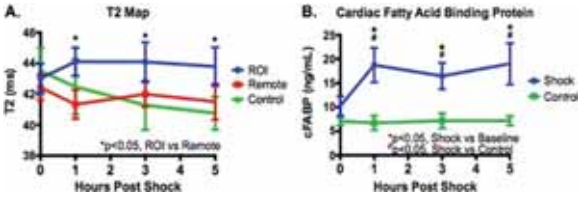
Purpose: Defibrillation and cardioversion are often life saving interventions. Regarding serologic parameters, it is controversial if they can cause myocardial damage. Edema is an early feature of acute myocardial injury and can be detected non-invasively with T2 mapping cardiovascular MRI (CMR).
Methods: Sixteen swine were anaesthetized; ten were treated with 5x200J transthoracic shocks and six served as control. At baseline, 1h, 3h and 5h post shock, serology samples and T2 maps in 3 short axis slices at 3T were obtained. Serology tests included porcine cardiac fatty acid binding protein (cFABP), total creatine kinase (CK) as well as the porcine cardiac isoform (CK-MB) and porcine ultra-sensitive troponin I (usTnI). After euthanization, myocardial tissue samples were obtained for hematoxyline-eosine staining from regions deemed affected by T2 maps (ROI) or 3 random samples in the control pigs.
Results: There was an 83% increase in cFABP after 1h post-shock ($p<0.05$) that remained elevated (Fig. 2b). CK-MB and usTnI did not change, however total CK increased from 633±81.9 U/L at baseline to 7397±941.3 U/L at 5h post shock ($p<0.01$) attributable to skeletal muscle damage. There was no change in CK in the control animals. In CMR, T2 increased in the affected ROI at 1h, 3h and 5h post defibrillation (Fig. 1a), which differed from the remote myocardium of the same animals ($p<0.05$). The change in T2 corresponded to defibrillation pad locations. The interstitial and intracellular space of affected areas were both singificantly increased by 953% and 185% respectively, compared to control samples (p=0.02).



Changes in T2 and cFABP after shocks.

Conclusion: Both cFABP as a myocardial necrosis marker and T2 mapping of myocardial edema can detect acute myocardial injury after transthoracic electric shocks in-vivo

P4009 | BEDSIDE
Cardiac magnetic resonance in patients with antiarrhythmic devices, analysis of image quality,reproducibility and diagnostic effectiveness

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CMR in patients with antiarrhythmic devices has been considered of limited diagnostic yield due to artifacts. The aim was to assess effectiveness and reproducibility of CMR in this setting.
Methods: Consecutive patients with devices were prospectively included. Artifact area (AA) was assessed in steady state free precession (SSFP) cine, spoiled gradient- echo perfusion and late enhancement (LGE) sequences. Reproducibility of CMR data and effectiveness of scan were also analyzed.
Results: 68 patients, 43 males (63%), mean age 60 years (range 12-87) were included, 15 (22%) had ICDs and 53 (78%) PMs. Image quality was considered excellent in 38 (56%) of patients. AA in cine, perfusion and LGE sequences significantly correlated with device mass and volume. The scan was considered ineffective in 13 patients (20%) and this was significantly associated to ICDs (OR: 18 p<0,001), greater mass and volume of device (OR: 1,05 p<0,001/OR: 1,07 p=0,004) and greater extent of AA in SSFP cine and spoiled LGE sequences (OR: 1,01 p<0,001/OR: 1,02 p=0,04). Data regarding reproducibility are shown in the table.

Intraclass correlation of CMR data

	Interobserver intraclass correlation		Significance	Intraobserver intraclass correlation		Significance
LVEF	0,77	0,35–0,99	0,002	0,9	0,58–0,97	<0,001
RVEF	0,44	0,38–0,87	NS	0,95	0,61–0,99	0.002
LVEDV	0,94	0,79–0,91	<0.001	0,98	0.83–0,99	<0.001
RVEDV	0,73	0,05–0,95	0,019	0,96	0,64–0,95	P=0,001

LVEF, left ventricle ejection fraction; RVEF, right ventricle ejection fraction; LVEDV, left ventricle end diastolic volume; RVEDV, right ventricle end diastolic volume.

Conclusions: CMR could be performed with excellent image quality in 56% of patients. Reproducibility was good excluding RVEF data. The scan was considered ineffective in 20% of patients and this was significantly associated with ICDs, greater mass and volume of device and greater AA in cine SSFP and spoiled LGE sequences.

P4010 | BEDSIDE
Relation between site of origin of monomorphic ventricular arrhythmias and myocardial tissue characteristics in non-ischemic left ventricular heart disease

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Purpose: Left Ventricular (LV) scar is a potential substrate for Ventricular Arrhythmias (VAs). Analysis of QRS morphology on ECG during VA has been demonstrated to accurately identify the site of origin of monomorphic VA among pts with ischemic LV scar. Aim of the present study was to investigate the relation between site of origin of monomorphic VA and myocardial tissue characteristics among pts with non-ischemic LV structural heart disease.
Methods: 26 consecutive pts (96% males, mean age 48±13 years) with

monomorphic VAs (i.e. frequent ventricular premature beats, recurrent non-sustained and sustained ventricular tachycardia) and non-ischemic LV structural heart disease were included in the study. Non-ischemic LV structural heart disease was defined on the basis of 1) cardiac Magnetic Resonance Imaging (cMRI) evidence of LV Late Gadolinium Enhancement (LGE), a surrogate of scar, with non-ischemic (intramyocardial or subepicardial) distribution and 2) absence of significant coronary artery disease on exercise stress testing, multi-slice computed tomography or invasive coronary angiography. Site of origin of VA was identified analysing QRS morphology on ECG during VA as previously suggested by Segal and colleagues (J Cardiovasc Electrophysiol. 2007;18:161-168). The relation between site of origin of VA and myocardial tissue characteristics as evaluated by cMRI was investigated.
Results: Mean LVEDV and mean RVEDV were 96±24 ml/m^2 and 80±13 ml/m^2, respectively. LV dilatation was observed in 10 (38%) pts; none had RV dilatation. Mean LVEF and mean RVEF were 57±12% and 67±8%, respectively. Reduced LV and RV systolic function were observed in 14 (54%) and 1 (4%) pts, respectively. Mean number of LV segments with LGE per patient was 4.8±3.8. A total of 127 (28%) LV segments showed LGE; 42 LV segments had intramyocardial LGE and 71 LV segments had subepicardial LGE. Site of origin of VA was located at basal- or mid-posterior LV wall in 17 (65%) pts, posteroapical LV wall in 4 (15%) pts, mid-anterior LV wall in 1 (4%) patient and basal- or mid-septum in 4 (15%) pts. Site of origin of VA matched with the presence of LV LGE in 22 (85%) pts. At the site of origin of VA, LGE was intramyocardial in 6 and subepicardial in 16 pts.
Conclusions: In patients with non-ischemic LV structural heart disease, VAs usually originate from scar zone. In these patients, identification of scar using cMRI with LGE technique may be of value for mapping and ablation procedures.

P4011 | BEDSIDE
Evaluating the impact of the revision of the taskforce criteria for the diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC)

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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically determined cardiomyopathy associated with ventricular arrhythmia and sudden cardiac death. In 2010 the criteria used to diagnose the condition were revised. The aim of this study was to investigate the impact of the 2010 revisions on the prevalence of ARVC criteria determined by cardiac magnetic resonance (CMR) imaging in a consecutive series of patients with a clinical suspicion for ARVC.
Methods: Retrospective analysis was performed on the CMR scans of all patients referred with a clinical suspicion of ARVC between 2011 and 2013 at a single regional centre. Presence or absence of major and minor CMR task force criteria (TFC) was determined using both the original and the revised criteria. Patient records were also reviewed to determine the prevalence of non-imaging criteria.
Results: 401 consecutive patients were included (mean age 41.2±16.8 yrs, 55% male). 216 patients (53.9%) satisfied at least one non-imaging criterion for a diagnosis of ARVC. Utilising the original criteria, 16 patients (3.9%) satisfied major CMR criteria compared with 12 patients (3%) with the revised criteria (p=0.42).
Of the 16 patients initially classified as having major CMR criteria in the original guidelines 4 (25%) did not fulfil any of the revised TFC. Using the original criteria, 115 patients (28.7%) satisfied minor CMR criteria compared with 18 patients (4.5%) with the revised TFC (p<0.001); 97 patients (84.3%) with minor original TFC did not have any of the revised TFC. This discrepancy was primarily due to the exclusion of regional wall motion abnormalities in the absence RV dilatation as a criterion, in the revised TFC.
Using the full original TFC, 13 patients (3.2%) satisfied criteria for definite ARVC, 22 (5.5%) for borderline ARVC and 72 (18%) had possible ARVC. When the full revised TFC were used 17 patients (4.2%) satisfied criteria for definite ARVC, 20 (5%) for borderline ARVC and 72 (14.5%) had possible ARVC.
Application of the revised CMR TFC significantly improved the positive predictive value for combined CMR major and minor criteria in diagnosing ARVC from 8.4% to 40%. Despite this improvement in specificity, CMR's sensitivity for the diagnosis of ARVC was not significantly reduced (70.6% vs. 84.1%).
Conclusion: CMR plays an important diagnostic role in the evaluation of patients with possible ARVC. The revision of the ARVC task force imaging criteria has improved CMR's accuracy in the diagnosis of the condition.

P4012 | BEDSIDE
Computed tomography versus magnetic resonance for characterization of left atrium anatomy before 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 by computed tomography (CT) or magnetic resonance (MR) for the characterization of left atrium (LA) anatomy before the procedure. However, no comparative data between CT and MR have been described regarding to the impact of different imaging modality. The aim of this study is to compare the procedural characteristics, overall radiation exposure and clinical outcomes between RFCA guided by image integration with CCT versus CMR.
Methods and materials: Four hundred consecutive patients with drug-refractory paroxysmal or persistent AF were randomized to CT (Group 1; N: 200; mean age 61.6±10.9 yo; male:155) or MR (Group 2; N: 200; mean age 59.7±10.4 yo; male:166) for evaluation of LA before RFCA. CT was performed with 64-slices scanner (Discovery CT 750HD, GE Healthcare, Milwaukee, WI) and MR was performed with 1.5-T scanner (Discovery MR450, GE Healthcare, Milwaukee, WI) using a non-triggered contrast enhancement magnetic resonance angiography sequence. All patients were subsequently treated by image integration-supported RFCA. Left atrium diameter, left atrium volume, variant of pulmonary veins anatomy, pulmonary veins ostial dimensions, procedural characteristics, overall radiation exposure and rate of AF recurrence 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 (557±302 vs. 523±265 days, respectively, p:0.24). Group 1 showed higher LA volume versus group 2 (117±46 vs. 101±40 mL, p<0.001). The procedural characteristics [fluoroscopy time (32.6±16.0 vs. 35.0±16.6 min, p:0.15); procedural duration (180.2±59.0 vs. 182.8±53.5, p:0.65, pulmonary veins identified (4±0.1 vs. 3.9±0.2, p:0.08); pulmonary veins targeted (3.9±0.4 vs. 3.9±0.4, p: 053); pulmonary veins isolated (3.9±0.4 vs. 3.9±0.4, p:0.9)] and the rate of AF recurrence (29% vs. 26%, p:0.5) were similar between the two groups. Group 1 showed a higher overall cumulative radiation exposure (40.4±23.7 vs. 32.8±23.5, p<0.005). and LA volume measured by MR was the most robust independent predictor of AF recurrence at multivariate analysis [(HR: 1.08 (1.01-1.15), p:0.02]
Conclusions: CT and MR appear to provide similar information before RFCA. However, MR integration-supported RFCA procedure seems to be associated with a lower overall cumulative radiation despite similar outcome in comparison with CT-guided RFCA.

P4013 | BEDSIDE
Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a MRI study

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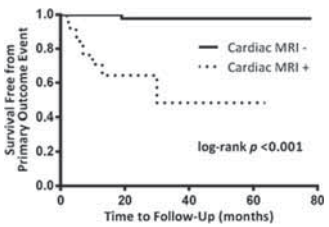
Purpose: Routine diagnostic work-up occasionally does not identify any abnormality among patients with monomorphic ventricular arrhythmias of left ventricular origin (VAs-LV). Aim of the study was to investigate the value of cardiac magnetic resonance imaging (cMRI) for the diagnostic work-up and prognostication of these patients.
Methods: 46 consecutive patients (65% males, age 44±15 years) with monomorphic VAs-LV and negative routine diagnostic work-up were included. 74 consecutive patients (60% males, age 40±17 years) with apparently idiopathic monomorphic VAs of right ventricular origin (VAs-RV) served as control group. Both groups underwent cMRI study using a 1.5 Tesla scanner to assess LV and RV function, myocardial fatty replacement, myocardial edema and necrosis/fibrosis and were followed-up for 23±20 months. Primary outcome event was an arrhythmic composite end-point of sudden cardiac death (SCD) or aborted SCD.
Results: The 2 groups did not differ in age (p=0.14) and gender (p=0.57). No significant difference was observed between patients with VAs-LV and VAs-RV regarding biventricular volumes and systolic function. cMRI demonstrated myocardial structural abnormalities in 19 (41%) patients with VAs-LV vs. 4 (5%) patients with VAs-RV (p<0.001). Primary outcome event occurred in 9 patients; 8 of these patients had myocardial structural abnormalities on cMRI (Figure). Myocardial structural abnormalities on cMRI were significantly and independently related to the primary outcome event (HR 28.9, 95%CI 3.4-247.0; p=0.002).



Conclusions: Myocardial structural changes are detected by cMRI in a non-negligible proportion of patients with apparently idiopathic monomorphic VAs-LV and are associated with worse outcome. cMRI should be implemented in the routine diagnostic work-up of these patients.

MYOCARDITIS AND PERICARDITIS: NEW DEVELOPMENTS

4037 | BEDSIDE
Immunosuppressive therapy in virus-negative inflammatory lymphocytic cardiomyopathy - who benefits most?

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Introduction: Immunosuppressive therapy appears to be beneficial in patients with virus-negative lymphocytic inflammatory cardiomyopathy. It was the aim of this single-center study to identify potential baseline characteristics that may predict positive response to therapy.
Methods: Virus-negative inflammatory cardiomyopathy was diagnosed in endomyocardial biopsies of 93 patients. Cortison and azathioprin for six months in addition to standard heart failure therapy was started in 79 patients. Endomyocardial biopsy and hemodynamic evaluation was repeated at six-months follow-up. Patients were classified as responders if NYHA class improved by at least one class or remained stable in class I and serum NT-proBNP dropped by $\geq$30%.
Results: At this stage complete 6-months follow-up is available in 61 patients (age: 46$\pm$11.3, female: 34%, median disease duration: 3 months [0.25-42]). Compared to baseline we observed a significant improvement in NYHA class (I/II 59%, III/IV 41% before vs I/II 98%, III/IV 2% after therapy, $p<0.001$) and NTproBNP (852 ng/l [49-6118] vs 276 ng/l [45-8099], $p<0.001$) in the entire cohort. Also left ventricular ejection fraction (LV-EF) (29$\pm$12% vs 44$\pm$12%, $p<0.001$) and left ventricular enddiastolic volume index (LVEDVI) (121$\pm$39 ml/m^2 vs 107$\pm$36 ml/m^2, $p<0.001$) improved, as did cardiac index (2$\pm$0.6 l/min/m^2 vs 2.4$\pm$0.6 l/min/m^2, $p<0.001$) and pulmonary capillary wedge pressure (15mmHg [4-42] vs 11mmHg [6-26], p=0.001).
Responders (n=35, 57%) were characterized by higher NYHA class (III/IV 54% vs 23%, p=0.014), higher NTproBNP levels (1387 ng/l [53 - 6118] vs 406 ng/l [49 - 5329], p=0.018), lower LV-EF (26$\pm$11% vs 34$\pm$13%, $p<0.001$) and higher leucocytes (7.7 G/l [4.4 – 15.4] vs 6.4 G/l [4.2 – 12.6], p=0.007) at baseline. Interestingly, no significant differences were found between groups with regard to hemodynamics, LVEDVI and the extent of myocardial inflammation/fibrosis. Standard heart failure therapy was comparable between groups at baseline and 6-months follow-up. Multivariate logistic regression analyses including disease duration, LV-EF, LVEDVI, CI, leucocytes, CD14 positive lymphocytes/mm^2 revealed high leucocytes and low LV-EF at baseline as independent predictors of positive response to therapy.
Conclusion: From our data it appears that a positive response to immunosuppressive therapy in virus-negative lymphocytic inflammatory cardiomyopathy is more likely in patients with higher leucocytes and low LV-EF at baseline.

4038 | BEDSIDE
Vasculotropic parvovirus infection impairs outcome in inflammatory cardiomyopathy

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Purpose: To evaluate outcome of patients with virus associated inflammatory cardiomyopathy. Parvovirus B19 infections are acquired by majority in the childhood and persist lifelong within bone marrow precursor cells and the vascular endothelium in a high percentage of the general population. Because many infected patients remain asymptomatic, the clinical relevance of erythrovirus detection in myocardial tissue has remained doubtful.
Methods: The study group comprised of 423 consecutive parvovirus positive and 177 virus negative patients (441 man, mean age 53.0$\pm$12.6 years) presenting with symptomatic heart failure and global systolic left ventricular dysfunction below 45% (mean EF 29.5$\pm$8.9%). The patients who clinically presented as suspected myocarditis in the past (n=310) or dilated cardiomyopathy (n=290) were followed 60 months to compare outcome with respect to biopsy-based quantitative information on myocardial inflammation and virus infection.
Results: The frequency of virus positive patients was not different between patient groups with clinically suspected myocarditis and DCM (p=0.661). Biopsy analyses confirmed myocarditis and inflammatory cardiomyopathy in 37.6% and 27%, respectively with comparable numbers of inflammatory cells in virus negative and positive patients. Five year survival was impaired in B19V positive patients if infiltrating CD3-positive lymphocytes exceeded 10 cells/mm^2 ($p<0.001$) whereas mortality was not associated with elevated inflammatory cells in virus negative patients (p=0.837).
Conclusion: Inflammatory cardiomyopathy in the presence of a vasculotropic B19V infection is associated with a higher mortality than in patients with non infectious myocardial inflammation. This suggests that endothelial cell infection may constitute a cofactor that aggravates inflammatory cell associated myocardial injury and outcome.

4039 | BEDSIDE
18F-FDG PET and high-sensitivity troponin T as prognostic markers in giant cell myocarditis

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Purpose: Introduction of potent immunosuppressive therapy has improved the prognosis of giant cell myocarditis (GCM). In our recent study transplant-free survival at 5 years was 52%. The purpose of this study was to identify predictors of poor outcome in GCM.
Methods: We collected data from 35 patients with histologically verified GCM treated from May 1991 to November 2013. Eight patients were diagnosed postmortem or from explanted hearts. We analyzed 18F-FDG PET and cardiac MRI studies in all patients. We graded the rest perfusion and 18FDG-uptake based on AHA 17 segment model. A segment with a clear mismatch, defined as perfusion defect and increased 18FDG-uptake, was considered abnormal. MRI chamber volumes, wall thickness, segmental wall motion, edema-analysis and late-enhancement gadolinium uptake pattern were analyzed.
Results: Mean age at symptom onset was 49 (range 14-69). There were 12 males (34%) and 23 females (66%). Mean first measured ejection fraction was 39% (range 5-72). Patients were followed for 20,5$\pm$25,8 months (range 0,03-80,4, median 9,8). Adverse cardiovascular endpoints included 3 deaths, 8 transplants and 15 ventricular arrhythmias requiring intervention.
Initial symptoms, ejection fraction, age or sex did not predict cardiovascular events. Hs-TnT values were measured in 20 patients. Patients were divided into two groups based on their response to immunosuppressive therapy. In 13 patients, immunosuppressive therapy reduced hs-TnT to 15 ng/l or less; 5 of them (38%) had an adverse cardiovascular event (5 ventricular arrhythmias). In 7 patients hs-TnT remained $>$15 ng/l despite immunosupression and 6 of them (86%) had an adverse cardiovascular event (2 deaths, 3 transplantations and 1 ventricular arrhythmia) (p=0,008, log-rank).
Ten patients underwent 18F-FDG PET. The 4 patients that had an abnormal perfusion-18F-FDG uptake pattern in $\geq$1 segment of the left ventricle had an adverse cardiovascular event (3 ventricular arrhythmias and 1 transplantation). In 6 patients without the mismatch, only 2 had an adverse cardiovascular event (2 ventricular arrhythmias) (p=0,025, log-rank). Perfusion-18F-FDG mismatch in $\geq$1 segment was associated with more adverse events (mean 4,5 vs. 0,3 per patient, p=0,019).
Ten patients underwent cardiac MRI. Neither late enhancement nor other measured parameters were significantly associated with adverse cardiovascular events.
Conclusions: Hs-TnT is a promising marker of treatment response in GCM. The presence of abnormal perfusion-18F-FDG uptake pattern is associated with adverse cardiovascular events.

4040 | BENCH
Role of calpain in Coxsackievirus B3-induced myocarditis

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Purpose: To observe the role of calpain in the pathogenesis of Coxsackievirus B3 (CVB3) induced myocarditis via overexpressing the specific endogenous calpain inhibitor calpastatin in the myocardium.
Methods: Calpastatin transgenic mouse was injected intraperitoneally with CVB3 to establish the viral myocarditis model. At the harvest time, heart weight/body weight ratio were calculated, HE staining of the heart tissue sections were analyzed and the pathological score was calculated and compared. The peripheral myocardium injury biomarkers of CK-MB and cTnI were detected.CVB3 capsid protein VP1 and virus titers were detected using molecular biology method. Fibrogenic agents of Smad3, MMP2 were detected and analyzed. The expression alteration of IL17, IFNγ and perforin were observed.
Results: The calpain activity in the heart tissue of Tg-CAST mouse was suppressed significantly. Comparing with the wild type control, in the CVB3 infected Tg-CAST mouse, the heart weight/body weight ratio decreased significantly, the inflammatory infiltration attenuated accompanied by a decrease in the pathologic score and lower levels of peripheral CK-MB and cTnI concentrations. VP1 and virus titers in the myocardium of Tg-CAST mouse decreased significantly indicating that the virus replication was suppressed. Myocardium fibrosis agent of smad3 showed a decrease in expression, as well as the MMP2 expression and activity. Similarly, the inflammatory factors of IL17, IFNγ and PFN were reduced in the myocardium indicated by both the WB detection and IHC methods.
Conclusions: Calpastatin overexpression showed significant heart protection effect, indicating the role of calpain in the pathogenesis of viral myocarditis. Further studies showed that calpain activity was correlated with CVB3 replication, myocardium fibrosis and inflammation infiltration, which highlights the potential of calpain as a novel target of viral myocarditis treatment.

4041 | BENCH
Roles of miRNA21 in Coxsackievirus B3 (CVB3)-induced cardiac microvascular endothelial cells apoptosis via modulating the target gene of PDCD4

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Purpose: To investigate the role of miRNA21 in Coxsackievirus B3 (CVB3)-induced cardiac microvascular endothelial cells (CMVECs) apoptosis via targeting the programmed cell death protein (PDCD4) gene.
Methods: 1. CMVECs were infected with CVB3 and then the differentially expressed miRNAs were screened using miRNA chips and identified with RT-PCR. The target genes were predicted via searching data bases of miRanda and TargetScan.
2. After transfection of miRNA21 mimics, miRNA21 inhibitors or sham control respectively, the apoptosis was observed via Annexin V/PI double staining. Caspase3 activity was assayed. PDCD4 protein expression was detected.
3. Co-transfect the CMVECs with the recombinant plasmids PGL3-PDCD4-3'UTR-WT or PGL3-PDCD4-mut3'UTR and miRNA21mimics together and detect the luciferase activity.
4. To observe the effect of PDCD4 on AP1 transcription activity, construct plasmids overexpressing PDCD4 and synthesize PDCD4 siRNA, then co-transfect CMVECs with AP-1-luciferase plasmid and PDCD4 gene or PDCD4 siRNA followed by luciferase reporting gene activity assays.
Results: Screened with miRNA chips and identified with RT-PCR, in CMVECs infected with CVB3 for 48 hours, miRNA21 was upregulated by 3.65 folds comparing with the normal controls. After searching in databases of miRanda and TargetScan and systemic literary review, PDCD encoding gene was predicted as the target gene.
Comparing with the normal controls, apoptosis rate, caspase3 activity were enhanced in CMVECs infected with CVB3 or transfected by miRNA21 mimics ($p<0.05$), while PDCD4 protein expression was downregulated ($p<0.05$). The CVB3-infected and miRNA 21inhibitor-transfected CMVECs showed the opposite outcomes with apoptosis and caspase3 activity suppressed and PDCD4 expression upregulated ($p<0.05$); The luciferase activity was decreased significantly in CMVECs co-transfected with PGL3-PDCD4-3'UTR-WT and miRNA21mimics, while no statistical difference was achieved in CMVECs co-transfected with PGL3-PDCD4-3'UTR-WT and miRNA21mimics; AP-1-luciferase activity was downregulated by 0.25 folds in PDCD4-overexpressing CMVECs and was up-regulated by 2.2 folds in PDCD4-siRNA-transfected CMVECs; The combining activity of AP1 and DNA was decreased by 30% in CMVECs overexpressing PDCD4 gene.
Conclusion: In CVB3 infected CMVECs, miRNA21 expression is upregulated and then inhibits PDCD4 gene transcription specifically by combing with the PDCD4-3'UTR site, which leads to AP1 transcription activity increasing and CMVECs apoptosis enhancement.

4042 | BEDSIDE
Gender and age differences in occurrence and in-hospital mortality of pericarditis

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Purpose: It is commonly thought that the risk of developing pericarditis is similar in men and women, but few epidemiological studies have been reported on pericarditis. Effect of age on susceptibility and outcome of pericarditis is also largely unknown.
We studied gender and age differences in pericarditis using a large nationwide hospital registry.
Methods: Data of all hospital treatment periods caused by pericarditis during 9.5 years (May 2000 - October 2009) were collected from national Finnish registry (FHDR) including all medical and cardiological admissions (1.7 million) of patients aged $\geq$16 years in 29 hospitals nationwide. Post-cardiotomy and post-myocardial infarction syndromes were excluded.
Results: Study period included 2274 admissions caused by pericarditis. Pericarditis patient was more commonly male (62.3% of patients; 95%CI 59.1-65.6%) than female (37.7%; 95%CI 35.2-40.3%) with age-adjusted relative risk of 1.65 (95%CI 1.52-1.80, $p<0.0001$). Median age of all pericarditis patients was 56 years (range 16-98 years). Pericarditis occurred most commonly at the age of 56-65 years in both genders. Of all medical hospital admissions 0.024% (95%CI 0.016-0.035%) were caused by pericarditis. Admissions were more commonly caused by pericarditis in men (RR 1.45; 95%CI 1.33-1.58, $p<0.0001$) and in younger patients (estimated decline of proportion 23% per 10-year increase of age; 95%CI 22-25%, $p<0.0001$). Gender did not affect the proportion of acute (59.9% of admissions) or chronic (36.2%) pericarditis, but chronic pericarditis became more common with increasing age (by estimated 27% per 10-year increase of age; 95%CI 23-32%, $p<0.0001$). Gender did not influence the proportion of idiopathic/viral (87.0% of patients), bacterial (1.4%) or rheumatic fever (1.5%) etiology, but systemic disease (2.9%) caused pericarditis more commonly in women (RR 4.04; 95% 2.35-6.96, $p<0.0001$). Total in-hospital mortality of pericarditis was 2.6% (95%CI 2.0-3.4%). Gender did not affect mortality, but mortality increased notably with age (RR 2.56; 95%CI 1.95-3.35 per 10-year increase of age, $p<0.0001$) and was higher in patients with chronic pericarditis (RR 4.55; 95%CI 1.08-19.15, $p<0.05$).
Conclusions: Pericarditis appears to be more common in men. Both genders are affected most commonly at the age of 56-65. Gender does not affect in-hospital mortality of pericarditis, but mortality increases with age and with chronic pericarditis.

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Interleukin-8 as a predictor of acute idiopathic pericarditis recurrences. A pilot study

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Purpose: Idiopathic recurrent pericarditis (IRP) is a frequent and troublesome complication of acute pericarditis with adverse impact on patient's quality of life. Since few clinical or laboratory parameters capable of predicting recurrences are available, we sought to investigate the possible role of pro-inflammatory cytokines towards this direction.
Methods: Twenty five consecutive patients with acute idiopathic pericarditis (AIP) were included in the study. Demographic, clinical, imaging and laboratory data were collected for each patient at baseline. Additionally several serum pro-inflammatory cytokines were measured by a multiplex assay (namely serum TNF-α, IFN-γ, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-17, IL-18, and IL-1β levels) using flow cytometry. Moreover, 20 age-matched healthy individuals were recruited as controls. Patients were followed prospectively for 20 months and the appearance of recurrences was recorded. In addition, a number of baseline parameters were examined as potential predictors for recurrent disease as well.
Results: After exclusion of 2 patients (8%) with secondary causes of pericarditis, 23 patients with AIP were included and followed prospectively. Among the latter patients 9 (39%) developed IRP, 35$\pm$5 days after the index episode. Patients with IRP were younger (mean age 41$\pm$16 years) and received less frequently colchicine (11%), compared to patients with no recurrent pericarditis (NRP) (55.8$\pm$16 years, p=0.04 and 50%, p=0.05, respectively). Among the different cytokines studied at baseline, interleukin-8 (IL-8) was more commonly detected among patients with IRP (4/9, 44%) compared to those with NRP (1/14, 7%, p=0.03) and controls (2/20, 10%, p=0.03). Moreover, there was a significant association between serum IL-8 detection and development of IRP (Spearman's ρ=4.41, p=0.035).
Conclusions: In this investigation, younger age, no treatment with colchicine and interestingly, detection of serum IL-8 in the sera of patients with AIP, were associated with disease recurrence.

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Post pericardiotomy syndrome in a large subgroup of the DECS study

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Purpose: To identify whether dexamethasone influenced the incidence and character of post pericardiotomy syndrome (PPS) after cardiac surgery. PPS is a common complication of cardiac surgery and is associated with increased morbidity.
Methods: We performed a blinded post hoc analysis of a large subgroup (n=822) of patients undergoing valvular surgery with or without CABG who were included in the DECS trial. The DECS trial was a large randomised trial investigating the effect of a single intraoperative high dose dexamethasone (1 mg/kg) on a composite endpoint of adverse cardiac events in patients undergoing cardiac surgery with use of cardiopulmonary bypass. In the current substudy, all medical charts, X-rays and echocardiograms were reviewed. PPS was diagnosed if two out of five listed symptoms were present: Unexplained fever $>$72 hours postoperatively, pleuritic chest pain, pericardial or pleural friction rub, new significant pleural effusion, new significant pericardial effusion. We used semi-quantitative scales to record pericadial en pleural effusions. Readmissions for PPS and interventions related to PPS (evacuation of pleural or pericardial effusions), were recorded as well.
Results: The incidence of PPS was 14.5%. A diagnosis of PPS was strongly correlated with increased length of hospital stay: 13 (9-18) versus 11 (8-14) days (median (IQR), $p<0.01$). 24.5% of PPS affected patients had a PPS related readmission or complication. The incidence of PPS was 13.5% in the dexamethasone group versus 15.5% in the placebo group (RR 0.88, CI 0.63-1.22, p=0.43). There were no differences between groups for the individual components of PPS, except that we found a higher percentage of patients with no pleural effusions in the dexamethasone treated group. We were not able to identify patients with "pleuritic chest pain", since this was not recorded specifically enough to distinguish it from normal postoperative pain and all patients had strong pain relieve regimes. The percentage of PPS related complications was not significantly different between dexamethasone and placebo treated individuals.
Conclusion: Prophylactic dexamethasone treatment did not prevent occurence of PPS or PPS related complications in patients undergoing valvular surgery with or without CABG.

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Tuberculous pericarditis: eighteen-year experience in a tertiary hospital

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Objectives: In the developed world tuberculous pericarditis (TP) is a rare clinical form of the disease and its management and prognosis are problematic. The aim was to evaluate the epidemiological and clinical spectrum of TP and the risk of constrictive pericarditis (CP).
Methods: A retrospective analysis of TP in our center from January 1995 to December 2013 is presented. Diagnosis was made based on clinical, microbiological, fluid analyses and histological data.
Results: Of a total of 1632 patients with tuberculosis, 18 patients had TP (1.1%). The mean age was 54±16.8 years, and 13 (72.2%) were men. Three of 18 patients (16.7%) were immigrants. Positive tuberculin skin test (TST) was positive in 8 patients (44.4%). No patients had HIV infection. At the time of diagnosis, 11 (61.1%) patients presented fever, 4 (22.2%) had unexplained weight loss, 12 (66.7%) had symptoms and signs of pericarditis and 4 patients (22.2%) had tuberculous disease in other locations. In 5 patients (27.7%) the diagnosis was made after pericardial fluid analysis. Median ADA value in pericardial fluid was 34 U/L (range 13-227 U/L).In 4 cases the diagnosis was confirmed microbiologically (1 from a biopsy and 3 from the pericardial fluid). In 5 patients underwent histopathological diagnosis. In 8 patients (44.4%), the diagnosis was based on clinical suspicion (positive TST and recent contact with a person with active tuberculous disease).
The therapy most frequently used was a combination of three drugs (13, 72.2%). Steroids were used in 11 patients (61%). Outcome was favorable in all patients but one, who developed a CP and died subsequently.
Conclusions: Diagnosis of TP is challenging. The evolution to a constrictive form is not so common if diagnosis is accurate, and treatment is established promptly.

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Analysis of the incidence and management of cardiac tamponade in 12.700 invasive examinations and interventional procedures

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Introduction: Cardiac tamponade is a rare but life-threatening complication of invasive procedures and percutaneous coronary intervention (PCI).
Methods: We performed a single-center analysis of the incidence of procedure-related cardiac tamponades during a 4-year period (2008-2011) in our university heart center. The following procedures were included in this study: diagnostic and therapeutic heart catheterization, electrophysiological examination and therapy (ablation, PVI) and electric device implantation (pacemaker, ICD, CRT, CCM). All cardiac tamponades had been detected in the catheterization lab by echocardiography and fluoroscopy and had been treated by immediate pericardiocentesis.
Results: During the 4-year period 12.762 invasive heart examinations and interventions, including 3450 PCI's, electrophysiologic examinations and ablations as well as 1686 device implantations, had been performed.
In total, 18 patients developed procedure-related cardiac tamponades (0.14%). 7 cardiac tamponades were detected after PCI (0.2%/PCI's; 0.05%/ total procedures). During device implantation 7 tamponades were recognized (0.4%/device implantations; 0.05%/total procedures). Rare causes of cardiac tamponade were: Perforation of the left ventricle after retrograde passage of severe aortic stenosis (N=1; 0.008%), after left ventricular biopsy (N=1; 0.008%), 1 after pericardiocentesis due to postsurgical pericardial effusion, and after PVI (N=1; 0.008%). In 3 patients autotransfusion was performed, in 3 patients a Graft-Stent was implanted due to coronary perforation and 6 of 17 patients had to treated by cardiac surgery (e.g. due to pacemaker lead perforation). The primary success rate of pericardiocentesis with hemodynamic resuscitation and stabilization of the patient in the cath lab was 100%. The mean amount of fluid, which has been evacuated out of the pericardial space, was 723±487 ml. In-hospital mortality after cardiac tamponade was 11% (2 of 18 patients), and was related to referral for emergent surgical treatment because of left ventricular perforation by pacemaker leads.
Conclusion: Rapid and successful therapy of the life-threatening complication of cardiac tamponade is the precondition for the performance of invasive and interventional procedures in modern cardiology. The incidence of cardiac tamponade (0.14%) in our university heart center was below the previously described complication rate of up to 0.3%.

CATHETER ABLATION – OLD SUBSTRATES, NEW STRATEGIES

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Characterization of the endocardial component of ventricular tachycardia reentrant circuits by postpacing interval electroanatomical mapping

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Reentry is the most common mechanism of monomorphic ventricular tachycardia (VT) in patients with structural heart disease (SHD). The reentrant circuit usually has a protected isthmus of slow conduction (ISC) which can be mapped by both activation and entrainment techniques and finally validated by ablation. However, the knowledge of other parts of the circuit is more limited.
Methods: 28 VTs in 27 consecutive patients (64,5±11,6 years, 85,7% male) with SHD and ablation attempt of sustained VT were prospectively enrolled in this study. Geometrical reconstructions of the left (LV), right (RV) or both ventricles were obtained by a 3D electroanatomical system. VT induction and entrainment for postpacing interval (PPI) mapping was attempted in all. The postpacing interval values were color-coded on the ventricular geometry in order to obtain 3D maps of the endocardial surfaces. VT activation and voltage electroantomical maps were also obtained from the data collected during geometrical reconstruction and entrainment.
Results: Most patients had ischemic cardiomyopathy (75%) and LV dysfuntion (ejection fraction 38,8±35,6%). 3 patients (3 VT) were withdrawn from the study because no VT or multiple and/or intolerant VTs were induced. A PPI map of at least 15 pacing sites (27,7±14) was obtained in 25 VTs in the remaining 24 patients. All VTs except 4 (4 patients) had endocardial areas with PPI matching (difference shorter than $<$5 ms) the VT cycle length ("PPI-0"). The endocardial surface with PPI-0 and with scar voltage values ($<$0.5 mV) were 28,6±45,21 cm^2 (range 0-229,3) and 15,3±16,5 cm^2 (range 0,4-61,5) respectively. There was a mismatch between the reentrant circuit location define by PPI and activation maps in 12 VTs. 5 VTs had a perimitral valve disposition of the circuit and the endocardial component of the circuit was confined within 1 (9 VTs), 2 (10 VTs), 3 (1 VTs) and 4 (5 Vts) ventricular walls (anterior, septal, inferior, lateral, or apical). The VT was successfully ablated at the endocardium by focal radiofrequency application in 20 VTs (80%) and in all of them the ISC (local activation preceding $>$60 ms the QRS complex onset) was located within the PPI-O area. The VT was successfully ablated at the epicardium by focal radiofrequency application in 5 patients (20%).
Conclusions: PPI maps allow precise determination of the endocadial component of reentrant VT circuits in patients with SHD. These circuits may have complex tridimensional dispositions around valve orifices or with components involving both the endo and epicardium

4052 | BEDSIDE
Catheter ablation of idiopathic ventricular tachycardia without the use of fluoroscopy

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Catheter ablation (CA) employing fluoroscopy is associated with a definite radiation risk for patients (Pts) and personnel. We report our experience of CA procedure for idiopathic ventricular tachycardia (VT), using electroanatomic mapping system (EAM) in conjunction with intracardiac echocardiography (ICE) without using fluoroscopy.
Methods: Informed consent was obtained and antiarrhythmic medication was discontinued before CA in all Pts. All procedures were performed with conscious sedation. A 3.5-mm externally irrigated radiofrequency (RF) ablation catheter (C) was advanced to the inferior vena cava (IVC) under EAM guidance (CARTO3). 3-D geometric contours of the IVC, RA and coronary sinus (CS) were created by sweeping the C tip. Subsequently 3 C were positioned respectively at His area, CS (if required) and RV using the 3D shell of RA. RV stimulation was performed to induce or to sustain VT. Isoproterenol infusion up to 5γ/min was used if necessary. Then a 10-Fr ICE C was inserted and sequential ICE contours to create a 3D map of the RV and/or the LV were acquired. Mapping was performed during VT or PVC using the 3D shell obtained with ICE focusing on the area of interest. Left sited VT were mapped with retrograde trans aortic approach. Local earliest activation, QS deflection in the unipolar derivation, optimal pace mapping or abnormal Purkinje potentials were used to guide ablation. RF energy was delivered up to 35 W, during VT or PVC. After ablation, isoproterenol was administered to assess for PVC/VT induction.
Results: 19 Pts (16 males, mean age 39.1 yrs) presenting idiopathic VT were treated without fluoroscopy. Twelve Pts presented with outflow tract PVC/VT (8 right, 4 left sited), 3 Pts with idiopathic left (fascicular) VT, 2 Pts with peritricuspidal PVC/VT, 1 with peri-mitral PVC/VT, 1 with left free-wall VT. The mean procedure time was 190±38 min. RA reconstruction and C positioning required a mean of 13±3 minutes. 3D shell of the ventricles were reconstructed with mean of 55±10 ICE contours, with a mean time of 24±8 min. Focus mapping and ablation required a mean of 38±18 min, acute success was achieved in all Pts. C manipulation was performed using multiple EAM projections and under direct ICE

visualization and without any need of fluoroscopy in all Pts. No complication occurred in any Pts. VT recurrences was documented in 2 Pts during a mean follow up of 16±4 months.
Conclusion: Fluoroless ablation of idiopathic VT is feasible, effective and safe using EAM and ICE, with a reasonable prolongation of procedure time

4053 | BEDSIDE
Outcomes of ablation of ventricular arrhythmias with the 56 hole open-irrigation radiofrequency catheter; a two center international experience

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Introduction: No data has been published on the use of the 56 hole, open irrigation, 3.5mm tip, radiofrequency (RF) catheter in ablation of ventricular arrhythmias (VA).
Methods: Between June 2011 and November 2013, we identified 242 patients who underwent 261 VA ablation procedures. Power was limited to a maximum of 30-40W (up to 50W in septal locations) with saline flow rates between 8-17 ml/min. Acute procedural outcomes and 30-day major complications were reported.
Results: A total of 261 ablations: 131 ventricular extrasystole (VE) and 130 VT ablations were undertaken. Indications included symptoms (n=144), ICD shocks (n=58) VT storm (n=21), reduced LVEF (n=30), and primary prevention of ICD shocks (n=8). 71% were males, mean age was 59±14, LVEF 44±15.4%. 82 patients had no structural heart disease, 97 had ischemic, and 63 had non-ischemic cardiomyopathy. 108 patients had ICDs; 64 for primary prevention, and 45 CRT-D. 81 patients (31%) had ≥1 previous ablation (range 1-5). A total of 402 VAs were targeted (248 LV, 77 RVOT, 47 LVOT, 30 RV) via an endocardial (n=236), epicardial (n=23) and surgical approach (n=2). The mean procedural time was 235±97 minutes. Acute procedural success was achieved in 237 (91%) patients; with 18 unsuccessful and 6 partially successful ablations. 15 (5.7%) major complications occurred within 30 day. Tamponade occurred in 4 (1.5%) patients: 3 occurred while mapping the RVOT/LVOT prior to ablation. One patient with history of fast pathway ablation developed heart block prior to RF application with catheter manipulation. Two (0.8%) patients suffered coronary artery injury requiring acute stenting. One patient had a small stroke 22 days following ablation. One suffered transient phrenic nerve palsy following epicardial ablation. Three (1.1%) patients developed heart failure requiring intubation or readmission. Three deaths were recorded (1.1%) due to advanced heart failure at 3, 19, and 29 days post procedure. In our cohort there was only one steam pop during ablation that was not associated with any complications.
Conclusions: Ablation of ventricular arrhythmias using a 56-hole open-irrigation RF ablation catheter appears safe with no apparent excess in complications at 30 days. Acute success and complication rates compare favorably with data from contemporary VA ablation trials.

4054 | BEDSIDE
The substrate for ventricular tachycardia in repaired tetralogy of Fallot are slow conducting anatomical isthmuses

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Introduction: In repaired Tetralogy of Fallot (rTOF), the majority of ventricular arrhythmias (VA) are sustained reentrant ventricular tachycardia (SMVT) related to four anatomical isthmuses. Specific anatomical isthmuses characteristics may be related to SMVT.
Methods: Seventy-three consecutive rTOF patients (40±16 yrs, 63% male) with documented SMVT (n=13) or considered at risk for VA underwent programmed stimulation (3 drive cycle length (CL), ≥3 extrastimuli, from ≥2 RV sites, isoproterenol) and electroanatomical substrate mapping (EAM). All identified anatomical isthmuses (AI) bordered by unexcitable tissue (patch, scar, valve annulus) were evaluated for width, length and conduction velocity (CV); AI 1:Tricuspid annulus (TA) and RVOT patch/scar, AI2: RV scar and pulmonary annulus (PA), AI3: PA and VSD patch, AI4: VSD patch and TA. The relation between VT reentry circuit sites and AI was determined by pace and/or entrainment mapping.
Results: Twenty-eight pts (all 13 with documented SMVT) were inducible for a median of 1.0 (1.0 – 1.8) SMVT; VTCL 252 ms (231 – 312). The number of identified AI 1, 2 and 3 was comparable for inducible and non-inducible (n=45) pts (AI1 27 vs 39, p=0.11; AI2 8 vs 11, p=0.62; AI3 26 vs 37, p=0.12). AI 4 was only present in 4 inducible pts. Inducible pts had significant narrower AI 1 and 3 (AI1 36±11 vs 43±10mm, p<0.01; AI2 25±11 vs 30±12mm, p=0.34; AI3 20±6 vs 26±8mm, p<0.01; AI4 19±5), significant longer AI 1, 2 and 3 (AI1 16±7 vs 12±4, p=0.02; AI2 22±7 vs 13±5, p=0.01; AI3 20±7 vs 16±8, p=0.03; AI4 16±7) and significant slower CV of AI 1,2 and 3 (AI1 0.80±0.42 vs 1.11±0.34m/s, p<0.01; AI2 0.59±0.28 vs 0.95±0.32m/s, p=0.03; AI3 0.35±0.18 vs 0.81±0.29m/s, p<0.01; AI4 0.72±0.67m/s). A critical SMVT reentry site was mapped to an AI in 24/27 pts. All AI containing reentry sites (n=28; AI1 8, AI2 2, AI3 17, AI4 1) had CV of <0.5 m/s (mean CV 0.33±0.08 m/s). In contrast, in 43/45 non-inducible pts all AI had CV of ≥0.5m/s.
Conclusion: In rTOF, slow conducting anatomical isthmuses with a CV<0.5m/s protected by unexcitable tissue are the dominant substrate for SMVT. The results of electroanatomical mapping obtained during stable rhythm may therefore significantly contribute to risk stratification for VT.

4055 | BEDSIDE
Catheter ablation of hemodynamically tolerated VT in patient with CAD and preserved systolic LV function

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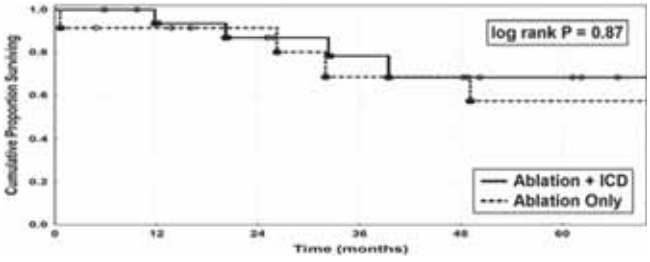
Introduction: Patients with coronary artery disease (CAD), hemodynamically tolerated ventricular tachycardia (VT) and LV ejection fraction (EF) >40% may benefit from catheter ablation without necessity of implantation of cardioverter-defibrillator (ICD). Our aim was to retrospectively analyze long-term results of VT ablation in this patient subgroup.
Methods: Out of 728pts, who underwent catheter ablation of VT between 2001 and 2012, we have identified 30pts (4% all pts, 1 women, mean age 68±10years) with CAD, tolerated VT and EF>40%. Mean LV EF was 47±5%, mean VT cycle length was 337±68ms. Catheter ablation was performed in order to abolish all inducible VTs. An ICD was implanted if sustained VT of any morphology remained inducible after ablation.
Results: Clinical VT and all inducible VTs were abolished in 83% and 60% of pts, respectively. An ICD was subsequently implanted in 53% of cases. Mean follow up was 43±34months. In the subgroup of pts with an ICD, adequate therapy was noted in 53% pts. In subgroup of pts without ICD, two subjects (15%) had recurrence of tolerated VT and were implanted with ICD. In total, 43% pts have died during follow up, mostly due to non-cardiac causes. Survival (figure) did not differ between both subgroups (p=0.87).



Conclusions: Hemodynamically tolerated VT eligible for catheter ablation in pts with CAD and preserved systolic function LV occurs infrequently. Despite high success of VT ablation of clinical VT, an ICD is indicated in considerable proportion of the cases due to inducibility of VT of other morphologies. Although ICD interventions are common in the group of pts with ICD, the long-term survival does not differ between pts with or without ICD.

4056 | BEDSIDE
Significant reduction of radiation exposure during electrophysiological procedures with the use of novel x-ray system using a crystalline detector

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Aim: Radiation exposure has been reduced in electrophysiological procedures (EP) by the use of mapping systems but remains a concern for electrophysiologists. We evaluated the impact of the use of a novel x-ray technology during EP procedures on fluoroscopy doses.
Methods: 148 consecutive patients undergoing ablation procedures or device implantations were included in our study. Procedures were performed using the Artis Q.Zen (Siemens, Forchheim, Germany; n=68) with new crystalline silicone detector enabling ultra-low-dose imaging and the Artis Q with an amorphous silicon detector (n=80). Patients were categorized into four groups – pulmonary vein

Table 1

	Artis Q	Artis Q.Zen	p-value
Overall	n=80	n=68	
FDP	1186 (276–2044)	549 (143–1281)	0.003
CDP	619 (0–1298)	204 (0–752)	0.184
CDP/F	3.58 (0–6.99)	1.38 (0–2.23)	0.006
PVI	n=31	n=26	
FDP	1771 (962–3789)	1235 (553–1970)	0.017
CDP	1212 (826–2948)	497 (113–1187)	<0.001
CDP/F	7.1 (5.1–9.1)	2.0 (1.2–2.4)	<0.001
CRT	n=7	n=10	
FDP	1816 (927–6350)	579 (286–971)	0.007
CDP	981 (213–3282)	351 (163–483)	0.070
CDP/F	4.7 (3.0–5.1)	1.4 (1.3–1.8)	<0.001

FDP: fluoro dosis product (μGy m^2), CDP: cine dosis product (μGy m^2), CDP/F: cine dosis per frame.

isolation (PVI), supraventricular tachycardia ablation (SVT), CRT (CRT) and pacemaker/ICD implantation (PMICD). In SVT and PMICD patients, only fluoroscopy was used while in PVI group cine acquisition was used for transseptal puncture,in CRT group for coronary sinus venogram. Cine dose was corrected for time and frame rate.
Results: The patients baseline parameters weight, height, BMI, and age did not differ. The results are shown in the table.
Conclusion: The use of a novel x-ray technology with a crystalline detector for noise reduction for standard EP procedures significantly reduces radiation doses. The use of this technology further improves safety of fluoroscopy based EP procedures.

4057 | BEDSIDE
Minimal invasive non-fluoroscopic imaging and catheter ablation of supraventricular arrhythmias

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Introduction: Although the "near zero-X-ray" or "no-X-ray" catheter ablation (CA) approach has been reported for treatment of various arrhythmias, few prospective studies have strictly used "no-X-ray," simplified 2-catheter approaches for CA in patients with supraventricular tachycardia (SVT). We assessed the feasibility of a minimally invasive, non-fluoroscopic (MINI) CA approach in such patients.
Methods: Data were obtained from a prospective multicenter CA registry of patients with regular SVTs. After femoral access, 2 catheters were used to create simple, 3D electroanatomic maps and to perform electrophysiologic studies. Medical staff did not use lead aprons after the first 10 MINI CA cases.
Results: 252 patients (age, 47±23 years; 18% <19 years; 57% women) referred for the no-X- ray approach were included. They were compared to 714 consecutive patients referred for a simplified approach using X-rays (age, 52±18 years; 7% <19 years; 55% women). There were only 17 cases (7%) with protocol exceptions that necessitated the use of X-rays. Ultimately, 235/252 patients underwent the procedure without fluoroscopy, with an acute success rate of 98%. The procedure times (62±24 vs. 63±29 min, P=NS), major complications (0% vs 0%, P=NS) and acute (98% vs. 98%, P=NS) success rates were similar in the "no-X-ray" and control groups. The MINI CA protocol group showed a very significant reduction in radiation exposure time (0.3±0.8 min) compared to ablations using fluoroscopy (8.1±7.4 min, P<0.001).
Conclusions: Implementation of a strict "no-X-ray, simplified 2-catheter" CA approach is safe and effective in majority of the patients with SVTs. No-X-Ray approach should be prospectively validated and implemented in training of new generation of adepts of modern electrophysiology.

4058 | BEDSIDE
Postero-septal epicardial accessory pathways - electroanatomical corelations

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Background: Radiofrequency (RF) catheter ablation is a highly effective curative treatment for Wolff-Parkinson-White syndrome. Epicardially located accessory pathways (AP) are sometimes the cause of failed endocardial catheter ablation.
Aims: To identify ECG characteristics that predicts an epicardial location for accessory pathways in the postero-septal region.
Methods: Fully pre-excited ECGs, EP characteristics and successful site of ablation were analyzed retrospectively in 54 patients with postero-septal pathways.
Results: In 20 out of 54 patients endocardial ablation failed (including irrigated-tip RF ablation) and successful application was located epicardially, into the coronary sinus (CS) tributaries (16 inside of a CS diverticulum, 4 into the proximal part of the mid-cardiac vein). In all patients with epicardial ablation an AP potential was recorded at site of successful ablation. The only ECG feature that predicted a successful epicardial ablation was an isoelectric or discretely biphasic appearance of the initial 40 ms of the QRS in lead V1 measured from the beginning of delta wave as assessed in 12 leads (98% sensitivity and 99% specificity).
Conclusions: APs are located epicardially in a substantial proportion of the patients with postero-septal pathways. An isoelectric or discretely biphasic appearance of the initial 40 ms of the pre-excited QRS in lead V1 predicts epicardial successful ablation, mainly in a CS diverticulum.

4059 | BEDSIDE
Characteristics of focal atrial tachycardias in a large real world cohort

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Introduction: Focal atrial tachycardias (FAT) are a rather rare form of supraventricular tachycardias and radiofrequency (RF) ablation has become a favored treatment option. We analyzed the characteristics of FAT and the outcome of RF ablation in a large "real world" cohort in Germany.
Methods: Patient and procedural data as well as acute and long-term outcome data from patients with FAT ablation were prospectively collected in 44 centers in Germany in the years 2007-2011.
Results: 604 pts. were treated for FAT in 610 procedures. 53 pts. (9%) had biatrial foci (BAF), 163 pts. (27%) left atrial foci (LAF) and 388 pts. (64%) right atrial foci (RAF). Pts. with BAF and LAF more often had valvular disease (35.8% BAF, 18.4% LAF, 6.7% RAF p<0,01) and were more often re-do procedures (22.2% BAF, 24.2% LAF, 13.0% RAF p<0,01). FAT site of origin are shown in the table. No difference for the acute ablation success rate could be observed 79.6% BAF, 87.3% LAF. 85.9% RAF p=0,37). The recurrence rate in 1yFU was 46.7% for BAF vs. 34.5% for LAF and 29.7% for RAF (p<0,01). Acute complications were more frequent in BAF pts. (major bleeding 3.8% BAF, 0% LAF, 0% RAF p<0,01; minor bleeding 7.7% BAF, 3.7% LAF, 0.8% RAF p<0,01). No other major complications occurred.

Origin of Focal Atrial Tachycardia

	Both atriums (n=53)	Left atrium (n=163)	Right atrium (n=388)
Location RA			
Crista terminalis	7,4%	–	26,1%
Septal	35,2%	–	29,9%
Multifocal	18,5%	–	7,7%
Sinus node	1,9%	–	6,6%
Other location	42,6%	–	34%
Location LA			
Pulmonary veins	18,5%	41,8%	–
Septal	31,5%	16,4%	–
Multifocal	44,4%	24,2%	–
Others	40,7%	37,6%	–

Conclusion: Referring to this data from a large "real world" cohort of patients RF is an efficacy treatment option for FAT with a good success rate ≥80% and an acceptably low complication rate. The recurrence rate for the whole cohort is notable.

4060 | BEDSIDE
Characterization of very low voltage/scar areas in patients with left atrial flutter by high density voltage maps

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Background: Circuits of left atrial flutter (LAFl) are delimited by scar areas (SA). We studied the location and extension of SA in patients without previous LA ablation.
Methods: 33 P included (67% women, age 71±10 years). High-density point-by-point activation/voltage maps were developed with a 3D navigator during LAFl or SR if the arrhythmia was unstable. Bipolar peak-to-peak amplitude at each point was shown. SA were defined by congruent points with <0,1 mV and normal tissue by >0,5 mV. Total endocardial surface (TES) and total scar areas (SA) surface were quantified by merging with a 3D TC image of the LA.
Results: 49 EP studies in 33 patients, 9 (27%) had a prosthetic mitral valve implated. In the first EP study in each patient the tisular substrate was characterized (number of points: 955±332, range 379-1481). TES was 114±31 cm^2. Median SA was 25±31 cm^2 (range 0-134 cm^2), constituting 20±21% of TES (range 0-86%). 2 P presented massive scar areas (>85%) and 1 P had no scar. Location of the widest scar area: anterosuperior wall 61%, posterior 15%, septal 6%, right PV antrum 6%, massive 6%, inferior 3%. 28 P had a secondary SA: posterior

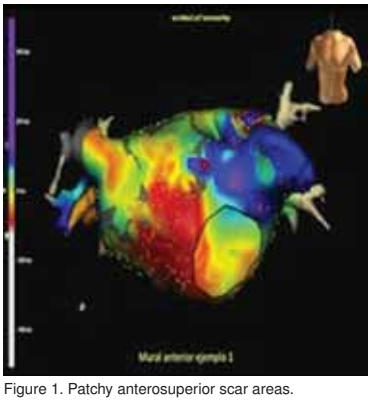

Figure 1. Patchy anterosuperior scar areas.

25%, septal 21%, anterior 18%, right PV antrum 18%, inferior 15%. 61 LAFl were studied, 23 (37%) could not be fully characterized. Detailed characterized circuits: 35% perimitral, 18% mural superior, 12% mural posterior, around right PV 10%, septal 10%, around left PVs 8%, LAA flutter 6%. 59/61 circuits laid adjacent or crossed through scar areas. No relationshipt was found between scar areas and number of LAFl per patient.
Conclusions: Prevalence of SA is high but their distribution heterogeneous. SA are located frequently on the anterosuperior and posterior walls of the LA. Characterizing these SA is relevant for LAFl mapping and ablation.

ARRHYTHMOGENESIS: FROM HORMONAL DRIVE TO IONIC HOMEOSTASIS

4061 | BENCH
Carotid body denervation prevents pulmonary edema, attenuates left ventricular remodeling and restores normal autonomic balance in chronic heart failure after myocardial infarction

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Purpose: Autonomic imbalance in chronic heart failure (CHF) predicts poor prognosis. It has been well established that the hypersensitive carotid body induces sympathoexcitatory hypertension and carotid body denervation (CBD) fully abolishes it. Since CHF sensitizes the peripheral chemoreflex, we hypothesized that CBD restores normal autonomic balance, thus improves CHF in a rat model of myocardial infarction-induced CHF (MI-CHF).
Methods: We created MI-CHF in 8 weeks Sprague-Dawley rats. Surviving rats at 2 weeks after MI were randomized into sham-operated (Sham; n=10) and CBD (n=10) groups. We removed the tissues around the carotid bifurcation and established CBD. In some rats (Sham; n=5, CBD; n=5), we telemetrically recorded blood pressure (BP) and heart rate (HR). A month after CBD, we compared physiological and histological findings between Sham and CBD.
Results: CBD did not change mean BP (94±6 vs. 100±4 bpm, n.s.), while significantly reduced HR (364±12 vs. 337±15 bpm, $p<0.05$). Power spectral density (PSD) analysis of HR demonstrated that CBD markedly increased the PSD in the high frequency range (29.0±8.2 vs. 81.0±9.5 n.u., $p<0.05$) and decreased the low frequency/high frequency ratio (1.8±0.5 vs. 0.6±0.2, $p<0.05$) indicating the restoration of autonomic balance. CBD significantly reduced biventricular weight (3.7±0.3 vs. 3.1±0.3 g/kg, $p<0.05$), lung weight (11.9±1.6 vs. 6.5±1.3 g/kg, $p<0.01$), left ventricle (LV) end-diastolic pressure (32.7±5.3 vs. 20.9±6.2 mmHg, $p<0.01$), and plasma norepinephrine (1048±997 vs. 384±202 pg/ml, $p<0.05$). Furthermore, CBD increased body weights (351±38 vs. 426±32 g, $p<0.01$) and LV dp/dtmax (4075±536 vs. 5118±809 mmHg/sec, $p<0.05$). Histological analysis showed CBD decreased the collagen volume fraction (6.0±1.3 vs. 4.7±1.6%, $p<0.05$) and the number of inflammatory macrophages (474±73 vs. 345±45 counts/mm^2, $p<0.05$) in the non-ischemic LV area.
Conclusion: The CBD induces sympathoinhibition prevents pulmonary edema, attenuates LV remodeling, restores normal autonomic balance and improves CHF in rats. CBD can be a novel neuro-modulatory therapy for CHF patients.

4062 | BENCH
miR-mediated BAG3 regulation may be lost in stress-induced Takotsubo cardiomyopathy

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Purpose: BAG3 protein is constitutively expressed in cardiomyocytes and is essential for the homeostasis of mechanically altered cells. BAG3 knock-out mice result in a lethal cardiomyopathy soon after birth and mutations of this gene have been associated with different forms of cardiomyopathies including Takotsubo (TTC). Up to date the pathogenetic mechanism leading to TTC has not been defined even if it has been suggested that excessive epinephrine levels may trigger the event. In this study we extended our previous genetic screening for BAG3 mutations to the 3'UTR of the gene and we studied how a particular mutation may be involved in the pathogenesis of TTC.
Methods: All patients were enrolled according to the Mayo Clinic diagnostic criteria of TTC. Patient cohort included 70 females (64.3±12 y.o.; range 35-82), donors were 81 healthy female, older than 50, with absence of evaluable cardiovascular disease. BAG3 gene was sequenced from gDNA and an in silico analysis was performed to identify potential miRNAs predicted to bind its 3'UTR. In vitro dual luciferase reporter assays were performed to verify miRNA binding to BAG3 3'UTR. miR and proteins levels were detected in cardiomyocytes after epinephrine stimulus by qPCR or Western blot respectively. BAG3 modulation after miR precursors or inhibitors transfection was assayed.
Results: We found that BAG3 protein levels increase in cardiomyocytes after epinephrine stimulation by a pERK-dependent pathway. Since stress-cardiomyopathy is reported to be triggered by epinephrine, we sequences BAG3 gene in TTC patients and donors and we found that patients carried more BAG3 mutations than the control group (27% and 53% of BAG3 wild types genotypes respectively, $p<0.05$). Moreover, we identified a frequent SNP in BAG3 3'UTR (minor allele frequency MAF=0.38 in TTC and MAF=0.26 in the control group, $p<0.05$). In vitro assays showed that this SNP in BAG3 3'UTR results in loss of miR-371-5p binding to the mRNA, moreover we found that epinephrine is able to up-regulate miR-371-5p expression in cardiomyocytes by a pERK-mediated mechanism. Indeed, the transfection of the pre-miR is able to induce BAG3 protein levels post-transcriptionally and the anti-miR (inhibitor) is able to inhibit BAG3 epinephrine-induced up-regulation.
Conclusion: We identified a novel pathway in cardiomyocytes that leads to an increase of BAG3 protein upon exposure to epinephrine, through an ERK dependent induction of miR-371-5p. Therefore, loss of miR-371-5p binding on BAG3 mRNA seems to play an important role in the pathogenesis of Takotsubo cardiomyopathy.

4063 | BENCH
Stabilization of RyR2 by inhibition of CaMKII-mediated aberrant Ca2+ release may suppress arrhythmogenesis in cardiac troponin T-related familial hypertrophic cardiomyopathy

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Background: Cardiac troponin T (cTnT) mutations that increase myofilament Ca2+ sensitivity cause Familial Hypertrophic Cardiomyopathy (FHC), which leads to sudden cardiac death in young age. However, the underlying mechanism by which the cTnT mutations lead to lethal arrhythmia remains elusive. Here, we investigated the pathogenic role of phosphorylation-mediated aberrant Ca2+ release via cardiac ryanodine receptor (RyR2) and therapeutic effects of dantrolene, which was found to stabilize RyR2 in catecholaminergic polymorphic ventricular tachycardia and failing hearts by correcting inter-domain interactions (i.e. unzipping to zipping), in transgenic mouse (TG) model with FHC-related cTnT mutation (TNT-delta160E).
Methods and results: In 6-months-old's TG, there was no appreciable difference in the structural or functional features of hearts, compared with non-TG. In response to isoproterenol (ISO; 10nmol/L), the Ca2+ spark frequency (SpF: $s^{-1}\cdot100\mu m^{-1}$ by fluo4) was much higher in TG cardiomyocytes (ISO-TG: n=11: 7.7±0.7; $p<0.01$) than in non-TG cardiomyocytes (n=6: 3.5±0.5). It was largely reversed by CaMKII inhibitor {KN-93 (1μM), n=6: 5.2±0.4; $p<0.05$}, but not by PKA inhibitor{H-89 (1μM), n=6: 7.3±0.4;n.s.}. Time from peak to 70% decline of Ca2+ transient was more prolonged in ISO-treated TG than in ISO-treated non-TG, whereas it was attenuated by KN-93. ISO-TG (but not ISO-treated non-TG: 0/14: n=14) showed spontaneous Ca2+ transient (sCaT) after 5Hz pacing (12/18: n=18), whereas it was again attenuated only by KN-93 (0/5: n=5). Moreover, dantrolene (1μM) attenuated ISO-induced SpF (n=6:5.2±0.3; $p<0.05$ vs ISO-TG), time from peak to 70% decline of Ca2+ transient and sCaT (3/10; n=10) in TG cardiomyocytes.
Conclusion: In FHC-linked cTnT-mutated hearts, aberrant Ca2+ release through defective RyR2 was induced by beta-adrenergic stimulation, and subsequent CaMKII activation. Stabilization of RyR2 by inhibition of CaMKII-mediated aberrant Ca2+ release might be a new therapeutic target for preventing the development of arrhythmias in FHC.

4064 | BENCH
Adrenergically-triggered calcium handling abnormalities and arrhythmias in induced pluripotent stem cell-derived cardiomyocytes generated from cpvt patients with ryanodine or calsequestrin mutations

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Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a familial arrhythmogenic disorder characterized by syncope and sudden death occurring during exercise or acute emotion. The disease is caused by abnormal Ca2+ handling resulting from mutations in the RYR2 or the CASQ2 genes. The present study had two aims: (1) Investigate cardiomyocytes derived from induced Pluripotent Stem Cells (iPSC-CM) generated from dermal fibroblasts obtained from CPVT patients caring the heterozygous R420Q mutation in the RYR2 gene (CPVT-RYR2R420Q-CM). (2) To compare isoproterenol-induced calcium handling disturbances in CPVT-RYR2R420Q-CM versus iPSC-CM generated from patients carrying the D307H mutation in the CASQ2 gene (CPVT-CASQ2D307H-CM). The major findings were: (1) While in healthy iPSC-CM, β-adrenergic stimulation with isoproterenol only increased the spontaneous firing rate, in CPVT-RYR2R420Q-CM isoproterenol caused delayed afterdepolarizations (DADs) and triggered activity blocked by the β-blocker Bisoprolol. (2) In both RyR2 and CASQ2 mutations, in the age range of 20-70 day-old embryoid bodies (EBs), the arrhythmogenic phenotype was age-dependent, being more pronounced in cardiomyocytes >50 day old. We propose that these age-dependent isoproterenol-

induced arrhythmias were due do maturational changes in the sarcoplasmic reticulum function and in its Ca2+ storage/release capacity. (3) Compared to healthy iPSC-CM, caffeine releases more Ca2+ in CPVT-CASQ2D307H-CM and less Ca2+ in CPVT-RYR2R420Q-CM. Additionally, while healthy iPSC-CM and CPVT-RYR2R420Q-CM demonstrated prompt recovery after caffeine-induced SR Ca2+ release, the CPVT-CASQ2D307H-CM demonstrated slower recovery. We conclude that these findings may result from one or more of the following mechanisms: (1) Different Ca2+ storing capacity of the RyR2 versus CASQ2 mutated iPSC-CM; (2) CPVT-CASQ2D307H-CM have unstable RyR2 channel due to non-functional CASQ2 which causes uncontrollable Ca2+ release; (3) The two mutations have different responsiveness to caffeine. Our results demonstrate that mutated iPSC-CM from CPVT patients, can be used to study the differences in the mechanisms underlying the arrhythmias and the calcium handing derangements in the RYR2 versus the CASQ2 mutations.

4065 | BENCH
Transient [Ca2+]i oscillations and long-term pro-fibrotic responses to UTP involve differential activation of P2Y2, P2Y4 and P2Y11 purinoceptors in rat cardiac fibroblasts

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Purpose: Cardiac fibroblasts (CF) play a crucial role in cardiac remodeling, electrophysiological changes and hemodynamic alterations following myocardial infarction. ATP and UTP are released in huge amounts during ischemia and reperfusion. Extracellular nucleotides may act as autocrine and/or paracrine mediators via the activation of a variety of P2 purinoceptors. Here, we investigated the role of uracil nucleotides on intracellular Ca2+ signaling and growth of cultured CF from rat ventricles.
Methods: The chemical coding of CF and the expression of P2 purinoceptors was assessed by immunofluorescence confocal microscopy. Intracellular calcium [Ca2+]i oscillations were monitored with a microplate reader after loading the cells with Fluo-4NW (2.5 μM, 45 min at 37ºC). CF proliferation/viability was evaluated using the MTT assay.
Results: Cultured CF co-express discoidin domain receptor 2 (DDR2) and alpha-smooth muscle actin (α-SMA), suggesting a myofibroblastic phenotype. UTP and UDP (100 μM) increased [Ca2+]i in rat CF respectively by 54±2% (n=13) and 35±3% (n=12). The preferential P2Y4 antagonist, Reactive Blue-2 (RB-2, 100 μM, n=9), and the selective P2Y11 antagonist, NF340 (10 μM, n=9), were more effective than Suramin (100 μM, n=10) in decreasing [Ca2+]i oscillations triggered by UTP (3 μM). Selective activation of P2Y4 receptors with MRS 4062 (10 μM, n=7), but not P2Y2 receptors with MRS 2768 (10 μM, n=4), mimicked the effect of UTP. Incubation of CF cultures with UTP (100 μM, n=4) increased cell growth. Suramin (30-100 μM) was more effective than RB-2 in decreasing the proliferation of CF. Rat CF in culture express higher amounts of P2Y2 receptor as compared to P2Y4 immunolabeling.
Conclusions: Data suggest that activation of the less abundant P2Y4 receptor is the main responsible for UTP-induced [Ca2+]i transients in rat CF. Stimulation of the P2Y11 receptor may also contribute to sustain [Ca2+]i at elevated levels following UTP application. The highly expressed P2Y2 receptor may exert a preferential role on CF proliferation promoted by UTP. In summary, UTP-sensitive P2Y2, P2Y4 and P2Y11 receptors can differentially affect [Ca2+]i levels and pro-fibrotic responses to UTP in rat CF and, therefore, may constitute important pharmacological targets for therapeutic intervention in the remodeling myocardium.

STATE OF THE ART – AORTIC STENOSIS: FROM EPIDEMIOLOGY TO TREATMENT

4070 | BEDSIDE
Is there any role for familial screening in bicuspid aortic valve and aortic disease?

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Introduction and objective: : Bicuspid aortic valve (BAV) is the most common congenital heart disease. Recent studies have shown a certain family aggregation, suggesting that echocardiographic screening in first-degree relatives (FDR) would permit early diagnosis of valve and/or aortic abnormalities in this population. The usefulness of this strategy, however, has not been demonstrated. We sought to assess the usefulness of systematic echocardiographic screening of FDR of patients with a confirmed BAV.
Methods: Ninety consecutive families of patients with a confirmed echocardiographic diagnosis of BAV (75% males; 75.6% anteroposterior configuration) were studied. A transthoracic echocardiogram was performed in FDR to assess valve features (opening configuration, presence of a raphe, degeneration and function) and aortic dimensions at different levels (root, AA, aortic arch).
Results: Of the 401 FDR recruited: 113 (28.1%) refused the study and 288 (71.9%) underwent screening (mean age: 36.1±19 years; 66.7% males). Twenty-one aortic valve abnormalities were encountered: 20 BAV and 1 quadricuspid valve, distributed in 17 of the 90 families, yielding a BAV family prevalence of 18.8% (Table 1).

Table 1

	Probands (N=90)	Positive FDR (N=21)	p
Male n (%)	67 (75)	14 (66.7)	p=1.000
Age (years) mean ± SD	49.6±15.5 (16–76)	36.1±19.8 (9–59)	p=0.501
BSA (m^2) mean ± SD	1,82±0.18 (1.3–2.2)	1.67±0.5 (0.25–2.4)	p=0.164
AP/no raphe	68 (75.6%)/25 (28.1%)	12 (66.7)/4 (22.2)	p=0.073/p=0.187
MS AO stenosis	15 (16.7)	1 (5.3)	p=0.296
MS AO regurgitation	39 (43.3)	1 (5.3)	p=0.001

BSA: body surface area; SD: standard deviation; SV: sinus of Valsalva; AA: ascending aorta; Ao: aortic; MS: moderate-severe;.

The prevalence of BAV among the FDR screened was 7.3%, higher than that reported in the general population (0.5-1.0%). The number of FDR required to screen for identifying a new BAV case is 14, in contrast to 100 in the general population.
Conclusions: BAV prevalence is higher in FDR of BAV patients than in the general population. Echocardiographic screening of FDR is a useful approach for identifying asymptomatic cases, that should therefore be offered to all FDR of BAV individuals.

4071 | BEDSIDE
Does body mass index affect left ventricular remodeling in different categories of severe aortic stenosis?

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Purpose: We aim to evaluate how body mass index (BMI) may have differential effects on left ventricular (LV) remodeling in patients with severe aortic stenosis (AS).
Method: We studied 508 patients with severe AS (valve area $<1cm^2$). Concomitant significant valvular lesions were excluded. These were divided into 4 categories according to flow (low flow (LF), stroke volume index, SVI <35 ml/m^2) and mean gradient (low gradient (LG), <40 mmHg). Patients were grouped by BMI into underweight (<19 kg/m^2), ideal weight (19 – 23 kg/m^2), overweight (24 – 27 kg/m^2) and obese (>27 kg/m^2). Echocardiographic parameters were examined.
Results: The degree of LV remodeling was significantly different across different categories of AS in patients who are not underweight, with the largest LV mass index in the normal-flow group but higher relative wall thickness (RWT) in the low-flow group. Underweight patients did not show difference across categories for LV mass index and RWT. LV end-diastolic volume index was relatively higher in the normal-flow categories across all BMI groups (trend in the underweight group) but end-systolic volume index was only significantly different in the ideal weight group.

Table 1

	Low-flow low-gradient (n=167)	Low-flow normal-gradient (n=40)	Normal-flow low-gradient (n=214)	Normal-flow normal-gradient (n=87)	p
LV ejection fraction (LVEF, %)					
Underweight (n=30, 6%)	55±19	59±18	65±6	65±6	0.38
Ideal (n=176, 35%)	45±20	54±15	58±12	60±14	<0.01
Overweight (n=187, 36%)	49±18	59±15	58±13	62±13	
Obese (n=115, 23%)	56±16	57±20	61±10	62±10	0.23
LV mass index (g/m^2)					
Underweight	98±31	103±27	118±32	140±32	0.15
Ideal	110±35	114±22	116±28	155±28	<0.01
Overweight	111±31	111±25	127±32	143±32	
Obese	104±28	127±29	115±40	137±40	
Relative wall thickness					
Underweight	0.53±0.10	0.54±0.08	0.48±0.07	0.38±0.05	0.07
Ideal	0.48±0.15	0.65±0.24	0.39±0.08	0.49±0.11	<0.01
Overweight	0.50±0.13	0.54±0.07	0.41±0.09	0.50±0.12	
Obese	0.51±0.13	0.55±0.10	0.42±0.07	0.46±0.10	
End diastolic volume index (ml/m^2)					
Underweight	55±23	48±19	67±12	78±12	0.05
Ideal	62±26	48±20	76±19	75±19	<0.01
Overweight	59±26	50±10	80±22	71±18	
Obese	52±20	54±18	69±18	70±10	
End systolic volume index (ml/m^2)					
Underweight	34±32	32±34	30±11	36±11	0.97
Ideal	37±27	22±14	29±15	28±16	0.04
Overweight	54±41	37±17	56±32	45±28	0.11
Obese	47±39	47±44	46±29	44±17	0.99

Conclusion: Different categories of severe AS affect LV remodeling of all BMI except the underweight group. Further studies on the prognostic significance are warranted.

4072 | BEDSIDE

Prognostic value of aortic valve area flow rate ratio in aortic stenosis with preserved ejection fraction: Japanese Multicenter Aortic Stenosis (JUST) study

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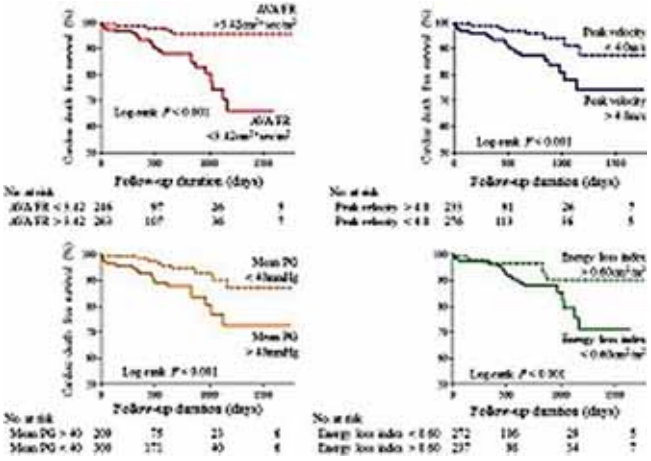
Purpose: Accurate assessment of disease severity is critical for the subsequent appropriate treatment in patients with aortic stenosis (AS). The purpose of this study was to examine the prognostic value of a new index, aortic valve area flow rate ratio (AVA/FR), in patients with severe AS.
Methods: This retrospective study included 509 consecutive patients with severe AS (indexed aortic valve area <0.6 cm^2/m^2) with preserved left ventricular ejection fraction ($\geq$50%) who had been enrolled from 4 Japanese institutions. AVA was calculated using the continuity equation. The primary endpoints were cardiac death (CD) and major adverse cardio-cerebrovascular events (MACE).
Results: During a mean of 1097days follow up, 247 patients (42.4%) had MACE including 39 CD (6.7%). Kaplan-Meier analysis showed that all AS severity criteria had a significant prognostic power for predicting CD (Figure). Cox proportional-hazard analysis revealed that lower AVA/FR was independently associated with both MACE and CD (hazard ratio: 0.371 and 0.354, all $P<0.001$), respectively. AVA/FR <3.42 cm^2·sec/ml was the best cut-off criteria for predicting CD.



Conclusions: AVA/FR is a novel index for predicting future prognosis in patients with severe AS, better than conventional severity.

4073 | BEDSIDE

Reliability of aortic stenosis severity classified by 3-dimensional echocardiography in prediction of cardiovascular events

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Background and aim: Doppler echocardiography derived aortic valve area (AVA) is commonly used to determine the severity of aortic stenosis (AS). However discrepancies of severities between AVA and pressure gradient were sometimes observed. The main pitfall is an error of left ventricular (LV) stroke volume (SV) calculation with LV out-tract diameter and time-velocity integral in the continuity equation. In contrast, 3-dimensional echocardiography (3DE) allows measuring LV volume more accurately. Then, we hypothesized that AVA estimated by the continuity equation with 3DE derived LVSV might be more closely related with clinical severities in patients with AS.
Methods: First, in 361 patients with moderate ($1.5>$AVA >1.0 cm^2) to severe AS (AVA <1.0 cm^2), AVA was compared between Doppler method (AVA-Dop) and 3DE (AVA-3D), and the determinants of differences between the methods were identified. Second, in a part of patients (n=276), clinical courses were investigated to identify the differences of clinical impacts between the methods. The primary end-point was major adverse cardiovascular events (MACE), including cardiac death, aortic valve replacement (AVR), and any cardiovascular events.
Results: Indexed AVA-DOP (iAVA-Dop) was significantly higher than iAVA-3D (0.56 ± 0.17 vs. 0.47 ± 0.16 cm^2/m^2, $p<0.001$). Differences between iAVA-Dop and iAVA-3D was significantly higher in female ($p<0.001$) and patients with upper septal hypertrophy (USH, $p<0.001$). In addition, the differences were negatively correlated with body surface area ($r=-0.26$, $p<0.001$), and positively with LV ejection fraction ($r=0.33$, $p<0.001$) and LV end diastolic volume (LVEDV, $r=0.41$, $p<0.001$). In a least square multiple regression analysis, USH and LVEDV were selected as significantly determinants (USH: $p<0.001$, $\beta=-0.06$, LVEDV: $p<0.001$, $\beta=-0.002$). In the outcome study, 129 (47%) patients met MACE (follow up 342 ± 343 days). The events were occurred in almost severe AS based on the AVA-3D, however, the significantly high number of patients with events were classified into moderate AS if AVA-Dop was used. (moderate/severe: Doppler; 35 (27%)/94 (73%) vs. 3D; 15 (12%)/114 (88%),p=0.001).
Conclusions: Doppler method may underestimate AS severity, particularly, in patients with USH. In contrast, 3DE volumetric method has a potential to accurately classify AS severities and contribute predicting cardiovascular events.

4074 | BEDSIDE

Surgical sutureless and transcatheter aortic valves: haemodynamic performance in propensity-score matched high-risk populations with severe aortic valve stenosis

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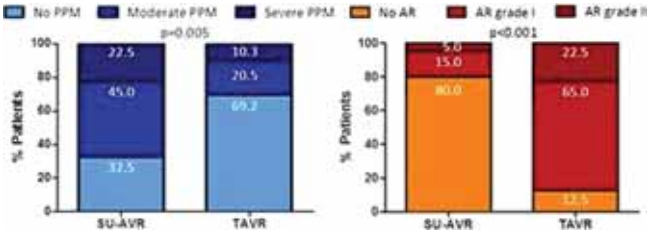
Purpose: High operative risk patients with severe aortic stenosis are candidates for surgical sutureless aortic valve replacement (SU-AVR) or for transcathter aortic valve replacement (TAVR). The current study aimed at comparing the hemodynamic performance of both valves after SU-AVR and TAVR, assessed by echocardiography, in propensity-score matched populations.
Methods: Of 258 patients who underwent successful TAVR and SU-AVR for severe aortic stenosis, 80 (79 ± 5 years old, 100% men) were included in the current analysis based on propensity score 1:1 matching for clinical and hemodynamic parameters at baseline. All subjects had hemodynamic echocardiographic evaluation at baseline and discharge.
Results: Compared with SU-AVR, patients undergoing TAVR had larger aortic valve area index (1.00 ± 0.30 vs 0.76 ± 0.22 cm^2/m^2, $p<0.001$) lower transaortic pressure gradient (8.14 ± 4.21 vs 10.72 ± 4.01 mmHg, p=0.006), less frequent prosthesis patient mismatch (PPM) (30.8 vs 67.5%, p=0.001) and low-flow (46.2 vs 72.5%, p=0.02) but more frequent aortic regurgitation (87.5 vs 20%, $p<0.001$) (Figure). The only variable independently associated to the low-flow state at discharge was the presence of PPM (OR 4.70, p=0.004) and to PPM at discharge the SU-AVR type of procedure (OR 3.90, p=0.02).



PPM and AR after SU-AVR vs. TAVR

Conclusion: TAVR is associated with better hemodynamics than SU-AVR, in terms of aortic valve area, pressure gradients, PPM and stroke volume, but show higher incidence of aortic regurgitation.

COMPUTED TOMOGRAPHY FOR FUNCTIONAL ASSESSMENT OF CORONARY ARTERY DISEASE

4076 | BEDSIDE

Diagnostic performance of non-invasive fractional flow reserve derived from coronary computed tomography angiography: influence of vessel territory and calcification

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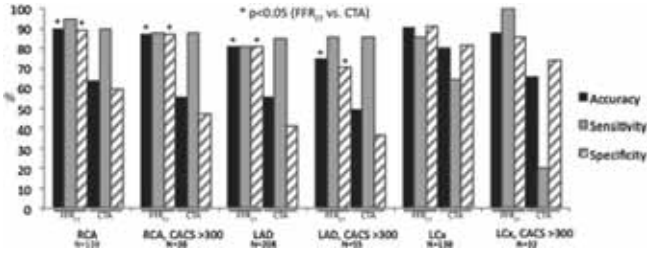
Purpose: Non-invasive fractional flow reserve derived from standard acquired coronary CT angiography (CTA) datasets (FFRct) has shown high diagnostic accuracy in diagnosing lesion-specific ischemia. We aimed to determine the diagnostic performance of FFRct in relation to vessel territory and coronary calcification.
Methods: We performed CTA, FFRct, and FFR with blinded independent analysis. Lesion-specific ischemia was defined by FFRct or FFR $\leq$0.80, CTA steno-

sis >50% was considered obstructive. The diagnostic performance of CTA and FFRct using FFR as the reference standard was evaluated separately in RCA, LAD, and LCx. Outcomes were related to per-patient coronary calcification as assessed by coronary artery calcium score (CACS, cut-off 300).
Results: Out of 254 patients (64±10 years; 62% male; 484 vessels) 214 patients (422 vessels) had CACS performed. Mean (±SD, range) CACS was 302 (±468, 0-3599); 33% had CACS >300. The diagnostic performance of FFRct and CTA in RCA, LAD, and LCx including subgroups with CACS >300 is shown in the figure.



Conclusions: FFRct accurately identifies patients with or without ischemia irrespective of vessel territory. This finding was consistent even in patients with high levels of coronary calcification. The diagnostic performance of FFRct outperforms CTA irrespective of vessel territory and coronary calcification.

4077 | BEDSIDE
Coronary CT angiography-derived fractional flow reserve, performed on-site using a novel reduced-order model, validated by invasive fractional flow reserve

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Purpose: Pressure wire based fractional flow reserve (invasive FFR) has become the reference standard to determine the functional severity of angiographic coronary artery disease. The feasibility of non-invasive coronary blood flow simulations using Computational Fluid Dynamics have recently been reported. In this study, we investigate the performance of novel FFR-CT program allowing for complete on-site FFR-CT computation.
Methods: 106 patients underwent a CCTA followed by an invasive FFR measurement, in total 189 vessels were interrogated with a FFR pressure wire. In 80 (42%) of the 189 vessels a hemodynamic significant stenosis was measured (invasive FFR ≤0.80). The FFR-CT was performed using a reduced-order patient specific model for coronary circulation (cFFR version 1.4).
Results: A moderate too good direct correlation between FFR-CT and invasive FFR (Pearson's correlation r=0.58) was observed. The average value for FFR-CT was 0.77 (SD 0.15) compared with an average of 0.81 (SD 0.15) for invasive FFR. The sensitivity, specificity and accuracy of FFR-CT was respectfully 86% (77-93%), 65% (55-74%) and 74% (68-80%), with an area under the curve of 0.83.
Conclusions: This study provides proof of concept for a reduced-order computational fluid dynamics model in coronary blood flow computation, allowing for on-site FFR-CT computations.

4078 | BEDSIDE
Assessment of myocardial viability after acute myocardial infarction: a head-to-head comparison of the perfusable tissue index by PET and delayed contrast-enhanced CMR

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Purpose: Early recognition of viable myocardium is of great clinical importance after acute myocardial infarction (AMI). Delayed contrast-enhanced magnetic resonance imaging (DCE-CMR) has been validated extensively for the detection of viability. An alternative method for detecting viability is the perfusable tissue index (PTI), a positron emission tomography (PET) derived parameter, which is inversely related to the extent of myocardial scar (nonperfusable tissue). The aim was to investigate the predictive value of PTI on recovery of LV function after percutaneous coronary intervention (PCI) for AMI.
Methods: Twenty-six patients with AMI successfully treated by PCI were included. Subjects were examined one week and three months after AMI with [15O]H2O PET and DCE-CMR to assess PTI, regional function and scar. Viability was defined as recovery of systolic wall thickening (SWT) ≥3.0 mm at follow-up.
Results: A total of 396 segments were available for serial analysis. At baseline, 166 segments were dysfunctional, of which 125 (75%) exhibited significant DCE and were located in the myocardial territory supplied by the culprit-artery. Fourty-nine of these dysfunctional segments showed full recovery during follow-up (viable), whereas 76 segments remained dysfunctional (nonviable). Baseline PTI of viable segments was 0.94±0.07 and was significantly higher compared to non-viable segments (0.80±0.11, p=0.01). The optimal cut-off value for the PTI was 0.85 with a sensitivity of 92% and specificity of 71%, and an area under the curve (AUC) of 0.88. In comparison, a cut-off value of 40% for the extent of DCE resulted in a sensitivity of 75% and a specificity of 65%, and an AUC of 0.75 (p=0.02 vs PTI).
Conclusions: This study shows that assessment of myocardial viability shortly after reperfused AMI is feasible with PET, and that the PTI is a good prognostic indicator for recovery of contractile function when compared to DCE-CMR.

4079 | BEDSIDE
Diagnostic accuracy of transluminal attenuation gradient on 320-detector row CT for detection of functionally significant stenosis assessed by Fractional Flow Reserve (FFR)

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Background: Coronary-computed-tomography-angiography (CTA) has limited specificity for predicting functionally significant stenoses. The opacification gradient of iodinated contrast across coronary stenosis particularly on a 320-detector-row CT which enables near isophasic, single-beat imaging of the entire coronary tree may provide an accurate assessment of functional significance of coronary stenosis.
Method: Patients who underwent CTA on a 320-detector row CT as well as FFR assessment on invasive-coronary-angiography for evaluation of chest pain were recruited. We assessed the diagnostic accuracy of 3 opacification gradients (TAG320, Ga and Gs) to predict functionally-significant-coronary-stenosis using a customised semiautomated software. The luminal-radiological-contrast-attenuation (Hounsfield-Units, HU) was measured at 1-mm intervals along the artery from ostium to a distal level where the cross-sectional-area fell below 2.0 mm^2. TAG320 was defined as the linear-regression-coefficient between luminal attenuation and axial distance. Ga and Gs were defined as the change in HU with respect to the coronary artery lumen area and short axis diameter respectively. Functionally-significant-coronary-stenosis was defined as ≤0.8 on FFR.
Results: In 119 patients (age 64±9 years, 56 males, 185 vessels), TAG320 in FFR-significant-vessels was significantly lower when compared with FFR non-significant-vessels (-21 vs -13 HUs/10 mm, P<0.001]. On receiver-operating-characteristic (ROC) analysis, the AUC for TAG320 predicting FFR ≤0.8 was 0.82 compared to Ga 0.58, Gs 0.61 and CTA 0.8. The combined TAG320 and CTA assessment had an area-under-the-curve (AUC) of 0.88.

Diagnostic accuracy to predict FFR

	CTA	TAG320 <−15.37 HU/10mm	CTA + TAG320
Sensitivity,%	95	85	80
Specificity,%	65	81	95
PPV,%	65	76	92
NPV,%	95	89	87
Diagnostic accuracy,%	77	83	89

Conclusion: TAG320 is superior to Ga and Gs for detecting functionally significant coronary stenoses. Combined TAG320 and CTA may have incremental predictive value for predicting functionally significant coronary stenosis.

4080 | BEDSIDE
Diagnostic accuracy of computed tomography angiography for the detection of coronary artery disease in patients referred for transcatheter aortic valve implantation

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Purpose: To retrospectively determine the diagnostic accuracy of a standardized computed tomography angiography (CTA) for the detection of significant coronary artery disease (CAD) in patients with aortic stenosis referred for transcatheter aortic valve implantation (TAVI).
Methods: A consecutive series of 475 patients (194 male, mean age: 82±6 years) with acceptable dual-source CTA data quality obtained during the routine diagnostic work-up before TAVI were included in the analysis. A total of 6,603 coronary segments in 1,899 coronary arteries ≥1.5 mm in diameter and 271 grafts were evaluated for the presence of significant CAD defined as ≥50% decrease in vessel diameter. Results were compared with invasive coronary angiography as the standard of reference.
Results: Prevalence of significant CAD was 57% (270/475), and 5,925 coronary

Diagnostic accuracy of pre-TAVI CTA

	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Coronary segments	5925	81	80	38	96
Coronary vessels	1899	95	60	53	96
Bypass grafts	257	97	94	72	99
Patients (all)	475	98	37	67	94
Patients (fully evaluable)	216	97	57	66	96
Patients with prior CAD	254	98	23	81	82
Patients without prior CAD	221	97	43	47	97

CAD: coronary artery disease; CTA: computed tomography angiography; NPV: negative predictive value; PPV: positive predictive value; TAVI: transcatheter aortic valve implantation.

segments (90%) and 257 grafts (95%) were evaluable on CTA. In the per-patient analysis, sensitivity (Se), specificity, positive and negative predictive value (NPV) were 98%, 37%, 67% and 94%, respectively. CTA showed satisfactory ability to exclude significant CAD in the following subgroups: (1) patients (216/475) with fully evaluable coronary segments (Se: 97%, NPV: 96%), (2) patients (221/475) without prior CAD (Se: 97%, NPV: 97%), and (3) bypass grafts (Se: 97%, NPV: 99%).
Conclusions: A comprehensive evaluation of a pre-TAVI CTA could prove to be a useful rule-out test for significant CAD in selected subgroups of patients with fully diagnostic CT data, patients without previously known CAD, and bypass grafts.

4081 | BEDSIDE
Comparison of Agatston score and global plaque volume using multi-detector computed tomography in a large patient cohort

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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 correlation between Agatston score and the total burden of coronary plaque.
Patients and methods: Data sets of 1405 consecutive patients referred for coronary computed tomography (CT) angiography due to suspected coronary artery disease were included in this analysis. All CT examinations were performed with a 64-slice CT scanner, a first or a second generation dual source system (Siemens Healthcare, Forchheim, Germany). The total Agatston score was quantified in native data sets using semi-automatic software. In coronary CT angiography data sets, the entire coronary tree was visually assessed for the presence of calcified and non-calcified plaque using the 18-segment coronary model recommended by the society of cardiovascular computed tomography. Each coronary segment was visually evaluated for the presence of calcified and non-calcified plaque defined as lesions that were distinguishable from the surrounding connective tissue, with a CT density above or below the contrast enhanced lumen for calcified and non-calcified plaque, respectively, and could be identified in two independent planes.For segments deemed to have plaque, parallel cross-sections of 1 mm slice thickness and 1 mm distance were obtained. Non-calcified and calcified plaque cross-sections were manually traced to obtain the plaque volume. The volume of calcified and non-calcified plaque in all coronary segments was added together to obtain the global plaque burden.
Results: The mean age of all 1405 patients (61% males and 38% females) was 64±12 years and mean BMI was 19±13 kg/m^2. The mean heart rate during CT acquisition was 59±9 bpm. The mean Agatston score was 143±338 and the mean volume of total plaque was 1.89±5 mm^3. The total Agatston score showed a very close and significant correlation to total plaque volume (r=0.885, p<0.0001, figure 1). 43% of the patients (607 patients) had an Agatston score of 0 and 38% of patients had no identifiable plaques (537 patients). In 14% of patients with a 0 calcium score (88 patients), non-calcified plaque was identified in one or more segments of the coronary tree (mean volume: 1.1±1.8 mm^3).
Conclusion: In a large patient cohort, global measures of calcified and total plaque burden show a very close and significant correlation. However, in 14% of all patients with a zero calcium score, non-calcified plaque is present, which might influence risk modification strategies.

STATE OF THE ART – FUNCTIONAL IMPORTANCE OF REGULATORY RNA SPECIES

4082 | BENCH
CARMEN, a long noncoding RNA controlling cardiogenesis in cardiac progenitor cells

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Purpose: Cardiovascular disease and in particular heart failure are major causes of morbidity and mortality in the Western world. The mammalian heart has limited regenerative capacity. Therefore, the notion of promoting cardiac regeneration in the damaged heart has recently engendered considerable research interest. Development of the cardiovascular system, including the heart, is a multistep process coordinated by a network of specific transcriptional programs. In this context, it is emerging that the noncoding portion of the genome is dynamically transcribed, generating thousands of long noncoding RNAs (lncRNAs), which are central orchestrators of these networks. Controlled expression of cardiogenic lncRNAs in undifferentiated stem cells could therefore provide new ways of directing precursor cells toward the cardiac fate.
Methods: For these reasons, we profile the human long noncoding transcriptome during cardiogenesis in isolated human cardiac precursor cells (CPC) using custom microarrays designed to target annotated lncRNAs (GENCODEv7). We identified numerous lncRNAs, which are differentially expressed during CPC differentiation. Amongst the most upregulated lncRNAs was one originating from the mir-143/145 locus, which was named CARMEN (Cardiac Mesoderm Enhancer-associated Noncoding RNA).
Results: CARMEN is conserved in mammals. Therefore, we first validated the modulated expression of CARMEN in various human and mouse models of cardiogenesis. In particular, CARMEN is upregulated in differentiating mouse embryonic stem (mES) cells and P19 embryonic carcinoma cells, suggesting a role for CARMEN during cardiac mesoderm specification and subsequent differentiation into cardiomyocytes. We then generated a shRNA hairpin able to knockdown CARMEN in mES and P19 cells. Consistently, silencing of CARMEN interferes with the normal cardiogenic program in these two cell types.
Conclusions: We demonstrated that CARMEN has a crucial role in cardiogenic differentiation. Our finding that CARMEN is required for cardiac specification suggests that lncRNAs represent a class of molecular modulators that could be useful to force undifferentiated stem cells to adopt a cardiac fate. To conclude, identification and functional characterization of cardiogenic lncRNAs should provide new therapeutic targets for inducing efficient cardiac regeneration in the diseased heart.

4083 | BENCH
Functional importance of cardiac enhancer-associated noncoding RNAs during cardiac development and disease

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Purpose: Cis-regulatory modulation of tissue specific gene expression is central to the correct execution of gene regulatory networks (GRNs) that underpin cardiac development and disease. The key information processing units within GRNs are enhancers. Enhancer function is thought to be mediated by long distance genomic interactions and epigenetic remodelling at target gene promoters. In the heart, the existence of cardiac enhancer-derived transcripts such as noncoding RNAs has not been established. The main purpose of our study is to characterise cardiac enhancer expression during heart development and pathological cardiac remodelling.
Methods: We utilised a genome-wide epigenomic screen to identify approximately 3,000 fetal cardiac enhancers. The expression of seven enhancer-associated transcripts was then measured during heart development and in different model systems of cardiac differentiation. Furthermore, we evaluated whether enhancers demonstrated active transcription in the damaged heart as part of the reactivation of the fetal gene program, a hallmark of the response of the adult heart to stress.
Results: Enhancer expression correlated with the emergence of active enhancer chromatin states, the initiation of RNA polymerase II at enhancer loci and expression of putative target genes. Some of these transcripts are polyadenylated, multi-exonic long non-coding RNAs. Orthologous human sequences also exhibit enhancer-associated p300 enrichment in the fetal and adult human heart, with orthologous enhancer-derived transcripts being upregulated during cardiac differentiation of isolated human cardiac progenitor cells. Enhancer-associated noncoding RNA knockdown resulted in specific downregulation of its predicted target gene. Moreover, we demonstrate that the re-activation of the fetal gene programme in response to myocardial stress is accompanied by increased expression of fetal cardiac enhancer transcripts.
Conclusions: In this study we show that fetal cardiac enhancers generate noncoding RNAs during cardiac development in vivo and during cardiogenic differentiation of precursor cells in vitro. We also demonstrate that enhancer-associated noncoding RNA expression is regulated in pathophysiological models of heart disease in vivo. Altogether, these findings indicate that the activity of cardiac enhancers and expression of their target genes rely on the production of enhancer-derived noncoding RNAs.

4084 | BENCH
MicroRNA-33a, embedded in Srebf2 gene, regulate lipogenetic pathway in vivo

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Background: MicroRNAs (miRs) are small non-protein-coding RNAs that bind to specific mRNAs and inhibit translation or promote mRNA degradation. Recent reports, including ours, indicated that miR-33 located within the intron of sterol regulatory element binding protein (SREBP) 2 controls cholesterol homeostasis and can be a possible therapeutic target for treating atherosclerosis. Unexpectedly, miR-33 deficient (miR-33–/–) mice developed severe hepatic steatosis and the mechanisms were investigated.
Methods and results: miR-33–/– mice showed marked worsening of high fat diet (HFD) -induced hepatic steatosis. The liver weight of miR-33–/– mice were about 1.5 times heavier that that of miR-33+/+ mice and histological examination revealed that miR-33–/– mice fed HFD developed severe fatty liver with accumulation of lipid droplets. The total triglyceride levels in the liver were significantly increased in miR-33–/– mice fed HFD compared with miR-33+/+ mice fed HFD.

In order to determine the cause of the hepatosteatosis observed in miR-33–/– mice fed HFD, we analysed the gene expression profiles by microarray analysis using the liver of miR-33+/+ and miR-33–/– mice fed normal chow at the age of 16 weeks when their weights were the same. As a result, genes involved in fatty acid metabolism were upregulated in miR-33–/– mice. We searched for potential target genes of miR-33 and found that one of the targets is SREBP-1. We confirmed that miR-33 targeted the 3'UTR of SREBP-1 in vitro. The expression of SREBP-1 and de novo fatty acid production were significantly increased in miR-33–/– mice. We further intercrossed miR-33–/– mice with Srebf1+/– mice and fed them HFD. Hepatic steatosis was reversed in miR-33–/–Srebf1+/– mice compared with miR-33–/–Srebf1+/+ mice under pair-feeding conditions. The expression levels of genes involved in fatty acid synthesis, including Scd1, Fasn, Acc1, and Pparg were increased in miR-33–/–Srebf1+/+ mice compared with miR-33+/+Sregf1+/+ mice, and this was reversed in miR-33–/–Srebf1+/– mice.
Conclusions: These results demonstrate that miR-33 defficiency showed severe hepatic steatosis under HFD and miR-33 regulates lipogenic pathway through regulating SREBP-1 as a novel target. In sterol-depleted conditions, acetyl-CoA might be preferred as a substrate for cholesterol production and not for fatty acid production by the downregulation of SREBP-1 through the upregulation of miR-33. On the contrary, in cholesterol-rich condition, acetyl-CoA might be preferred as a substrate for fatty acid production through the downregulation of miR-33.

4085 | BENCH
Endothelial microparticles reduce ICAM-1 expression in a microRNA-222-dependent mechanism

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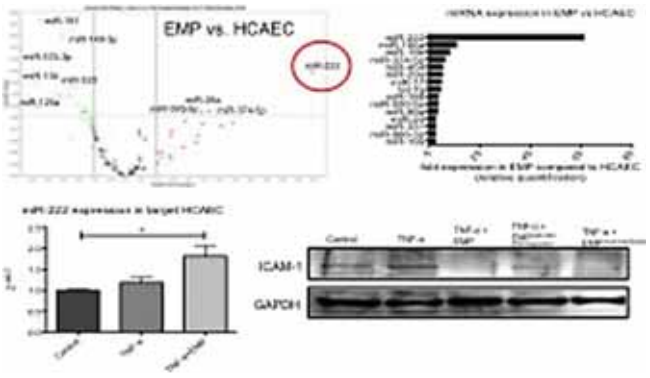
Objective: Endothelial microparticles (EMP) are released from activated or apoptotic endothelial cells (ECs) and can be taken up by adjacent endothelial cells, but their effect on vascular inflammation after engulfment is largely unknown. We sought to determine the role of EMP in endothelial cell inflammation.
Methods and results: In vitro, EMP treatment significantly reduced TNF-α-induced endothelial ICAM-1 expression on mRNA and protein level, whereas there was no effect on VCAM-1 expression. Reduced ICAM-1 expression after EMP treatment resulted in diminished monocyte adhesion in vitro. In vivo, systemic treatment of ApoE–/– mice with EMP significantly reduced murine endothelial ICAM-1 expression and infiltration of macrophages into atherosclerotic plaques. In order to explore the underlying mechanisms, Taqman microRNA-array was performed and microRNA (miR)-222 was identified as the strongest regulated miR between EMP and endothelial cells. Following experiments demonstrated that miR-222 was transported into recipient endothelial cells by EMP and functionally regulated expression of its target protein ICAM-1. Interestingly, after simulating diabetic conditions, EMP derived from glucose-treated ECs contained significantly lower amounts of miR-222 and showed reduced anti-inflammatory capacity in vitro and in vivo.



Conclusions: Endothelial microparticles promote anti-inflammatory effects in vitro and in vivo by reducing endothelial ICAM-1 expression via the transfer of functional microRNA-222 into recipient cells. In pathological hyperglycaemic conditions, EMP-mediated miR-222-dependent anti-inflammatory effects are reduced.

4086 | BENCH
Hypoxia-sensitive long non-coding RNAs (LNCRNAs) in endothelial cells

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Introduction: During angiogenesis, either pro- or anti-angiogenic signalling guides endothelial cells to sustain vascular integrity. One of the most potent pro-angiogenic signalling cascades involves hypoxic conditions. The role of non-coding RNAs, such as microRNA (miR), has been extensively studied in the past. Here, we questioned if human long non-coding RNAs (LncRNAs) would be differentially expressed after hypoxic treatment in human umbilical vein endothelial cells (HUVECs).
Methods and results: HUVECs were cultured under normoxic or hypoxic (0.1% O2, 24 h) conditions and total RNA was analyzed by microarray and RNA-sequencing analysis. We identified a set of deregulated LncRNAs after hypoxic intervention. Expression levels of hypoxia-sensitive LncRNAs were validated via qRT-PCR. With this approach, we identified the intergenic highly upregulated LncRNA HSLINCR. Of note, hypoxia induced HSLINCR specifically in the cytoplasm of endothelial cells. However no association of HSLINCR to Argonaute 2 (Ago2), a prominent RNA-binding protein, was found. Loss of function experiments using siRNA revealed a crucial participation of HSLINCR in intercellular processes, e.g. proliferation, cell cycle progression and capillary tube formation. Interestingly, endogenous HSLINCR knockdown altered gene expression profiles related to cell cycle control and angiogenesis. More specifically, the GATA2-SIRT1 axis and ERK signalling were disturbed by transient repression of HSLINCR. Overexpression studies were also applied to study enhanced HSLINCR expression in various settings in vitro.
Conclusion: In summary, based on arrays and RNA sequencing of LncRNAs in endothelial cells, we here report functional relevance of a single hypoxia-sensitive intergenic LNCRNA HSLINCR in human endothelial cells after hypoxia.

STATE OF THE ART – RENAL DENERVATION FOR HYPERTENSION: END OF THE BEGINNING OR BEGINNING OF THE END?

4102 | BEDSIDE
Prediction of blood pressure reduction after renal denervation based on intraprocedural norepinephrine spill-over drop reflecting sympathetic nerve disconnection

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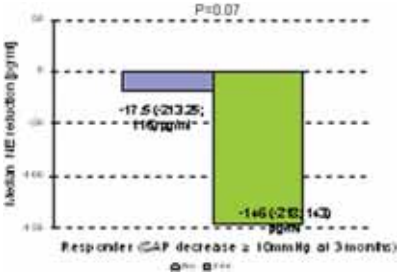
Background: Catheter-based renal denervation (RDN) is a promising new treatment option for refractory hypertension. Interestingly, only 50-70% of patients have a relevant reduction in 24h ambulatory blood pressure (BP) after RDN and the characteristics predicting the BP response are still unclear.
Methods: In this prospective study, we evaluated 40 patients with RDN for the changes of pre- and postprocedural norepinephrine (NE) and epinephrine (E) levels measured from the renal artery (RA) and vein (RV) with complete ABP follow-up. We defined the respective spill-over for ΔNE and ΔE as the difference RV-RA and compared this difference before and after the procedure, reflecting the extent of renal nerve disconnection.
Results: At three months, we observed a reduction of the mean systolic ABP from 179±21mmHg to 171±22mmHg (P=0.08). There was a significant decrease of the ΔNE RV-RA spill-over comparing pre- with post-procedural levels (160pg/ml±211 decrease to 104pg/ml±151, P=0.05), reflecting the effective renal nerve disconnection during RDN with decreased nerval NE release. There was no significant change for the epinephrine spill-over (90pg/ml±355 vs. 57pg/ml±202, P=0.41), serving as a control parameter. There was a strong trend for a higher NE spill-over reduction for patients with BP response (P=0.07 for patients with ≥10mmHg systolic BP reduction).



NE spill-over reduction and BP response.

Conclusions: The decrease of norepinephrine spill-over (veno-arterial difference) during RDN is an easily assessable physiologic marker reflecting the direct effects of RDN leading to disconnection of sympathetic nerves. There is a correlation between BP response and reduction of the NE spill-over during RDN with predictive value for the procedural success.

4103 | BEDSIDE

Renal denervation with cryoenergy as second-line option in the treatment of resistant hypertension in non-responders to radiofrequency ablation

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Aims: Renal denervation (RDN) with radiofrequency (RF) is beeing used to treat resistant hypertension (rHTN). As 15-30% of treated patients are non-responders to RDN, we investigated whether RDN with cryoenergy can serve as second-line option.
Methods and results: Ten non-responder patients (mean age 55 years, 6 male) with rHTN were treated with cryoenergy for RDN. In order to qualify as non-responders, patients had to reveal systolic 24-h ambulatory BP (ABP) ≥150 mmHg (median ABP 179/100 mmHg, median office-based BP [OBP] 193/108 mmHg) despite treatment with ≥4 different antihypertensive drugs (mean 6), and further did not show a reduction of systolic ABP ≥10 mmHg at ≥3 months after RDN with RF. The 3/6/12-month follow-up (FU) comprised clinical and biochemical evaluation, OBP, and ABP measurement. At 6 months duplex sonography was performed additionally.
Results: Cryoablation with a 7 French cryoablation catheter (Freezor Xtra; Medtronic Inc.) was performed in all patients without complications (4 applications in both renal arteries, each 4 minutes, temperature -75 °C). At 3/6/12 months we found reduction in systolic OBP of -28/-39/-53 mmHg (n=10/8/5; p for all <0.01), diastolic OBP of -18/-14/-30 mmHg, systolic ABP of -25/-27/-48 mmHg (n=9/6/6, p for all <0.05), and diastolic ABP of -17/-13/-27 mmHg, respectively. During FU, no complications occurred and the renal function remained unchanged. Three patients performed additionally bicycle exercise tests (up to 125 W) at 6 months, with adequate increase in BP and heart rate.
Conclusion: The significant reduction in systolic OBP and ABP observed, qualifies RDN with cryoenergy as second-line therapeutic option in non-responders to RDN with RF.

4104 | BEDSIDE

Renal sympathetic denervation is inferior to adjusted drug treatment in patients with true treatment resistant hypertension, a randomized controlled trial

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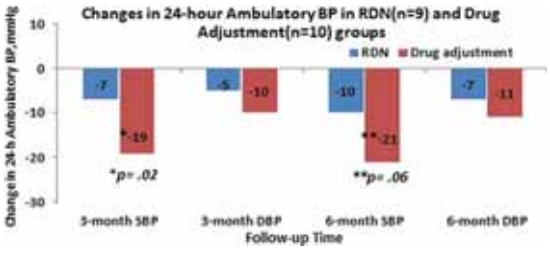
Purpose: Renal sympathetic denervation (RDN) has been introduced as a new treatment of hypertension that is resistant to drug treatment (TRH). However, the randomized and controlled documentation that RDN lowers blood pressure (BP) is limited. We aimed to investigate the BP lowering effect of RDN versus clinically adjusted drug treatment in true TRH after excluding patients with poor drug adherence.
Methods: Patients with apparent TRH (n=65) were referred specifically for RDN and those with secondary and spurious hypertension (n=26) were excluded. TRH was defined as office systolic BP>140 mmHg despite maximally tolerated doses of at least 3 antihypertensive drugs including a diuretic. Additionally, ambulatory daytime systolic BP>135 mmHg following witnessed intake of antihypertensive drugs was required, after which 20 patients had normalized BP, indicating poor drug adherence. Patients with true TRH were randomized and underwent RDN (n=9) versus adjusted drug treatment (n=10).
Results: 24-hour ambulatory systolic and diastolic BPs in the drug adjustment group changed from 151±12/85±6 mmHg (±SD) at baseline to 130±12/74±7 mmHg at 6 months (p=0.001 and p<0.0005, systolic and diastolic BP, respectively), and in the RDN group from 149±9/89±15 to 139±10/82±4 mmHg (p=0.02 and p=0.01, respectively). The absolute reduction in systolic BPs were higher in the drug adjustment group at 3 and 6 months compared to RDN group (p=0.02 and p=0.06, respectively). Pulse pressure, daytime and nighttime ambulatory BPs changed in parallel to the 24-hour ambulatory BPs.



Conclusions: Our data suggest that RDN has inferior lowering effects compared to adjusted drug treatment in patients with true treatment resistant hypertension after excluding patients with confounding poor drug adherence.

4105 | BEDSIDE

Effects of spironolactone and renal denervation on blood pressure in patients with resistant arterial hypertension: a case-control study

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Purpose: Both spironolactone and catheter-based renal denervation (RDN) are used to treat patients with resistant arterial hypertension. It is not known which method is more effective. The aim of our study was to compare the effects of spironolactone and RDN on office and ambulatory blood pressure in patients with resistant hypertension.
Methods: Office blood pressure and daytime, night-time and 24-hour ambulatory blood pressure (ABPM) were evaluated at baseline and after 3 months in 24 patients who undervent RDN using the Symplicity Catheter System (Medtronic, Mountain View, CA, USA). Using the propensity score method we identified 44 matched controls from the ASPIRANT-EXT trial database treated by spironolactone (25 mg daily), whose blood pressure (BP) was assessed at baseline and after 8 weeks of treatment. Statistical significance of differences was analysed using Mann-Whitney U test for continuous variables or Fisher exact test for categorical variables.
Results: Both groups were well matched in baseline characteristics. Mean baseline office BP was 161/90 mmHg and mean 24-hour ambulatory BP was 148/83 mmHg while patients were using mean 4.7 antihypertensive drugs. BP change after treatment in both groups is shown in Table 1. With the exception of office diastolic BP, spironolactone treatment lead to greater BP reductions than RDN.

Table 1

Blood pressure (mm Hg)	RDN (N=24)	Spironolactone (N=44)	Between-group difference	P
Systolic				
ABPM systolic daytime BP	–6.05 (±16.20)	–11.31 (±13.41)	–5.3 (–13.0; 2.5)	0.082
ABPM systolic night-time BP	–2.75 (±18.38)	–11.42 (±14.71)	–8.7 (–17.3; –0.1)	0.002
24-h ABPM systolic BP	–5.25 (±16.52)	–11.41 (±11.92)	–6.2 (–13.4; 1.1)	0.022
Office systolic BP	–14.50 (±21.52)	–18.91 (±17.26)	–4.4 (–14.2; 5.4)	0.236
Diastolic				
ABPM diastolic daytime BP	–2.35 (±7.54)	–5.57 (±8.24)	–3.2 (–7.6; 1.1)	0.067
ABPM diastolic night-time BP	0.50 (±9.58)	–3.88 (±9.39)	–4.4 (–9.5; 0.7)	0.010
24-h ABPM diastolic BP	–1.95 (±7.71)	–4.66 (±7.28)	–2.7 (–6.7; 1.3)	0.171
Office diastolic BP	–7.09 (±9.03)	–5.73 (±15.51)	1.4 (–5.8; 8.5)	0.446

Conclusions: Spironolactone reduced BP more effectively than renal denervation in this case-control study. A randomized controlled trial comparing the efficacy of these two methods is warranted.

STATE OF THE ART – AORTIC STENOSIS: NEW CHALLENGES

4115 | SPOTLIGHT

Prediction of the prevalence of aortic stenosis in the elderly in Iceland in the future: The AGES-Reykjavik study

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Purpose: To evaluate the prevalence of significant aortic valve stenosis (AS) in a randomly selected study population of elderly individuals representing the general population of Iceland. Further more, to predict the number of individuals likely to have severe AS in the coming decades.
Methods: Echocardiography and computer tomography (CT) data from individuals who participated in the AGES-Reykjavik study were used. Echocardiography data from 685 individuals (58% females) aged 67- 95 years (mean 76±6 years) were used. Severe AS was defined as an aortic valve area index of <0.6 cm^2/m^2. An aortic valve calcium score by CT was available in a study cohort of 5256 individuals (58% females) who's age ranged from 67 to 96 years (mean 76±6 years). A ROC analysis on the relation between the echocardiography data and the aortic valve calcium score on CT defined a score >500 to indicate severe AS with a sensitivity and specificity of 70% and 95%, respectively. Data from the "Statistics Iceland" institution on the current size, age and sex distribution of the population and it's prediction in to the sixth decade was also used.
Results: By echocardiography the prevalence for severe AS in both sexes for the age groups <70, 70-79 and ≥80 years was found to be 0.92%, 2.4% and 7.3%, respectively. By CT, the prevalence was 0.80%, 4.0% and 9.5%, respectively. Overall, in individuals >70 years and the genders combined, the prevalence of severe AS by echocardiography and CT was 4.3% and 5.9%, respectively. A prediction on the number of elderly according to age groups for the coming decades, until 2060, showed that the largest increase will be in the age groups 70-79 years and >80 years. The number of elderly individuals over >70 years predicted to have severe AS by echocardiography will increase from 1230 in the year 2012, to 2989 in 2040 and 3954 in 2060. By CT assessment in the same age category,

however, 1762 individuals had severe AS in 2012, and their number is predicted to increase to 4184 and 5495 in the years 2040 and 2060, respectively. Thus, the relative increase by echocardiography and CT data was predicted to be similar.
Conclusion: In a study cohort of elderly individuals representative of the general population in a Nordic country, the overall prevalence of severe AS by echocardiography and CT in individuals >70 years was found to be 4.3% and 5.9%, respectively. With the rapid increase in the elderly population the number of patients with severe AS will have increased 2.4 fold by the year 2040 and is predicted to more than triple in the next half a century.

4116 | BEDSIDE
Predictors of long-term outcomes in asymptomatic or minimally symptomatic patients with significant aortic stenosis undergoing treadmill stress echocardiography

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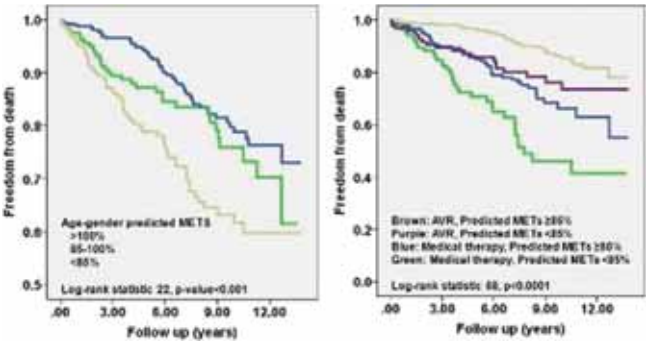
Background: Management of asymptomatic patients with significant aortic stenosis (AS) is controversial & exercise stress echocardiography (ESE) can aid in symptom assessment and timing of aortic valve replacement (AVR). We sought to assess the predictors of outcomes in asymptomatic/minimally symptomatic patients with moderate-severe & severe AS undergoing ESE.
Methods: We studied 755 asymptomatic/minimally symptomatic patients (age 66±13 years, 71% men, 29% coronary artery disease or CAD) with AV area (AVA) ≤1.3 cm^2 that underwent ESE between 2000-12. Clinical, echocardiographic & exercise variables [metabolic equivalents (METs), % of age-gender predicted METs & heart rate recovery (HRR) at 1st minute post-exercise] data were recorded. Endpoint was all-cause mortality.
Results: Mean glomerular filtration rate (GFR), ejection fraction, AV gradients, AVA, indexed left atrial dimension (iLAD), METs and HRR were 85±33 ml/kg/1.73 m^2, 47±20%, 26±12 mm Hg, 1.02±0.2 cm^2, 2±0.4 cm/m^2, 7.8±3 and 27±12 beats/minute, respectively. 54% achieved >100% age gender predicted METs, while 21% were between 85-100% and 24% <85%. Over 4.7±3.8 years, 422 (56%) underwent AVR (59% combination surgeries) & there were 146 (19%) deaths. On multivariable Cox Hazard analysis, % age-gender predicted METs (Hazard ratio or HR 0.87 [0.82-0.92]), abnormal HRR (HR 2.69 [1.85-4.01]), GFR (HR 1.12 [1.07-1.31]), AV surgery as time-dependent (HR 0.43 [0.29-0.67]), iLAD (HR 2.2 [1.27-3.79]) & CAD (HR 2.08 [1.22-3.57]) independently predicted mortality (all p<0.01).



ESE and long term outcomes in AS.

Conclusion: In asymptomatic/minimally symptomatic patients with moderate-severe & severe AS undergoing ESE, a higher % of age-gender predicted METs & AV surgery improved survival, while abnormal HRR, low GFR, higher iLAD & CAD were associated with reduced survival.

4117 | BEDSIDE
Clinical outcome of patients with aortic stenosis and coronary artery disease undergoing incomplete treatment strategies

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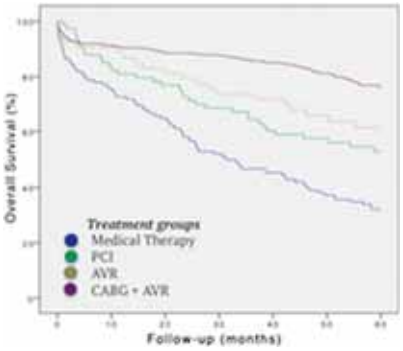
Purpose: Current guidelines recommend aortic valve replacement (AVR) with coronary artery bypass graft (CABG) in patients (pts) with moderate-to-severe aortic stenosis and significant coronary lesions. In real world, this is not always feasible due to advanced age and comorbidities. We sought to evaluate clinical outcome of pts treated not according to recommendations.
Methods: From 2002 to 2010, we retrospectively included 583 pts with moderate to severe aortic stenosis and at least one significant coronary lesion (diameter stenosis>50%): 134 (23%) were treated with medical therapy only (Gr 1), 74 (13%) with percutaneous coronary intervention (PCI) (Gr 2), 54 (9%) with AVR (Gr 3), and 321 (55%) with combined CABG and AVR (Gr 4). Primary endpoint of the study was overall death up to 5 years.
Results: Pts' characteristics like logistic euroSCORE (Gr 1: 18±13 vs. Gr 2: 16±15 vs. Gr 3: 15±14 vs. Gr 4: 11±10, p<0.01) and number of vessels diseased (Gr 1, 1.75±0.9 vs. Gr. 2, 1.85±0.9 vs. Gr 3, 1.28±0.6 vs. Gr 4, 2.13±1 years, p<0.01) were significantly different among the 4 groups. At median follow-up of 59 months, overall death significantly decreased along the groups (Gr 1, 88 [67%] vs. Gr 2, 34 [47%] vs. Gr 3, 20 [38%] vs. Gr 4, 74 [23%], p<0.01) (see figure). Compared to Gr 1, Cox-regression analysis adjusted for potential confounders showed a significant decrease in risk of death of Gr 2 (HR: 0.61 [0.4-0.94], p=0.027), Gr 3 (HR: 0,58 [0.44-0.77], p<0.01) and Gr 4 (HR: 0.6 [0.53-0.68], p<0.01).



Kaplan-Meier for survival at 60 months.

Conclusions: In pts with aortic stenosis and at least one significant coronary lesion, we confirm that medical therapy only is associated with the worst clinical outcome. Our data suggest that when combined CABG and AVR is not feasible, PCI or AVR alone significantly improve long-term survival.

4118 | BEDSIDE
Frailty: incidence and prognostic value in high risk patients with severe aortic stenosis treated with transcatheter aortic valve implantation or aortic valve replacement

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Aim of the study: To compare the incidence of frailty in patients with severe aortic stenosis treated with transcatheter aortic valve implantation (TAVI) or aortic valve replacement (AVR) and to assess the influence of frailty on midterm outcome.
Methods: We enrolled 178 consecutive patients treated with TAVI (112pts) or high-risk AVR (66pts) in our Institution. AVR was considered at high risk based on age >75 years or Logistic EuroSCORE ≥20. Frailty was defined as: body mass index <20kg/m^2 or baseline serum albumine <3.5 g/dL or Geriatric Status Scale 3/3 (two of following items/3 if incontinence: totally dependence for transfers, totally dependence in one or more activities of daily living; bowel and bladder incontinence, dementia).
Results: Patients in the AVR group were younger (80±4 vs. 82±6 years, p=0.01), had lower logistic EuroScore (12.3±6.3% vs. 22.1±13.3%, p<0.001), and less frequently presented with NYHA class III/IV (43.9% vs. 87.5%, p<0.001) or unstable angina (0 vs. 3.7%,p<0.001). The incidence of frailty was 18.0% (3.0% AVR vs. 26.8% TAVI, p<0.001) so distributed: no patient in the AVR group had GSS 3, while it was 5.4% in the TAVI group; BMI <20kg/m^2 1.5% AVR and 8.0% TAVI (p=0.06); serum albumine <3.5g/dL 1.5% AVR and 16.2% TAVI (p<0.001). One year mortality was 18.3% (10% AVR vs. 20% TAVI, Figure 1). At Cox regression analysis, the presence of a frailty status at baseline was a predictor of midterm mortality either alone (HR 2.7, CI 95%1.5-4.9, p<0.001) or corrected by Logistic EuroSCORE (Frailty: HR 2.6, CI 95% 1.5-4.9, p=0.001; Logistic EuroSCORE HR 1, CI 95% 0.99-1.03, p=0.56).

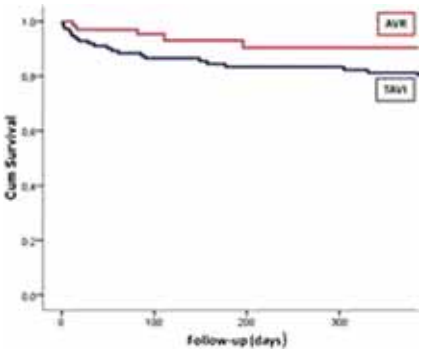

Figure 1

Conclusions: The incidence of frailty is higher in patients treated with TAVI and is

associated with a poorer outcome. Hence, frailty appropriate diagnosis may help to avoid futile procedures.

4119 | BEDSIDE

Outcome of patients with severe prosthetic aortic stenosis undergoing redo surgical aortic valve replacement

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Purpose: With improved survival of patients undergoing primary aortic valve replacement (AVR), reoperation for severe prosthetic aortic stenosis (PAS) is increasing. We sought to determine outcomes of severe PAS patients undergoing redo surgical AVR.
Methods: We studied 345 consecutive patients with severe PAS (63±15 years, 55% men) that underwent redo-AVR between 2000-12 (excluding transcatheter AVR). Clinical, echocardiographic & surgical data were recorded. PAS was defined as AV area <1 cm^2 &/or transvalvular mean gradient ≥40 mm Hg. A composite outcome of death & admission for congestive heart failure was recorded.
Results: There were 17% patients in Functional class (FC) I, 58% in Class II & 25% in Class III-IV. 27% had atrial fibrillation (AF). Average Euroscore, left ventricular ejection fraction & mean AV gradient were 10±3, 54±12% & 53±16 mm Hg, while 26% had >II+ aortic regurgitation (AR). There were 72% bioprostheses, 15% mechanical & 14% homografts. Only 39% had an isolated AVR, the rest were combination surgeries (only 1.7% needed another redo AVR in follow-up). At 4.4±4 years, 81 (24%) patients had events (18% deaths, including 2.3% at 30-days). After adjusting for clinical, echo and surgical variables, increasing Euroscore (Hazard ratio or HR 1.21 [1.11-1.32], p<0.001), worsening FC (HR 1.72 [1.13-2.61], p=0.01), AF (HR 2.05 [1.22-3.46], p<0.001) & AR degree (HR 1.32 [1.05-1.67], p=0.01) predicted worse outcomes. Kaplan-Meier curves of PAS patients are shown in Fig. 1A, B. Freedom from event was similar for different AV prosthesis (log-rank 4, p=0.1).

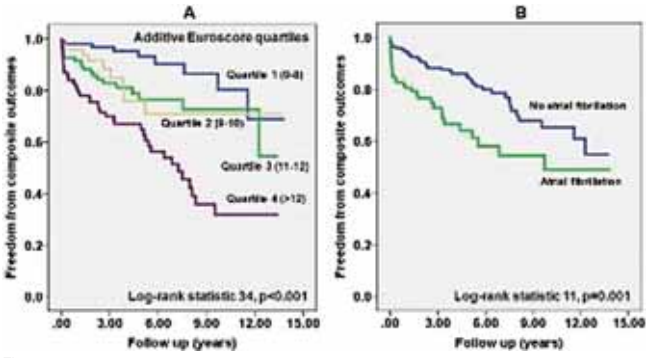

Figure 1

Conclusions: At an experienced center, patients with severe PAS undergoing redo AVR have excellent short-term outcomes, with long-term outcomes predicted by increasing Euroscore, worsening FC, AF & degree of concomitant AR.

STATE OF THE ART – STRUCTURAL HEART INTERVENTION BEYOND TAVI

4125 | BEDSIDE

Implantation of one versus two clips in MitraClipTherapy: Differences in patient characteristics and outcomes in the German TRAMI registry

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Purpose: MitraClip has emerged as a viable option for percutaneous treatment of mitral regurgitation in surgical high risk patients. Although initially designed as one-clip strategy, it has been rapidly found that more than one clip is feasible and may be necessary to yield a satisfactory result. No data comparing one- and multiple-clip strategies are available.
Methods: The German TRAMI registry prospectively enrolled 803 patients who underwent MitraClip therapy at 21 German centers between August 2009 and July 2013. 1 clip was used in 461 patients (57.4%), 2 clips in 312 (38.9%), and 3 or more clips in only 30 patients (3.7%). We compared baseline characteristics and short-term outcomes in patients with 1 and 2 clips, respectively.
Results: Patients with 2-clips strategy were more likely to be male (68.9% vs. 54.7%, P<0.0001) and taller in body height (172±9 cm vs. 168±9 cm, P<0.0001). Moreover, the prevalence of dilated cardiomyopathy (14.1 vs. 8.2%, P<0.05), the history of previous cardiac decompensation (61.6 vs. 51.0%, P<0.01), and implantable cardioverter defibrillator therapy (45.2 vs. 32.7%, P<0.05) were significantly more frequent. In addition, patients with 2 clips had larger left ventricular dimensions (left ventricular enddiastolic diameter 60 [54-68] mm vs. 58 [51-65] mm, P<0.05) and were less likely to have preserved ejection fraction (26.4 vs. 33.6%, P<0.05). There was a trend to higher NT-pro BNP levels (3863 [2089-7100] vs. 3272 [1450-6151]), and more patients exhibited a positive troponin test (40.4 vs. 30.6, P<0.05). Patient allocation to non-surgical treatment was more often done by the heart team (65.1 vs. 56.4%, P<0.05) reflecting the more complex patient population. Procedural success (defined as successful clip placement and residual regurgitation grade mild or less) was lower (80.5 vs. 89.1, P<0.001) in patients with two clips, and total procedure time (114.5±52.1 min vs. 90.9±50.7 min, P<0.0001) and radiation time (32.2±30.8 vs. 26.0±71.2 min, P<0.0001) were longer. Finally, patients with 2 clips were more prone to experience rapid re-hospitalization within a median of 8 weeks after discharge because of heart failure (9.0 vs. 3.4%, P<0.01). Apart from that, acute and short-term safety was similar between the two groups.
Conclusions: Selection criteria for a two-clip strategy are influenced by constitutional (male gender, height) and cardiomyopathy-related factors (etiology, left ventricular dimensions). It should be kept in mind that these patients are more prone to procedural failure and rapid re-hospitalization. 6 month follow-up data will be available early in 2014.

4126 | BEDSIDE

Percutaneous ventricular restoration (PVR) using the Parachute device in ischemic dilated heart failure patients: pooled analysis of the first 100 patients treated with 12 month follow-up

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Background: Left ventricle (LV) remodeling after anterior wall myocardial infarction (AWMI) leads to increased LV volumes, myocardial stress, and ultimately heart failure (HF). Treatment options are limited for these high-risk HF patients. We performed a pooled analysis of the first 100 patients treated for 1 year follow-up with the Parachute device.
Aims: To confirm the acute safety and acute and long-term efficacy of PVR using an expanded range of Parachute device sizes in patients with ischemic HF with prior AWMI.
Methods: One hundred patients with NYHA class II-IV HF secondary to AWMI, with akinetic or dyskinetic wall motion abnormality, and LV ejection fraction <40%, were enrolled into 3 non-randomized trials in the United States and Europe. Major endpoints were death and repeat hospitalization.
Results: As of the last data cut in late 2013 when 79 patients had been treated for 1 year, the 1-year mortality rate was 3.8% and the combined death and HF hospitalization rate was 17.7%. The 1-year paired hemodynamic results on 73 patients showed that heart rate and blood pressure remained stable, while statistically significant improvement was seen in LV volume, LV contractility, and LV filling pressure as demonstrated by left atrial volume reduction. Functional improvement (measured by NYHA class) was improved in 59% of patients and maintained in 33% at 1 year. The full cohort of 100 patients will be available for the ESC congress.
Conclusions: This pooled analysis of PVR using an expanded range of Parachute device sizes in patients with ischemic HF and prior AWMI confirms the safety and longer term efficacy of this approach to treating HF.

4127 | BEDSIDE

Bleeding risk and clinical benefit of WATCHMAN left atrial appendage closure in patients eligible for oral anticoagulation: a pooled analysis of the PROTECT-AF and PREVAIL randomized clinical trials

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Purpose: Left atrial appendage closure (LAAC) with the WATCHMAN is non-inferior to warfarin for prevention of cardiovascular death, stroke, or systemic embolism. The relative benefit of LAAC in warfarin-eligible patients according to bleeding risk has not been evaluated.
Methods: Results from the PROTECT-AF and PREVAIL trials, which compared WATCHMAN LAAC with warfarin in warfarin-eligible patients, were pooled and categorized according to HAS-BLED score<4 (low) or ≥4 (high). No points were assigned for liver disease or labile INR, as these data were not collected. A pro-

portional hazards model was used to assess the relationship between HAS-BLED category, treatment group, major bleeding, and efficacy events occurring >7 days post-implant. Rates are reported as events/patient-years.
Results: A total of 307 patients had low and 768 patients had high HAS-BLED score. High HAS-BLED score was associated with a significantly greater adjusted bleeding risk (HR 2.17, 95% CI 1.16-4.50, p=0.024), and LAAC with a significantly lower adjusted bleeding risk (HR 0.55, 95% CI 0.34-0.89, p=0.014).The bleeding reduction with LAAC was most pronounced among patients with high HAS-BLED scores (see table), although there was no significant interaction between treatment group and HAS-BLED score (p=0.37). The adjusted rates of primary efficacy events were lower (HR 0.61, 95% CI 0.40-0.95, p=0.027) and ischemic strokes similar (HR 1.09, 95% CI 0.54-2.34, p=0.82) with LAAC and were not influenced by HAS-BLED score.

Bleeding events in the pooled trials

HAS-BLED score category	WATCHMAN		Warfarin	
	% (n/N)	Events/Pt-Years N=693	% (n/N)	Events/Pt-Years N=382
0–3	3.1% (6/193)	1.3 (6/454)	3.5% (4/114)	1.4 (4/286)
4+	5.8% (29/500)	2.0 (29/1468)	11.2% (30/268)	4.1 (30/728)

Bleeding events after 7 days were significantly lower with WATCHMAN with or without adjustment for HAS-BLED score, and the reduction in bleeding was most pronounced in patients with higher HAS-BLED scores.

Conclusions: In the PROTECT-AF and PREVAIL trials, patients randomly assigned to LAAC had a lower risk of bleeding with or without adjustment for HAS-BLED score. Patients with higher HAS-BLED scores receiving LAAC had a numerically greater reduction in bleeding events, with similar efficacy and ischemic stroke reduction compared with warfarin, suggesting that the WATCHMAN device may be of particular benefit in patients at highest risk of bleeding.

4128 | BEDSIDE
Mid-term follow-up after transseptal transcatheter mitral valve-in-valve and valve-in-ring implantation

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Purpose: Redo surgery following failed mitral valve replacement or repair may be associated with high morbidity and mortality. We sought to evaluate the feasibility as well as the immediate and mid-term results of transseptal transcatheter heart valve (THV) implantation in patients with failed mitral bioprostheses (BP) and ring annuloplasty (RA).
Methods and results: Transseptal implantation of a balloon-expandable THV was performed in 17 patients after failed mitral surgery (6 BP, 11 RA) between March 2011 and February 2013. The procedure was performed on an elective basis in 14 patients and attempted as an emergency rescue intervention in 3 patients. Mean age was 61±24 years. All patients were in New York Heart Association (NYHA) class ≥III. Furthermore, the risk of redo surgery was high (Logistic EuroSCORE 37±29%, EuroSCORE II 20±22%, STS 18±22%). The procedure was successful in 15 patients (88%). Two complications occurred during emergency procedures: 1 procedural death and 1 THV migration. Mean gradient decreased from 12±6 to 8±3 mmHg and residual regurgitation was trace or less in 12 patients (75%) and mild in 4 patients (25%). During a mean follow-up of 22 months, 4 patients died: 1 from a non-cardiac cause, 2 from sudden death, and 1 from an unknown cause. The 18-month survival was 68±14% in the overall population and 78±14% for patients who underwent an elective procedure (Fig. 1). One patient underwent mitral valve replacement due to early paravalvular mitral regurgitation. At last follow-up, 12 patients were in NYHA class ≤II (75%) and 4 in class III (25%).

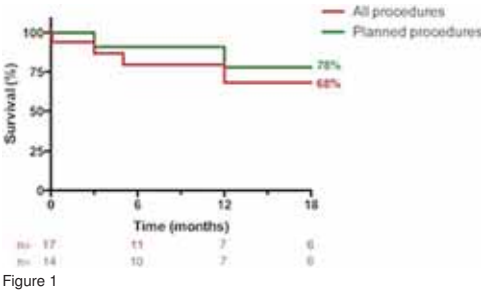

Figure 1

Conclusions: This single-centre series suggests that transfemoral THV implantation for failed mitral surgery is feasible in selected patients and improves early hemodynamic and mid-term functional status.

4129 | BEDSIDE
Early and late complications after transcatheter pulmonary valve implantations

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Transcatheter pulmonary valve implantation (TPVI) is a valid alternative to reoperation in patients with right ventricular outflow tract (RVOT) dysfunction after surgical correction of congenital heart disease. The aim of this report was to analyze complications after TPVI in short- and middle-term follow-up.
Patients and methods: Between Dec. 2008 and Dec. 2013 TPVI was performed in 51 pts (aged 25.3±8.2 y) with RVOT dysfunction after surgical correction of tetralogy of Fallot (n=30), pulmonary atresia (n=9), aortic stenosis (Ross operation, n=5), others (TGA, DORV, pulmonary stenosis, CATII, n=7). RVOT was reconstructed with the full conduit in 30 pts and with a patch in 21 pts. Valve implantation was preceded with bare metal stent insertion in all pts. Melody valve was used in 32 pts, SAPIEN™ in 19 cases.
Results: TPVI was successfully performed in 46 pts (90.2%): pulmonary gradient decreased from 79.5±36,7 to 36,6±20.4, p<0,0001, pulmonary competence was restored. Serious procedural and/or in-hospital complications were observed in 5 pts. Urgent operation was necessary in 3 pts (ES) because of tricuspid valve damage (2 pts) or stent migration during valve implantation (1 pt). Elective surgery was performed in 2 pts after MM implantation (calcified aortic homograft rupture and early valve compression). None of surgical revision procedures led to mortality. Pulmonary oedema in the 1st hour after TPVI was observed in 1 case, transient fever in 23 pts in the first 2 days after TPVI (MM-20 pts, 63% and ES-3 pts, 19%). In one case right bundle branch block developed during the procedure. There were no significant vascular access site complications observed.
46 pts after successful TPVI were observed for 29.4±18.8 months (1 mo-5 yrs). Survival in follow-up was 95.7% (2 pts died because of infective endocarditis), freedom from reintervention – 87.0%. Freedom from infective endocarditis was 89.1%. Infective endocarditis was diagnosed in 5 pts 3 months - 3 years after the procedure (fever -5 pts, pulmonary valve dysfunction - 4 pts, vegetations - 1 pt). Neither stent rupture nor noninfective valve degeneration were observed.
Conclusions: (1) TPVI is a safe and efficient procedure both for pts with full conduit and selected pts with patched RVOT dysfunction; (2) Infective endocarditis was the main cause of mortality, morbidity and re-intervention.

STATE OF THE ART – RETHINKING CURRENT HEART FAILURE THERAPIES

4139 | SPOTLIGHT
The SODIUM-HF (Study of Dietary Intervention Under 100 MMOL in Heart Failure) Pilot Results

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Background: Guideline recommended level of dietary sodium intake for heart failure (HF) patients is variable reflecting limited randomized controlled trial (RCT) evidence. The objective of this pilot study was to determine the feasibility of conducting a RCT comparing a low-sodium to a moderate-sodium diet in HF patients.
Methods: HF patients were randomized to low (1500 mg/day) or moderate-sodium (2300 mg/day) diet. Patients received structured dietary counselling and menu plans; dietary intake was evaluated using 3-day food records. The endpoints were KCCQ scores and BNP from baseline to 6 months of follow-up.
Results: 38 pts were enrolled (19/group). After 6 months, median sodium intake dropped from 2137 to 1398 mg/day in the low-sodium and 2678 to 1461 mg/day in the moderate-sodium diet group. Median BNP levels changed over 6 mo in the low-sodium diet group (216 to 71 pg/ml, Δ51 pg/ml [-2,331], p=0.006) and in the moderate-sodium diet group (171 to 188 pg/ml, Δ36 pg/ml [-51,62], p=0.7; p=0.17 between groups). Over 6m, median KCCQ scores increased in low-sodium diet group (63 to 75, Δ9 [2,15], p=0.006), and trended to increase in the moderate-sodium group (66 to 73, Δ6 [-1,15], p=0.07); p=0.4 between groups. At 6m, a post hoc analysis based on the dietary sodium intake achieved (> or ≤1500 mg/day)

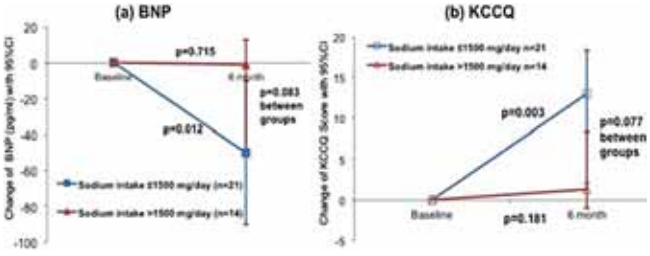

Figure 1

showed an association between achieved dietary sodium and improvement in BNP levels and KCCQ scores (Fig. 1a and b, respectively).
Conclusions: The dietary intervention was feasible and effective in reducing sodium intake in HF patients. A dietary sodium intake ≤1500 mg/day was associated with lower BNP levels and improved quality of life in HF patients and informs the design of an adequately-powered, clinical event driven RCT.

4140 | BEDSIDE
Maintenance of normal serum K+ with ZS-9 once daily in patients with CHF: subgroup analysis of a phase 3 multicenter, randomised, double-blind, placebo-controlled trial of patients with hyperkalaemia

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Hyperkalemia (HK) limits use of RAAS inhibitors (RAASi) in patients (pts) who derive the greatest cardiovascular or survival benefit, such as those with congestive heart failure (CHF), chronic kidney disease (CKD), or diabetes. ZS-9, a nonabsorbed cation exchanger designed to entrap potassium (K+) in the gut, significantly reduced serum K+ vs placebo (PBO) over 48 hr with excellent tolerability in pts with CKD and HK. We performed a predefined subset analysis in pts with CHF from a large phase 3 trial of ZS-9 for HK.
Methods: Pts (N=753) with K+ 5.0-6.5 mmol/L were randomized (1:1:1:1:1) to ZS-9 (1.25g, 2.5g, 5g or 10g) or PBO orally 3X daily for 48 hr (acute phase). At the end of this phase, pts with K+ 3.5-5.0 mmol/L (n=542) were re-randomized 1:1 to the same ZS-9 dose given acutely or PBO once daily (QD) for Day 3-15 (extended phase) (if they were on ZS-9 acutely), or re-randomized to 1.25g or 2.5g ZS-9 QD (if they were on PBO acutely). RAASi were kept constant during the study. We used unpaired t-test to compare serum K+ in the subset of pts with CHF treated with the highest ZS-9 dose (10g) vs PBO.
Results: Of 753 pts, 300 (40%) had CHF at baseline as determined by investigator, of whom 72% were on RAASi. Mean baseline K+ was 5.3 mmol/L in pts with CHF. Of the CHF pts, 204 entered the extended phase. Of these, 26 remained on 10g ZS-9 and 23 were switched to PBO. Their extended phase baseline K+ was comparable (4.4 vs 4.5 mmol/L) and similar to the overall group (4.5 [n=63] vs 4.4 [n=61] mmol/L). On Day 15, mean K+ (mmol/L) was 4.5 in CHF pts on 10g ZS-9 vs 5.0 in those switched to PBO (p=0.002; Fig. 1).

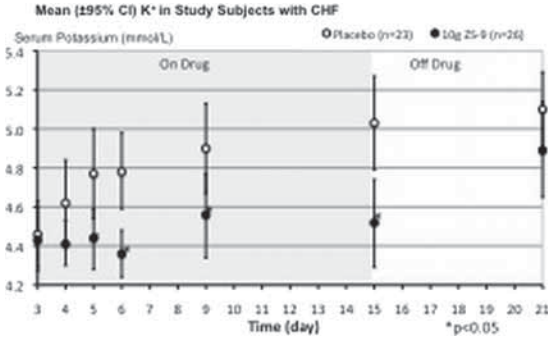

Figure 1

Conclusion: 10g ZS-9 once daily maintained mean serum K+ <5.0 mmol/L in pts with CHF despite RAASi continuation in most pts, indicating that ZS-9 facilitates use of RAASi in pts with CHF and HK.

4141 | BEDSIDE
Ant-inflammatory treatment with colchicine in stable chronic heart failure: a prospective, randomized study

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Background: Chronic heart failure (CHF) has been shown to be associated with inflammatory activation and inflammation has been designated as a therapeutic target in CHF.
Objectives: The purpose of this study was to test the efficacy of a 6-month course of anti-inflammatory treatment with colchicine in improving the functional status of patients with stable CHF.
Methods: Patients with stable CHF were randomized to colchicine – 0.5 mg twice daily – or placebo for 6 months. The primary endpoint was the proportion of patients achieving at least one-grade improvement in New York Heart Association (NYHA) class.
Results: 267 patients were available for final evaluation of the primary endpoint: its rate was 11% in controls and 14% in the colchicine group (odds ratio 1.40; 95% confidence interval 0.67-2.93; p=0.365). The rate of the composite of death or hospitalization for heart failure was 9.4% in the control group, compared with 10.1% in the colchicine group (p=0.839). The Kaplan-Meier mean hospitalization-free survival was 24.8 weeks (95% confidence interval 24.1-25.5) in controls compared to 24.7 weeks in the colchicine group (95% confidence interval 24.0-25.5). The changes in treadmill exercise time with treatment were insignificant and similar in the two groups (p=0.938). C-reactive protein and interleukin-6 were both significantly reduced in the colchicine group (-5.1 mg/l and -4.8 pg/ml, respectively; p<0.001 for both, compared to the control group).
Conclusion: According to this prospective randomized study, anti-inflammatory treatment with colchicine in patients with stable CHF, although effective in reducing inflammation biomarker levels, did not affect in any significant way patient functional status (in terms of NYHA class and objective treadmill exercise tolerance) or the likelihood of death or hospitalization for heart failure.

4142 | BEDSIDE
Heart Failure and autoantibodies against the beta1 adrenoreceptor

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Activating Antibodies specific for the β1-adrenergic receptor (AA-bAK) are found in patients with heart failure (HF) of various etiologies. Earlier studies have shown that passive transfer of AA-bAK induces HF in rodents, indicating a pathophysiological role in the generation of HF. So far, detection of AA-bAK had been difficult and methods applied were not suitable for clincial routine. Recently, we have established an ELISA based assay to detect AA-bAK. In this study we want to investigate if AA-bAK are present in patients with heart failure and if the levels are modified by treatment with carvedilol or bisoprolol.
An ELISA to detect AA-bAK was developed by CellTrend. AA-bAK were measured in 556 patients from the CIBIS-ELD trial population. 115 patients suffered from HF with preserved ejection fraction (HFpEF) and 454 with reduced ejection fraction (HFrEF). 198 healthy volunteers without relevant cardiovascular diseases served as controls (58.3±7.4 years, 33.7% male). Patient with ejection fraction (EF) <55% (1±0.271) or LVEDD >55 cm were statistically significant higher compared to the other patient groups as well as controls. In a multivariate analysis with sex, NYHA, BMI, systolic and diastolic blood pressure as covariates, only the relation to LVEDD remained significant.The level of AA-bAK correlated negatively with the EF in the follow up visit (r=-0.108, p=0.048). AA-bAK correlated positively with basal heart rate (r=0.062, p=0.028) and with the heart rate at follow up 12 weeks later (r=0.141, p=0.004). We observed a negative correlation to the change in HR during the study period (r=0.099, p=0.045). There was no relation of baseline AA-bAK to either pre-study use of beta blockers. A follow up sample after 12 weeks showed also a significant correlation with LVEDD and a negative with EF. AA-bAK at follow up were significantly higher in patients treated with bisoprolol compared to carvedilol (p=0.05), however, no differences were observed for the final dosis of either carvedilol or bisoprolol achieved.
We found autoantibodies against the b1-adrenoreceptor in patients with heart failure. They correlated negatively with ejection fraction and positively with heart rate at baseline and in the follow up. The presence of AA-bAK were independent of the presence or dosage of beta blocker. Further studies have to evaluate the relevance of this new biomarker.

4143 | BEDSIDE
Changes in ventricular ectopy with cardiac resynchronization therapy and associated clinical outcome

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Background: Patients with frequent ventricular ectopy on pre-implantation Holter derive less benefit from cardiac resynchronization therapy (CRT), but it is unclear if changes in ventricular ectopy after CRT implantation affect subsequent clinical outcome.
Methods: In the MADIT-CRT study, 698 CRT-D patients underwent 24 hour (h) Holter monitoring pre-implantation and 1 year post-implantation. The mean number of ventricular premature complexes (VPCs) per hour was calculated. A high level of VPCs was defined as >10 VPCs/h. Changes in VPCs/h from pre-implantation to 1 year Holter were evaluated. Starting follow-up at 1 year and adjusting for relevant factors, Cox regression analyses were used to investigate the risk of heart failure (HF) or death associated with changes in VPC level.
Results: At 1 year, 241 (35%) patients had experienced a reduction in ectopy >50%. Patients with a 1 year unchanged low VPC level (≤10 VPCs/h) were at the lowest risk of HF/death (figure).
When compared to patients with an unchanged high level (>10 VPCs/h), patients who had a reduction in VPCs from >10 VPCs/h to ≤10 VPCs/h had a 60% reduced risk of HF/death (HR=0.40 [0.17-0.93], p=0.034), similar to the risk in

patients with an unchanged low level of VPCs (HR=0.35 [0.18-0.66], p=0.001) (figure). When compared to patients with an unchanged low VPC level, an increase in VPCs to >10 VPCs/h was associated with a significant increase in the risk of HF/death (HR=2.97 [1.35-6.51], p=0.007), similar to the risk of patients with an unchanged high level of VPCs (HR=2.90 [1.51-5.56], p=0.001).

Changes in ectopy and risk of HF/death.

Conclusion: Reduction in ventricular ectopy to ≤10 VPCs/h in patients receiving CRT was associated with a significant reduction in the risk of HF/death, whereas an increase to >10 VPCs/h was associated with an adverse prognosis.

STATE OF THE ART – INNOVATION IN ACUTE CORONARY SYNDROMES

4153 | BEDSIDE

Impact of coronary plaque morphology assessed by optical coherence tomography on cardiac troponin elevation in patients with non-st segment elevation acute coronary syndrome

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Background and aims: Elevations of cardiac troponin (cTn) frequently occur after percutaneous coronary intervention (PCI), and it is unclear whether a new cTn release following PCI provides additional prognostic significance. We used optical coherence tomography (OCT) to study the relationship between pre-PCI plaque morphology and post-PCI cTn elevations in patients with non-ST-segment elevation acute coronary syndrome (NATE-ACS). We further assessed the association between post-PCI cTn elevations and adverse cardiac event during follow-up.
Methods and results: We studied 181 patients with NSTE-ACS who had identifiable native de novo culprit lesions suitable for PCI and OCT examination. All patients underwent OCT imaging before stent implantation. Cardiac troponin I (cTnI) was analyzed on admission, before PCI, and after PCI, and periprocedural myocardial injury (PMI) was defined as a patient showing stable pre-PCI cTnI values or fall, followed by post-PCI cTnI rise >20%. Forty patients (22.1%) with increasing cTnI values before PCI were excluded from subsequent analyses. We finally evaluated 141 patients with stable or falling cTnI values after admission. Clinical and OCT findings were compared between patients with (n=61, 43%) or without (n=80, 57%) PMI. After PCI, long-term follow-up data were collected. Thin-cap fibroatheroma (TCFA) was defined as lipid-rich plaque (one or more quadrants) with fibrous cap thickness <70μm. PMI was associated with prior PCI (PMI: 29.5% vs non-PMI: 6.2%, P<0.001), angiographic lesion length (PMI: median 15.6 mm [IQR: 12.3-18.1] vs non-PMI: 12.2 mm [IQR: 10.5-16.7], P=0.007), presence of OCT-derived TCFA (PMI: 60.7% vs non-PMI: 30.9%, P<0.001), and plaque rupture (PMI: 42.6% vs non-PMI: 25.9%, P=0.036). In multivariable analysis, presence of TCFA (odds ratio, 3.19; 95% confidence interval, 1.50 to 6.76, P=0.003) and prior PCI (odds ratio, 7.25; 95% confidence interval, 2.36 to 22.27, P=0.001) were independent predictors of PMI. At a median follow-up of 17 months, event free survival (ACS, stroke, cardiac death) was significantly worse in patients with PMI (log-rank test $\chi 2 = 6.90$, P=0.009).
Conclusions: OCT analysis showed that post-PCI myocardial injury occurs more frequently in lesions with TCFA in NSTE-ACS patients treated by stent implantation. OCT may allow identification of NSTE-ACS patients who are likely to have PCI-related myocardial injury, who may have higher risk of adverse cardiac events during follow-up despite otherwise successful PCI.

4154 | BEDSIDE

A novel cloud-based mobile 12-lead ECG optimized EMS and significantly reduced door-to-reperfusion time for STEMI patients

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Current ACCF/AHA guidelines recommend that 12-lead ECG should be performed in prehospital care for ST-elevation myocardial infarction (STEMI) as Class IB, whereas it still remains underachieved because optimal standard ECG system is not yet established. To expand the availability of prehospital 12-lead ECG, we developed a mobile 12-lead ECG system EC-12R characterized by a modern Android application coupled with secure cloud computing-based telecommunication system on cellphone infrastructure (MCECG). We conducted two clinical trials to clarify the feasibility and clinical efficacy of MCECG. Trial A: To test whether this can contribute to appropriate use of emergency service, we installed MCECG in 5 clinics located at 64±39 km distance from the center hospital. With accurate diagnosis in the case of EMS dispatch based on instantly shared 12-lead ECG with EMS personnel and cardiologist, patient transfer by EMS was required for only 4 cases out of 32 (12.6%). Case-Control Trial B: To test whether MCECG achieves reduction of myocardial ischemic time of STEMI patients, we equipped a rapid response car with MCECG (Fig. 1). Door-to-reperfusion time for STEMI was significantly shortened in MCECG group compared to conventional group (56.1±13.7 min, n=32 vs 74.0±14.1 min, n=76, p<0.001).

Figure 1

The results together demonstrate that MCECG is feasible and clinically effective, which is a noteworthy solution based on mobile ICT to expand practical use of prehospital 12-lead ECG for STEMI patients at inexpensive cost.

4155 | SPOTLIGHT

Effects of RVX-208 on major adverse cardiac events (MACE), apolipoprotein A-I and High-Density-Lipoproteins; A post-hoc analysis from the pooled SUSTAIN and ASSURE clinical trials

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Introduction: The epigenetic Bromodomain and extra-terminal (BET) inhibitor RVX-208 is characterized by bromodomain 2 selectivity and gene repression resulting in anti-inflammatory effects as well as activation of apolipoprotein A-I (apoA-I) transcription. The latter translates to an increase in plasma ApoA-I and HDLs. A surprise finding from the phase 2b program including the SUSTAIN (n=176, 1:1 randomization) and ASSURE (n=323, 3:1 randomization) clinical trials in cardiovascular disease (CVD) patients was the significant 55% relative risk reduction in Major Adverse Cardiac Events (MACE; death, non-fatal MI, revascularization, hospital admittance for cardiac reasons) (18/323 vs. 17/178, p=0.02 by log rank Kaplan-Meier).
The trials comprised of CVD patients with HDL cholesterol below 40mg/dL possibly explaining the high MACE rate observed. Patients were treated for 6 months with RVX-208 200mg per day or placebo added on top of standard of care, including either Rosuvastatin or Atorvastatin. In the two trials combined 331 patients received RVX-208 and 168 patients received placebo.
Methods: The below analysis was performed to assess if Reverse Cholesterol Transport markers including apoA-I, HDL-cholesterol and HDL particles by nuclear magnetic resonance (NMR) would help explain the observed MACE relative risk reduction.
Results: Assessing the difference between RVX-208 and placebo for change of the HDL variables and hsCRP at 6 months compared to baseline we observed a larger increase in the RVX-208 group for apoA-I (9.9% vs. 4.8%, p<0.001), HDL-cholesterol (7.69% vs. 0.0%, p<0.001), HDL-particle number (6.5% vs. 0.4%, p<0.001) and average HDL size (1.17% vs. 0.00%, p<0.01).
Conclusion: In summary RVX-208 treatment on top of standard of care generated significant elevations in plasma apoA-I and down-stream HDL variables compared to placebo. These findings may help explain the significant reduction of MACE observed in the RVX-208 treated patients compared to placebo control

in the two studies combined. These and additional analysis are useful in identifying the target responder population and designing future confirmatory trials.

4156 | BEDSIDE
Prognostic implications of major bleeding on mortality in ACS patients. An analysis of the PLATO trial

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Purpose: To evaluate the relative impact of PLATO major bleeding on short and long-term mortality according to the type of bleeding.
Methods: The PLATO trial is an international randomized trial comparing ticagrelor and clopidogrel in ACS patients. A Cox proportional hazard model with time-dependent indicator of bleeding assessed the relationship between major bleeding and mortality. We allowed for different bleeding effects for the short-term and long-term (within 30 days and more than 30 days after bleeding respectively). Models were adjusted for potential confounders previously identified in the PLATO study to be associated with mortality.
Results: Of 18 624 patients, 2 213 (11.9%) had at least one PLATO major bleeding event (493 spontaneous; 1515 CABG-related, 237 cath (PCI or angiography) -related; and 90 non-coronary procedure related major bleeding). Complete case data for all adjustment covariates was available on 14 509 patients. Adjusted impact on long and short term mortality according to the type of bleeding is presented in the table.
Conclusions: Major bleeding are overall associated with a higher short term but similar long-term mortality. However, we observed important variation of the impact according to the type of bleeding: spontaneous bleeding impacts both short-term and long-term mortality whereas cath - related bleeding doesn't seem to impact mortality.

4157 | BEDSIDE
Beneficial effect of thrombusaspiration in patients with STEMI - Results from the FITT-STEMI multicenter trial

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Introduction: Percutaneous coronary intervention (PCI) is the therapy of choice for a quick coronary recanalization in patients with ST-Segment Elevation Myocardial Infarction (STEMI). However, persisting thrombus burden frequently is responsible for impaired microcirculation. In the TAPAS trial, it was suggested that thrombus aspiration results in a significantly reduced mortality and re-infarction in STEMI patients after one year. However, in the recently published TASTE trial, no benefit for thrombus aspiration was observed. Thus, our aim was to investigate the outcome of STEMI patients with and without thrombus aspiration in a subanalysis of our multicenter FITT-STEMI trial.
Methods: Between 2007 and 2014 a total of 12,433 consecutive patients with STEMI were enrolled in the FITT-STEMI trial, 29 primary PCI hospitals in Germany and more than 100 associated non-PCI hospitals participated. Data from patient contact to balloon inflation were collected and analyzed and we compared all STEMI patients treated with thrombus aspiration versus conventional PCI without thrombus aspiration.
Results: Thrombus aspiration was performed during acute PCI in 1,219 of 12,433 patients with STEMI (9.8%). Contact to balloon (C2B) time did not significantly differ between patients treated with thrombus aspiration compared to conventional PCI (C2B median: 93 vs. 95 min.). The in-hospital mortality was significantly lower in patients treated with thrombus aspiration versus conventional PCI (5.9% vs. 7.8%, p=0.036). There was no significant difference in TIMI-Risk-Score (TRS) between patients with thrombus aspiration and conventional PCI (3.642 vs. 3.75). Regarding the effect of thrombus aspiration for different TRS subgroups, in patients with low risk (TRS 0-2, n=3,894 STEMI) interestingly no prognostic effect of thrombus aspiration was found (in-hospital mortality: 0.7% vs. 0.7%). In contrast, in patients with higher risk (TRS >2, n=6,879 STEMI) an almost significantly reduction of in-hospital mortality by thrombus aspiration compared to conventional PCI was observed (9.1 vs. 11.7%, p=0.063). Comparing the effect of thrombus aspiration for different treatment times, patients with C2B time >120 min. had a 2.1% reduction in mortality compared to only 1.2% for C2B time <120min.
Conclusion: In our multicenter trial, we show that thrombusaspiration during acute PCI leads to a significant improvement of prognosis, which is more related to those STEMI-patients with higher risk and prolonged C2B time. Therefore, further randomized trials are required to investigate the benefit of thrombusaspiration in this subpopulation.

STATE OF THE ART – THE GLOBAL THREATS OF SMOKING AND POOR DIET: MEETING THE CHALLENGES

4167 | BEDSIDE
Cigarette consumption reduces cardiac function and increase the risk for incident heart failure in the Multi-Ethnic Study of Atherosclerosis

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Background: Pack years of cigarette consumption (PYCC) reflects the accumulated lifetime exposure to smoking and is associated with reduced pulmonary function. However, the association with cardiac function or incident congestive heart failure (CHF) in the absence of cardiovascular disease has not been established. We hypothesized that PYCC had a significant relationship with left ventricle (LV) long axis strain (LAS), a sensitive marker of LV function, and with incident heart failure events in the Multi-Ethnic Study of Atherosclerosis (MESA), a population free from evident cardiovascular disease at inclusion.
Methods: At baseline, PYCC was registered in 6790 asymptomatic MESA participants (53% men). Moreover, long axis strain was assessed from conventional cine cardiac MR images in a randomly selected cohort (n=1656, 53% men). All participants were followed for a median of 7.0 years. We tested the association between PYCC and LAS using linear regression, and the association between PYCC and incident CHF using Cox regression analysis after adjustment for Framingham risk score for heart failure events (age, gender, BMI, heart rate, systolic blood pressure or hypertension, diabetes and LV mass indexed to body surface area).
Results: A total of 172 HF events were observed. PYCC was significantly associated with reduced LAS even after adjustment (Table). LAS was significantly higher in never smokers compared to ever smokers (11.9±2.4 vs 11.3±2.7, p=0.003). PYCC was significantly associated with incident heart failure events, before and after adjustment (Table), with a 6% increased risk per 10 PYCC. Differentiation between current and previous smokers did not significantly affect the results.

Correlations, PYCC

	n	Univariate	P	Multivariate	P
Linear regression, LAS	1656	–0.132	<0.001	–0.06 (–0.14, –0.02)	0.007
Cox regression, CHD-events	6790	1.06 (1.03–1.09)	<0.001	1.06 (1.02, 1.11)	0.004

Pack years of cigarette consumption (PYCC) significantly correlate with long axis strain (LAS) and congestive heart failure (CHF) development. Hazard ratio is reported for 10 PYCC.

Conclusion: Reduced left ventricle systolic function assessed by long axis strain is associated with pack years of cigarette consumption. Moreover, the risk for incident congestive heart failure increases with increasing lifetime cigarette consumption, independent of current smoking status.

Abstract 4156 – Table 1. Impact of major bleeding event

	Short term bleeding effect (bleed to 30 days post bleed)		Long term bleeding effect (>30 days post bleed)		P-value for difference) (short vs long)
Exposure	HR (95% CI)	P-value	HR (95% CI)	P-value	
Major bleeding overall	9.15 (7.40–11.32)	<0.001	1.27 (0.93–1.75)	0.133	<0.001
Major bleeding: spontaneous (non-procedure)	13.65 (10.39–17.93)	<0.001	3.29 (2.20–4.92)	<0.001	<0.001
Major bleeding: CABG-related	5.62 (4.14–7.63)	<0.001	0.84 (0.53–1.32)	0.454	<0.001
Major bleeding cath (PCI or angiography)-related	1.82 (0.81–4.10)	0.149	1.15 (0.51–2.60)	0.728	0.436
Major bleeding: non-coronary procedure or surgery	6.92 (3.61–13.25)	<0.001	2.01 (0.82–4.92)	0.127	0.026

4168 | BEDSIDE

Expired-air carbon monoxide is an independent determinant of 16-year risk of all-cause, cardiovascular and cancer mortality in a general population

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Purpose: Expired-Air Carbon Monoxide (EACO) measurement is a simple and cheap method fluently used to validate non-smoking status in ex-smokers. EACO is not a specific marker of smoking. It would be a marker of inhaled ambient Carbon Monoxide (CO) and of endogenous production related to inflammation. The effects on health of smoking and acute CO intoxication are well known but the association of EACO with health seems to have never been studied. The aim of this study was to assess 16-year risk of all-cause mortality according to EACO levels at the baseline, in a general population.
Methods: Our analysis was based on the Third French MONICA Cross-sectional survey on cardiovascular risk factors (1995-1996). Participants aged 35-64 were randomly recruited from the general population of three areas. Vital status was obtained 16 years after inclusion, and assessment of determinants of mortality was based on multivariable Cox modelling.
Results: EACO was measured in 2232 participants and 195 deaths occurred over the 16-year period (19.5% due to a cardiovascular (CV) cause and 51% due to a cancer cause). At the baseline, mean EACO was 11.8 (±7.4), 4.6 (±2.5), 4.3 (±2.2) ppm for current, past and non-smokers, respectively. Considering total mortality, after adjustment for smoking (and pack-years), sex, age, blood pressure, LDL-cholesterol, diabetes, gamma-glutamyl transpeptidase (GGT) and mean corpuscular volume (MCV) (as an objective marker of alcohol consumption), high school completion and centre, the hazard ratio (HR) for 1 ppm increase of EACO was 1.034[95% confidence interval: 1.009-1.060]. For CV mortality, after adjustment for sex, age, blood pressure, LDL-cholesterol, diabetes, GGT and MCV, high school completion and centre, HR was 1.046[1.001-1.093]. After additional adjustment for smoking, EACO was not yet associated with CV mortality (HR=0.991[0.929-1.057]). For cancer mortality, after adjustment for smoking, sex, age, GGT and MCV, high school completion and centre, HR for EACO was 1.042[1.014-1.071]. Interactions between CO and smoking were not significant.
Conclusions: In a general population, after extensive adjustment for risk factors and smoking, baseline EACO is an independent determinant for long term all-cause and cancer mortality. As expected, smoking is more predictive than EACO for CV mortality. Moreover, the effect of EACO being similar in smokers and non-smokers (none interaction), EACO is not specific to smoking and would be a marker of inhaled ambient CO and/or of endogenous production related to inflammation.

4169 | BEDSIDE

Fresh fruit consumption, blood pressure and cardiovascular disease risk: a prospective cohort study of 0.5 million adults in the China Kadoorie Biobank

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Purpose: To investigate the association of fruit consumption with blood pressure and risk of cardiovascular disease (CVD) among Chinese adults.
Methods: We analysed 7-year prospective data of 0.5 million individuals enrolled into the China Kadoorie Biobank from 10 diverse localities across China. Among the 451,682 participants with no prior history of CVD nor on anti-hypertensive treatment at baseline, there were 10,003 cases of ischaemic heart disease (IHD) and 15,922 cases of stroke (12,671 ischemic and 3,251 haemorrhagic) identified through electronic linkage with mortality and morbidity registries as well as with national health insurance system. Habitual consumption of fresh fruit (categorized into 5 groups), collected through an interviewer-administered computerized questionnaire, was related to measured systolic and diastolic blood pressure (SBP and DBP respectively) and incidence of IHD and stroke, using multivariable linear regression and Cox proportional Hazard models, with adjustment for potential confounders, including body mass index.
Results: The overall mean age was 50.5 years and mean SBP was 128.8 mmHg, with 18% participants reporting consuming fruit daily and 6.3% never/rarely. Individuals who consumed fruit more frequently had significantly lower blood pressure, with daily consumption associated with 3.4/1.4 mmHg lower SBP/DBP compared with never/rarely group. A dose-response relationship was observed between frequency of fruit consumption and risk of CVD, with the hazard ratio (HR) for daily vs. never/rare consumption being 0.76 (95% CI: 0.72-0.80) for IHD, 0.73 (0.70-77) for ischemic stroke, and 0.61 (0.53-0.70) for haemorrhagic stroke (see Figure). The magnitude of the associations were only slightly attenuated after the additional adjustment for SBP (HR = 0.78, 0.79, and 0.70, respectively). The strength of the associations were similar in both genders but were different across age-at-risk groups, with younger participants having a stronger association with IHD and ischemic stroke but a weaker association with haemorrhagic stroke.
Conclusions: In adult Chinese, regular fresh fruit consumption was associated with lower blood pressure and lower risk of cardiovascular diseases, largely independent of blood pressure.

4170 | BEDSIDE

Plasma concentrations of folate and vitamin B12 and risk of fatal and non-fatal cardiovascular disease: a nested case-control study nested in a population-based cohort

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Purpose: Despite plausible biological mechanisms, epidemiological evidence on the link between folate and vitamin B12 and cardiovascular risk remains inconsistent. We investigate the relationship between plasma concentration of folate and vitamin B12 and the risk of fatal and non-fatal cardiovascular disease (CVD).
Methods: The data come from the Health, Alcohol and Psychosocial factors In Eastern Europe (HAPIEE) prospective cohorts based in Krakow (Poland), Kaunas (Lithuania) and 6 Czech towns that followed up random population samples of men and women aged 45-69 since baseline in 2002-06. After median follow up of 6.5 years, all 495 incident cases of CVD (including 198 deaths) and 4,884 controls sampled from disease free subjects were included in a nested case-control study. Plasma concentrations of folate and vitamin B12 were analysed in a central laboratory. Odds ratios (OR) of fatal and non-fatal CVD by cohort-specific quartiles of plasma concentrations were estimated by logistic regression models controlling for potential confounders (age, sex, cohort, smoking, education and material deprivation). Since results were consistent across study centres, results of pooled analyses are presented.
Results: After adjustment for covariates, folate concentrations were inversely associated with mortality from all causes (OR for highest vs. lowest quartile 0.78, 95% CI 0.65-0.93 (p-value for trend by quartile 0.009). For CVD, the association was similar for non-fatal (OR for highest vs. lowest quartile 0.69, 95% CI 0.53-0.90, p for trend 0.005) and fatal CVD (OR 0.72, 95%CI 0.55-0.94, p-for trend 0.022). For the combined fatal and non-fatal CVD, the ORs quartiles 2, 3 4 vs. quartile 1 were 0.79 (0.65-0.95), 0.76 (0.62-0.92) and 0.70 (0.57-0.86), respectively, p for trend <0.001. Adjustment for further covariates did not change the results. We found no association of vitamin B12 with total mortality or with fatal or non-fatal CVD. Results were similar after excluding events in first 2 years of follow up.
Conclusions: In this large population based study, we found consistent and significant inverse associations of total and CVD mortality and non-fatal CVD with plasma folate but not with vitamin B12. The association with folate may be due redox and methylation status, although previous studies have not confirmed the role of homocysteine; alternatively, our finding of an apparently protective effect of folate may at least partly reflect higher intakes of foods associated with plasma folate, such as fruit, vegetables or cereals.

4171 | BEDSIDE

The association between adherence to the mediterranean diet and indices of glucose homoeostasis in predicting cardiovascular disease events; 10-year follow-up (2001-2011) of the Attica study

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Aims: The association between adherence to Mediterranean diet and fasting indices of glucose homoeostasis, on 10-year cardiovascular disease (CVD) risk, in a Greek adult population, was evaluated here.
Methods: From May 2001 to December 2002, 1514 men and 1528 women (>18 y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, Greece, were enrolled. In 2011-12, 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 (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria. Diabetes mellitus (type 2) and impaired fasting glucose (IFG) were defined according to the established ADA criteria. Insulin resistance was evaluated by HOMA-IR. Dietary habits were assessed through a validated food frequency questionnaire and a diet score (MedDietScore, range 0-55) was developed (higher values means greater adherence to the Mediterranean diet).
Results: The overall prevalence of diabetes at baseline examination was 7.9%

in men and 6.0% in women (p=0.05). Mean MedDietScore was 26.3±6.8 in normoglycemic, 25.7±6.4 in IFG and 22.2±5.8 in diabetic subjects (p<0.001). The 10-year incidence of CVD was 14.3% in men and 9% in women (p<0.001). MedDietScore was inversely associated with CVD events (relative risk=0.97, 95%CI 0.95, 0.99), after various adjustments; however, a significant interaction was observed between MedDietScore and diabetes status (p<0.001). Stratified analysis revealed that MedDietScore was inversely associated with CVD events (relative risk=0.97, 95%CI 0.94, 0.99) only among non-diabetic, whereas, no significant effect was observed among diabetic subjects (p=0.67). The aforementioned moderating effect of diabetes status was further confirmed by the mediating effect of HOMA-IR. Particularly, when HOMA-IR was entered in the model, MedDietScore was not associated anymore with CVD events (p=0.10).
Conclusion: An inverse association was observed between adherence to Mediterranean diet and CVD risk, only in normoglycemic people. The later observation stated a research hypothesis about the role of indices of glucose homeostasis on the pathway between diet and CVD risk.

STATE OF THE ART – NEW INSIGHTS INTO PREVENTION OF THROMBOEMBOLIC EVENTS IN ATRIAL FIBRILLATION

4181 | BEDSIDE
Implication of multiple risk factors for subsequent diagnosis of atrial fibrillation and risk of stroke in patients seen with hospitalization related to a cardiac condition

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Background: A substantial part of ischemic strokes (IS) occurs in patients with atrial fibrillation (AF) and 20% of all strokes are attributed to AF. We aimed to identify patients with a cardiac condition without diagnosed AF at higher risk of developing or having a subsequent diagnosis of AF based on multiple risk factors.
Methods: This was a longitudinal cohort study based on the national hospitalization database covering hospital care from 2008 to 2012 for the entire population. The population of individuals seen with a cardiac condition as a first diagnosis without prior AF were analyzed by calculating incidence rates of new onset AF.
Results: Of 1,081,969 patients with hospitalization related to a cardiac condition in the population in 2009, 255,553 had a previous history of AF and/or AF at baseline and were excluded. The analysis focused on 826,416 patients identified as not having AF at baseline or in their history. Their cardiac condition was hypertension (51%), heart failure (24%), coronary artery disease (40%), rhythm or conduction disturbances with no AF (23%) and/or valve disease (9%). A total of 61,062 (7.4%) of these patients were diagnosed as having AF during a follow-up of 17±15 months (yearly AF incidence rate 5.19 per 100 person-years). CHA2DS2-VASc score was significantly higher in these patients (4.63±1.66 vs 2.83±1.98 in those with no AF during FU, p<0.0001). Among these 61,062 patients, 3,623 (5.9%) also suffered stroke during follow-up and CHA2DS2-VASc score was even higher in these patients (5.29±1.60 vs 4.59±1.65 in those with AF and no stroke during FU, p<0.0001). Among them, 967/3,623 (27%) had a stroke before AF was diagnosed.
Conclusion: Hospitalization for a cardiac condition was associated with a substantial risk of AF during FU, in particular among individuals with higher CHA2DS2VASc score. This score appears to be a simple tool for identifying patients at higher risk of AF following cardiac hospitalisation in patients without known AF. Strategies aimed at preventing AF early during the course after hospitalisation or at better diagnosing AF in prevention of IS are warranted.

4182 | BEDSIDE
Risk of ischemic stroke or systemic embolism in aspirin-treated patients according to clinical presentation of atrial fibrillation: analysis of 6563 aspirin-treated patients in ACTIVE or AVERROES

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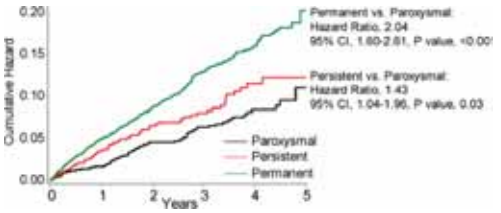
Background: Clinical presentation of atrial fibrillation (AF) as paroxysmal, persistent, or permanent reflects progressive stages of atrial dysfunction and there is a clinical impression that this reflects progressively higher risk of embolic events. However previous studies have not consistently shown AF type to predict stroke but have been hampered by methodological short-comings; low power, variable event ascertainment and variable anticoagulant use.
Methods: We analyzed the rates of stroke and systemic embolism in 6563 aspirin-treated patients with AF from the ACTIVE-A/AVERROES database according to AF presentation. All embolic events were adjudicated. Multivariable analyses were performed with adjustment for known risk factors for stroke.
Results: Mean age for patients with paroxysmal, persistent, and permanent AF was 69.0±9.9y, 68.6±10.2y, and 71.9±9.8y (p<0.001). CHA2DS2-VASc score was similar in patients with paroxysmal and persistent AF (3.1±1.4), but was higher in patients with permanent AF (3.6±1.5, p<0.001). Yearly stroke rates were 4.2, 3.0 and 2.1% for patients with permanent, persistent, and paroxysmal AF, respectively, with an adjusted hazard ratio of 1.83 (p<0.001) for permanent vs paroxysmal and 1.44 (p=0.02) for persistent vs paroxysmal. Multivariable analysis identified age, sex, history of stroke/TIA, and AF type as independent predictors of stroke risk, with AF type being the second strongest predictor after prior stroke/TIA.



Conclusion: In a large contemporary population of non-anticoagulated AF patients, the clinical presentation of AF was a strong independent predictor of stroke risk. Therefore, the clinical presentation of AF may be helpful to assess the risk/benefit of anticoagulant therapy, especially in low risk patients.

4183 | BEDSIDE
Oral anticoagulant use but not antiplatelet reduces stroke and mortality in patients with asymptomatic ambulatory atrial fibrillation

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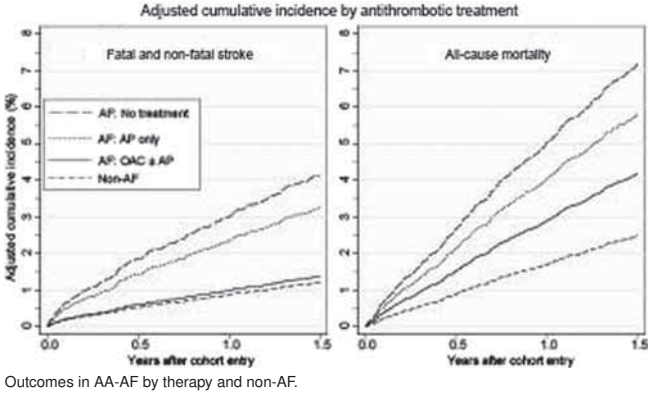
Purpose: To estimate risk of stroke and all-cause mortality in patients with incidentally detected asymptomatic ambulatory atrial fibrillation (AA-AF), and the response to antithrombotic therapy.
Methods: Cohort of 5,555 patients <85 years (mean age 70.9±10.1, 38.4% female) with incident AA-AF identified in the UK Clinical Practice Research Datalink 2001 – 2009, linked to hospital discharge diagnoses and causes of death. Patients with hospital-recorded AF, valvular disease, heart failure or use of antiarrhythmics, symptoms potentially indicative of AF, cardioversion, or use of oral anticoagulants (OACs) in the year prior to AA-AF were excluded. Non-AF cohort (24,705 patients) was generated matched on birth year, gender, and date of first AA-AF. Both cohorts were followed for 3 years for incident strokes, MI, all-cause mortality and major bleeding. Adjusted hazard ratios (HR) were used to assess prognostic significance of AA-AF and antithrombotic use on study outcomes compared to non-AF adjusting for potential confounders.
Results: Mean AA-AF CHA^2DS^2VASc score was 2.5±1.5. Stroke incidence rate (IR) was 19.4/1000 person-years (py) vs 8.4 (p<0.001) in non-AF cohort, mortality 40.1/1000 py vs 20.9 (p<0.001), and MI 9.0/1000 py vs 6.5 (p<0.001). OAC ± antiplatelet (AP) therapy significantly reduced risk of stroke and death compared to no antithrombotic therapy. For stroke this approximated non-AF. AP alone was associated with non-significant reduction of stroke and death. Both antithrombotics carried a similar small non-significant adjusted excess IR of major bleeding.



Outcomes in AA-AF by therapy and non-AF.

Conclusions: AA-AF is associated with an increased risk of stroke and death, with significant reduction in both associated with OAC but not AP use. This would justify consideration of widespread screening to detect unknown AF.

4184 | BEDSIDE
Persistence of vitamin K antagonist therapy in the real world

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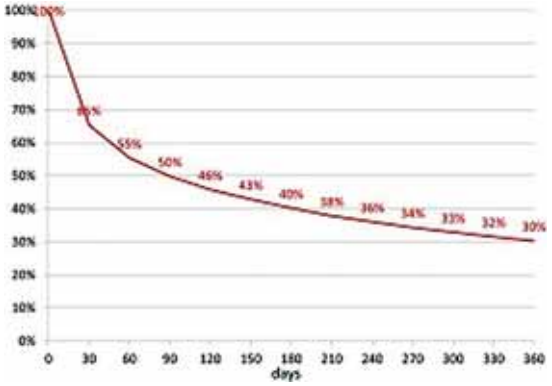
Introducton: Patient adherence and persistence of every chronic treatment has

a great importance to achieve benefits of treatment and to avoid adverse events. With anticoagulant therapy the risk of stroke is lower in AF. Oral vitamin K dependent anticoagulants (VKA) can effective decrease the risk of stroke.
Our aim was to investigate the one year persistence of the newly started VKA therapy in patients suffered from AF.
Patients and methods: Data was utilized from institutional database of the National Health Insurance Found (NHIF). The study included data for patients who newly started (not administered KVA therapy before one year) VKA therapy (acenocumarol or warfarin) between June 1 2011 and May 31 2012. Main outcomes measures were the persistence of VKA therapy in months, the percentage of patients persisting in therapy for 1-12 months and Kaplan–Meier plots. We analyzed the data by gender and age group too.
Results: 26.403 patients (12.634 men and 13.769 women) started VKAs. The most pronounced decrease of adherence occurred at the end of first month (-35%), it means the persistence was only 65% for one month. In the following months the persistence curve showed a moderate decrese because 35% of patients left VKA therapy between 1-12 months. The percentage of patients who persisted with VKA therapy after 12 month was only 30 percent overall. In age group 60-69 years was the best perstistence by 33% and the worst in age group under 39 year by 11%.



One year persistence of VKA therapy.

Conclusion: We have proved that patients with newly started VKA therapy suffered from AF, one year persistence of VKA therapy was very low, only 30%. The persistence has differed by age groups. It is well known that oral VKA therapy prevents the risk of stroke, but there are several factor affecting the persistence of VKA therapy.

4185 | BEDSIDE
Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicenter experience with the Amplatzer Cardiac Plug

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Aims: To investigate the safety, feasibility, and efficacy of left atrial appendage occlusion (LAAO) with the Amplatzer Cardiac Plug (ACP) in patients with atrial fibrillation (AF).
Methods and results: Data from consecutive patients treated in 22 centers were collected. A total of 1047 patients (age 75±8 years, 62% males) were included. Procedural success was 97.3%. In 216 patients (20.6%), LAAO was combined with another procedure. There were 45 (4.3%) peri-procedural major adverse events: death 8 (0.8%), stroke 9 (0.9%), myocardial infarction 1 (0.1%), cardiac tamponade 13 (1.2%), major bleeding 13 (1.2%), and device embolization needing surgery 1 (0.1%). Follow-up was complete in 98.2% of successfully implanted patients. Average follow-up was 13 months, accumulating 1345 patient-years. ASA monotherapy increased from 31% to 64% and warfarin monotherapy decreased from 16% to 1.6%. One-year all-cause mortality was 4.2%. A total of 63 deaths were reported at follow-up (17 due to cardiovascular causes). None was related to the device. There were 9 (0.9%) strokes, and 9 (0.9%) transient ischemic attacks at follow-up. The annual rate of systemic thromboembolism (peri-procedural + follow-up) was 2.3%, which translates into a 59% risk reduction. There were 15 (1.5%) major bleedings at follow-up. The annual rate of major bleeding (peri-procedural + follow-up) was 2.1%, which translates into a 61% risk reduction.
Conclusions: In this multicenter all comers study, LAAO with the ACP had a high procedural success and a moderate amount of peri-procedural complications. LAAO with the ACP showed a favorable outcome regarding efficacy for the prevention of AF related thromboembolism. Modification in antithrombotic therapy after LAAO resulted in fewer than expected bleeding events.

Results: Stroke & bleeding reduction.

Poster Session 5

THINGS YOU ALWAYS WANTED TO KNOW ABOUT SPORTS CARDIOLOGY

P4188 | BEDSIDE
A delayed increase in high sensitive Troponin I following high-intensity endurance cycling competition may have a potential role in the detection of unrecognized coronary artery disease

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Purpose: An increase in circulating cardiac Troponin levels may be observed following prolonged intense physical exercise. The precise cause and clinical significance of this troponin increase is unknown. The objective of this study was to describe the pattern of high-sensitive cardiac Troponin I (hs-cTnI) release following long-term cycling competition in presumably healthy amateur athletes.
Methods: Leisure sport cyclists without known coronary artery disease or cardiovascular medical treatment completing the 91 km mountain bike race were included in the study. Blood samples and rest ECG were aquired at 4 time-points: 24 hours prior to the race, and at 0, 3 and 24 hours following the race.
Results: A total of 97 cyclists, 74 (76%) males, mean age 43 (36-49) years, completing the race in 4:22±0:52 (h:min) with a mean heart rate of 156±16.7 bpm were included. Mean hs-cTnI value prior to the race was 4.0±3.7 ng/l (upper limit of normal: 30.0 ng/l).No patient had rest ECG or symptoms suggestive of coronary artery disease (CAD) during the race or for the first 24 hours following the race. Following the race, there was an increase in hs-cTnI in all participants that competed in the race. The mean hs-cTnI value immediately following the race was 61.4±54.8 ng/l, peaking at 3 hours to 90.8±113.9 ng/l, declining at 24 hours to 46.9±215.2 ng/l. All values were highly significantly different from baseline ($p<0.0001$). In 3 out of 4 individuals with the highest hs-cTnI levels, significant CAD was detected by CT coronary angiography. Revascularization was performed in two of these. No CAD was detected in individuals with a max hs-cTnI level <370 ng/l.
Conclusions: Hs-cTnI levels increased in all participants following the competition. Highly elevated hs-cTnI following the competition identified several cyclists with previously unrecognized significant CAD. These findings may suggest a potential role for hs-cTnI in the detection and monitoring of CAD among persons participating in prolonged high intensity endurance activity.

P4189 | BEDSIDE
Simultaneous pressure and volume registration demonstrates RV contractile impairment during exercise in endurance athletes with RV arrhythmias

G. Claessen[1], A. La Gerche[1], N. Pattyn[2], S. Dymarkowski[3], F. De Buck[4], J. Van Cleemput[1], P. Claus[5], H. Heidbuchel[1]. *[1]University Hospitals (UZ) Leuven, Campus Gasthuisberg, Dept. of Cardiology, Leuven, [2]Catholic University of Louvain (UCL), Dept. of Rehabilitation Sciences, Leuven, [3]University Hospitals (UZ) Leuven, Dept. of Radiology, Leuven, [4]University Hospitals (UZ) Leuven, Dept. of Anesthesiology, Leuven, [5]Catholic University of Leuven, Dept Cardiovascular Dis., Division Imaging & Cardiovascular Dynamics, Leuven, Belgium*

Introduction: At rest, right ventricular (RV) function may appear reduced in healthy endurance athletes (EAs), whereas RV functional reserve is normal. We sought to evaluate whether EAs with ventricular arrhythmias (EA-VA) of RV origin and apparently normal RV function at rest have impaired RV functional reserve during exercise.

Methods: Ten EAs, 8 EA-VAs and 7 healthy control non-athletes (NA) underwent cardiac magnetic resonance (CMR) imaging at rest and during incremental supine exercise on a CMR-compatible bicycle with simultaneous invasive hemodynamic monitoring. During real-time exercise and free-breathing, left ventricular (LV) and RV volumes were derived from real-time cine imaging and registered with simultaneous invasive measures of mean pulmonary artery pressure (mPAP).
Results: At rest, LV and RV function was similar between groups. However, as illustrated in Figure 1, EA-VAs had a smaller reduction in RV end-systolic volume (ESVi) from rest to peak exercise relative to EAs and NAs (interaction $P<0.0001$). RV end-diastolic volume (EDVi) decreased during exercise in EAs and controls, but not in EA-VAs (interaction $P<0.05$). Whilst the exercise-induced increase in LV ejection fraction (EF) was similar between groups, RVEF augmentation was impaired in EA-VAs (interaction $P<0.001$). There was no between-group difference in the slope of the relationship between mean pulmonary artery pressure (mPAP) and cardiac output (CO).

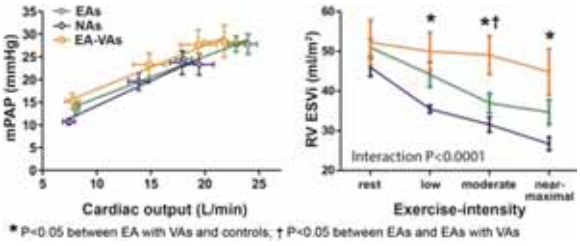

Figure 1

Conclusion: As compared with healthy EAs and NAs, EA-VAs have impaired RV functional reserve. The relationship between mPAP and CO was similar in all groups suggesting that the observed RV volume changes during exercise are due to RV contractile impairment rather than differences in afterload.

P4190 | BEDSIDE
RV functional impairment during exercise in endurance athletes with right ventricular arrhythmias

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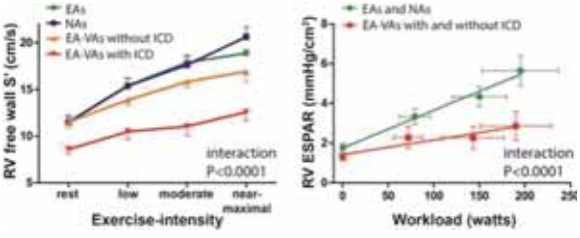
Introduction: Ventricular arrhythmias in endurance athletes (EA) frequently originate from a mildly dysfunctional right ventricle (RV). In athletes, it can be challenging to differentiate between low normal function due to physiological RV dilation and true RV contractile impairment. We evaluated whether RV dysfunction in EAs with ventricular arrhythmias (EA-VA) of RV origin becomes more apparent during exercise than at rest.
Methods: Ten EAs, 16 EA-VAs (50% with ICD) and 7 healthy control non-athletes (NAs) performed incremental exercise to near-maximal intensity. At rest, comprehensive echocardiographic measures included LV and RV strain/strain rate. Throughout exercise, echocardiographic measures included: 1) 2D RV areas to determine RV end-systolic area (RVESA) and RV fractional area change (RVFAC), 2) LV volumes to determine ejection fraction (LVEF), 3) systolic myocardial velocities of the tricuspid annulus (RV S') and 4) Doppler estimates of systolic pulmonary artery pressure (PASP). The RV end-systolic pressure-area relationship (ESPAR) was calculated as PASP/RVESA as a surrogate of RV contractility.
Results: At rest, LVEF, RVFAC, RV S' and PASP were all similar between EA-VAs, healthy EAs and NAs. Whereas resting LV strain and strain rate were also similar between groups, RV strain and strain rate were reduced in EA-VAs ($P<0.05$). From rest to peak exercise, LVEF augmentation was similar between groups. However, as illustrated in Figure 1, EA-VAs had an impaired increase in RVFAC and RV S' during exercise ($P<0.0001$ for interaction group*workload) and a reduced RV ESPAR ($P<0.0001$) relative to EAs and NAs.



Conclusion: Whereas RV dysfunction is only subtle at rest, EA with VAs of RV origin have an impaired RV contractile reserve which becomes more apparent during strenuous exercise.

P4191 | BEDSIDE
Arterial hypertension and cardiac remodeling in middle-aged endurance athletes

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Background: Extensive endurance training leads to cardiac adaptations and is an established risk factor for atrial remodeling and atrial fibrillation in the aging athlete. We investigated the contribution of a mildly elevated blood pressure (BP) to cardiac remodeling and supraventricular arrhythmias.
Methods: Amateur athletes who participated in the Grand Prix of Bern, a popular Swiss 10 mile race, were included. Athletes with an office blood pressure >140/90 mmHg were excluded. 24 hour ambulatory blood BP measurement was performed and athletes were stratified into a normotensive (NT) and a hypertensive (HT) group based on established cut-off values. Left atrial and left ventricular end-diastolic volume indices (LAVI, LVEDVI), left ventricular mass index (LVMI), left ventricular mass/volume index (LVMVI), tissue Doppler annular early and late diastolic velocities (Ea, Aa), and signal-averaged P wave duration (SAPWD) were measured. 24 hour Holter monitoring was performed and premature atrial contractions (PAC) were recorded.
Results: 87 runners were included in the final analysis. Mean age was 42±8 years. 33 (38%) athletes fulfilled the criteria for hypertension. Groups did not differ with respect to age, body mass index, cumulative training hours, an 10 mile race time. Mean systolic and diastolic BPs were significantly higher in the HT group (130±7 vs. 120±5 mmHg; $P<0.001$, and 84±4 vs. 76±3 mmHg; $P<0.001$). Hypertensive athletes had a higher LVMVI (0.95±0.21 vs. 0.85±0.16 g/ml; P=0.025), and a lower Ea (11.3±1.6 vs. 12.5±2.1 cm/s; P=0.006), compared to normotensive athletes. LAVI, LVEDVI, LVMI, Aa and SAPWD showed no significant differences between the groups. 12 (14%) runners had more than 1 PAC/hour (1.3 to 77.9) with no significant differences between the groups. In logistic regression models, including age, cumulative training hours and presence of hypertension, hypertension was an independent predictor for LVMVI (beta=0.227; P=0.027), and Ea (beta=-0.270; P=0.004). Cumulative training hours were independently associated with LAVI (beta=0.474; $P<0.001$), SAPWD (beta=0.481; $P<0.001$), LVEDVI (beta=0.336; P=0.001), and LVMI (beta=0.379; $P<0.001$).
Conclusion: In our study, one third of runners with a normal office blood pressure fulfilled criteria for arterial hypertension in 24 hour ambulatory BD measurement. Already modest BP elevations were associated with alterations of LV structure and diastolic function, but no with atrial remodeling or atrial ectopy.

P4192 | BEDSIDE
Myocardial blood flow and oxygen utilization in different ventricular regions of the healthy human heart in untrained subjects and endurance athletes at rest and during exercise

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Myocardial blood flow (MBF), oxygen extraction fraction (OEF), and oxygen consumption (MVO2) in human right ventricle (RV) has been measured in pulmonary hypertensive patients, but to the best of our knowledge never in healthy human subjects. These RV characteristics have neither been simultaneously compared against to those of left ventricle (LV) and septum of the heart. Furthermore, the effects of endurance training also remain incompletely understood. Consequently, in the present study MBF, OEF and MVO2 were measured in 12 healthy untrained young men (UT) and 12 healthy highly-trained endurance athletes (EA) in the RV, LV and septum at rest and during supine bicycle exercise (100 watts) with positron emission tomography and 15O-labelled tracers. Statistical analyses were performed with hierarchical linear mixed models, including two within factors, condition and wall region, and group as a between factor. $P<0.05$ was considered statistically significant. MBF was significantly lower in RV as compared to LV and septum in all subjects and consistently lower in all regions in EA compared to UT, both at rest and during exercise. As MBF, also OEF increased in response to exercise and similarly in all three regions, but there were significant regional differences and a region*group interaction. Regionally, OEF was mostly higher in RV (80±14% in UT and 78±11% in EA at rest and 87±7% in UT and 86±9% in EA during exercise) and septum (82±8% in UT and 74±9% in EA at rest and 84±15% in UT and 85±11% in EA during exercise) as compared to LV (62±10% in UT and 71±19% in EA at rest and 72±10% in UT and 86±12% in EA during exercise) both at rest and during exercise. For the interaction, OEF was higher in the LV in EA both at rest and during exercise, but not in the two other walls. As a result of these responses, MVO2 was consistently lower in all three walls in EA both at rest and during exercise, and MVO2 was significantly lower in RV (0.14±0.04 ml/g/min in UT and 0.10±0.04 ml/g/min in EA at rest and 0.30±0.12 ml/g/min in UT and 0.20±0.06 ml/g/min in EA during exercise) as compared to LV (0.16±0.05 ml/g/min in UT and 0.14±0.07 ml/g/min in EA at rest and 0.36±0.08 ml/g/min in UT and 0.31±0.09 ml/g/min in EA during exercise), but not to the septum (0.17±0.04 ml/g/min in UT and 0.13±0.05 ml/g/min in EA at rest and 0.29±0.12 ml/g/min in UT and 0.27±0.10 ml/g/min in EA during exercise). In conclusion, especially RV has perfusion and oxygen utilization features that are different from those of LV, but endurance training consistently

lowers the myocardial oxygen consumption in all three walls of the healthy human heart.

P4193 | BENCH
Occurrence of post-dive venous and arterial bubbles in divers with a patent foramen ovale: a randomized study

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Purpose: Patent foramen ovale (PFO) is a risk factor of decompression sickness (DCS) in divers due to paradoxical embolization of bubbles. Various diving restrictions are recommended to divers with PFO to prevent unprovoked DCS. To date, the safety of these recommendations has not been tested. The aim of this study was to test the effect of dive time and ascent rate restrictions on the occurrence of venous and arterial bubbles in divers with PFO after simulated dives. We compared a standardly recommended decompression regimen and a stricter regimen with slower ascent rate to a control dive known to produce significant amount of venous bubbles.
Methods: A total of 509 consecutive divers were screened for PFO using transcranial color coded sonography (TCCS). Forty-six symptomatic divers with a significant (grade 3) PFO were enrolled in this randomized study. All divers performed a simulated dive to 18 m in hyperbaric chamber. Divers randomized to group 1 (n=13) performed a standard Buehlmann regimen no-decompression dive (dive time 51 min, ascent rate 10 m/min), group 2 (n=14) performed the same regimen with a slower ascent (51 min, 5 m/min). Control group (n=19) performed a staged-decompression dive according to the US Navy decompression regimen (80 min, 9 m/min, decompression stop 7 min at 3m). Within 60 min after surfacing, presence of venous and arterial bubbles was assessed. Venous bubbles were assessed by pulse wave Doppler in the right ventricular outflow tract (RVOT), arterial bubbles by TCCS during native breathing and after Valsalva maneuvers.
Results: In all divers good visualization of RVOT and middle cerebral artery was possible. Group 2 had the lowest occurrence of venous and arterial bubbles, compared to group 1 (14% vs. 31%, p=0.38; 0% vs. 8%, p=0.48) and controls (14% vs. 74%, p<0.01; 0% vs. 32%, p=0.03). In group 1 fewer venous bubbles were detected (32% vs. 74%, p=0.03) compared to controls, but the reduction in arterial bubble occurrence (8% vs. 31%, p=0.42) was not significant.
Conclusions: The present study is the first study to demonstrate the effect of dive time and ascent rate restrictions on the occurrence of post-dive venous and arterial bubbles in divers with PFO. In our study the standardly recommended Buehlmann regimen reduced the occurrence of venous bubbles, but failed to eliminate arterial bubbles. However, this was achieved when combined with a slower ascent rate. Therefore, we suggest that stricter diving regimen might be necessary to prevent unprovoked DCS in divers with PFO. Clearly, this remains to be tested by clinical studies.

P4194 | BEDSIDE
Dynamic right ventricular adaptation induced by training in top-level athletes: an in-seasonal, speckle tracking study

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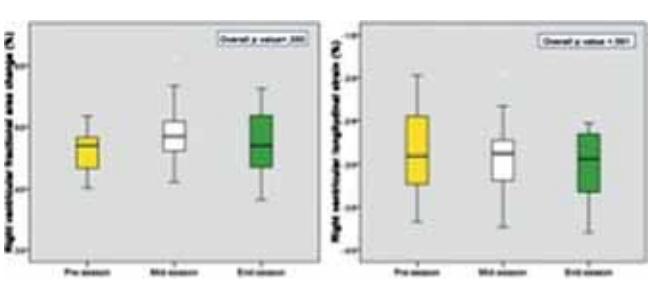
Background: Conflicting evidence exists concerning right ventricular (RV) morphology and function in top-level athletes. Although cross-sectional studies have been performed in athletes, longitudinal data investigating the in-seasonal changes in RV are not yet available. The aim of this study was to investigate whether morphological and functional RV changes can be observed in athletes during the season.
Methods and results: Twenty-nine top-level athletes (mean age: 20.9±6.7 years) were studied at pre-season, mid-season, and end-season time-points, using tissue Doppler imaging and 2D speckle-tracking echocardiography. RV basal and mid-cavity end-diastolic diameters (EDD) (overall p=.011 and p<.0001, respectively), and RV diastolic area (overall p<.0001) increased during the season. Conversely, RV outflow tract did not significantly vary (overall p=.960). No significant differences were observed during the season in RV diastolic functional parameters and in RV fractional area change (overall p=.350). Global RV longitudinal strain did not significantly change (overall p=.522), although apical longitudinal strain significantly increased (overall p=.017). On the left side of the heart, left ventricular mass increased during the season (overall p=.007). On multivariate analysis, left ventricular mass was identified as the only independent predictor of RVEDD at pre-season (β=0.69, p<.0001) and at end-season (β=0.82, p<.0001) time-points.
Conclusions: During the agonistic season, top-level athletes experienced an increase in RV chamber size as a physiological consequence of training-induced RV volume overload. This adaptation is not associated with an impairment of RV function or myocardial deformation and occurs in close association with changes on the left side of the heart.



P4195 | BEDSIDE
Exercise and risk of atrial fibrillation - a systematic review and network meta-analysis

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Purpose: There is some evidence that physical training, especially endurance training, increases the risk of atrial fibrillation. But results are conflicting and studies have used widely different assessments of physical activity. We performed a systematic review aiming to investigate the association of exercise with risk of atrial fibrillation, taking into account the intensity and duration of training.
Methods: We performed a systematic review of all studies investigating associations of exercise with risk of atrial fibrillation, using a predefined protocol. Because studies of total physical activity were scarce, we limited the analysis to studies reporting leisure-time activity. We quantified the exercise in the included studies as metabolic equivalent hours/week (METh/w). We thereafter used a network meta-analysis technique to summarize multivariable-adjusted risk estimates of atrial fibrillation across the different studies.
Results: Ten (eight cohort and two case-control) studies including a total of 111,282 persons and 4,633 atrial fibrillation cases fulfilled our inclusion criteria and were used for all analyses. There was a trend towards higher risk of atrial fibrillation with higher weekly amount of exercise (p=0.04). Compared to persons who exercised 0-5 METh/w, those who exercised more than 100 METh/w had a more than five-fold higher risk of atrial fibrillation, with statistically non-significant risk elevations in intermediate exercise groups (Fig. 1).

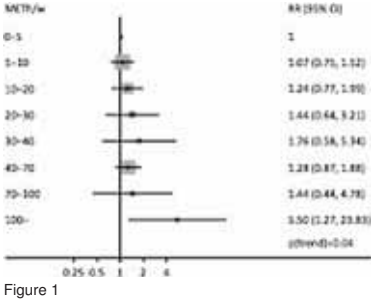

Figure 1

Conclusions: Higher weekly exercise amount was on average associated with higher risk of atrial fibrillation, across a variety of study samples and types. The risk increase was most notable for those with a very high exercise level.

P4196 | BEDSIDE
RV remodeling in college athletes engaged in mixed strength and endurance training: do the current echocardiographic reference values apply?

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Background and aims: Athletic participation is known to lead to ventricular remodeling. In this study, our objective was to determine the extent of right ventricular (RV) remodeling in Division I college athletes engaged in mixed strength and endurance training, using various scaling parameters. Defining upper thresholds of normal in athletes would be particularly useful for pre-participation screening for arrythmogenic right ventricular cardiomyopathy (ARVC).
Methods: Standard two-dimensional echocardiography was performed on 362 college athletes (mean age 18.4±1.1 years, males 70%, both strength and endurance sports) and 140 age and sex matched controls as part as the Stanford athletic screening program. Comparison of cardiac dimensions was performed using body size independent scaling parameters.

Results: Allometric scaling with BSA provided body size independent measures of RV end-diastolic area (RVEDA) as well as the right ventricular outflow tract (RVOT). Compared to age, sex and race matched controls, athletes have larger RV end-diastolic area (RVEDA) [12.4±2.3 vs. 11.3±2.5 cm^2/m^2, $p<0.001$], larger right atrial area (8.0±1.4 vs. 7.7±1.5 cm^2/m^2, p=0.01) and lower RV fractional area change (46±8 vs. 48±7%, p=0.007). Proximal RV outflow tract (RVOT) dimensions did not differ when scaled to height, or internally scaled to the LVOT (17.9±3.2 vs. 18.4±3.1 mm/m, p=0.07 and 1.4±0.2 vs. 1.4±0.2, p=0.64 respectively). More than 44% of athletes had RVOT values exceeding the American Society of Echocardiography unscaled criteria but only 7% exceeded thresholds in the ARVC scaled criteria.
Conclusion: Allometric scaling provides body size independent metrics for the right heart and provides useful threshold for pre-participation screening of college athletes. College athletes have larger right heart dimensions when scaled using body size independent metrics. ARVC scaled criteria provide useful thresholds for pre-participation screening of college athletes.

P4197 | BEDSIDE
Effect of remote ischemic preconditioning on the release of cardiac biomarkers after a 30 km run: a randomized trial

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Purpose: Elevated cardiac troponin (cTn) levels are frequently observed following prolonged endurance exercise. Several mechanisms may underlie exercise-induced cTn release, including an increase in cardiomyocyte permeability or cardiomyocyte injury due to ischemia. The aim of this study was to investigate whether remote ischemic preconditioning (RIPC), an established cardioprotective strategy that limits ischemia-reperfusion injury, has an effect on cTn and N-terminal pro-brain type natriuretic peptide (NT-proBNP) release after prolonged endurance exercise.
Methods: In a randomized crossover design, 26 healthy volunteers participated to an outdoor 30 km running trial preceded by RIPC of the forearm (4 x 5 min 220 mmHg unilateral occlusion) or a control intervention (4 x 5 min 20 mmHg unilateral occlusion). Cardiac troponin T (cTnT) and NT-proBNP concentrations were examined before, immediately after, 2 hours and 5 hours after exercise.
Results: In both trials, there was a consistent rise and fall of cTnT concentrations, from median baseline value of 5 ng/L (IQR 3-8) to 31 ng/L (IQR 23-50) immediately after the control trial ($p<0.001$). RIPC did not reduce exercise-induced cTnT release (median control 31 ng/L IQR 23-50 vs. RIPC 23 ng/L IQR 18-40 0h post-exercise, p=0.38). The effect of RIPC on exercise-induced NT-proBNP release was modest but statistically significant (median control 13 pmol/L vs. RIPC 10 pmol/L, p=0.03).
Conclusion: Brief episodes of upper limb ischemia-reperfusion preceding prolonged exercise decrease NTproBNP levels, but have no effect on cTnT release.

P4198 | BEDSIDE
Effects of high altitude exposure and of angiotensin receptor blocker/calcium channel blocker combination treatment on blood pressure response to submaximal exercise in hypertensive subjects

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Purpose: Acute exposure to high-altitude (HA) hypobaric hypoxia decreases exercise performance in healthy subjects, and increases systolic (S) and diastolic (D) blood pressure (BP). Little is known on BP responses to exercise in hypertensive subjects exposed to HA, and on effects of antihypertensive treatment in this setting.
We aimed to evaluate the effects of telmisartan 80mg–nifedipine slow release 30mg (T/N) combination treatment on exercise performance and BP response to exercise in hypertensive subjects exposed acutely to HA who underwent 6-minute walk test (6MWT).
Methods: Eighty-two mild-hypertensive participants of HIGHCARE-ANDES study (age 51.9±9.7; 47M/35F; BMI 28.2±3.5kg/m^2) performed a 6-minute walk test (6MWT) in 3 conditions: at sea-level (SL) off-treatment (SLbas); after 6 weeks of double-blind treatment with T/N (n=43) or placebo (PL, n=39) (SLtx); after the 1st full day of permanence at 3260m altitude (Huancayo-Perù; HA) under randomized treatment.
Results: Exercise performance and vital signs after the exercise were similar in both groups at SLbas. SBP/DBP at the end of the exercise was significantly lower in T/N than PL at SLtx (149.3±25.3/82.5±10.1 vs 162.1±24.6/92.9±13.1; $p<0.001$). At HA, SBP significantly increased in both groups, remaining significantly lower in T/N (159.1±24.6 vs. 185.7±25.6 mmHg, $p<0.001$). DBP did not differ between SLtx and HA in both groups, remaining lower in T/N (85.4±13.0 vs. 92.4±12.2, $p<0.01$). Mean end-exercise SpO2 decreased at HA in both groups, however, was significantly higher in T/N compared to PL (86.6±5.2 vs 84.2±6.0; $p\leq0.05$), whereas HR increased at HA, and did not show significant differences between groups. The 6-minute walking distance decreased significantly at HA, without differences between treatment groups, from 597±57 to 536.8±58.4m under T/N and from 599±61 to 537±56m under PL (both $p<0.001$).
Conclusions: T/N therapy effectively reduced BP and improved oxygen saturation at the end of exercise in hypertensive subjects exposed to HA, without affecting the six minute walking test performance. These results are relevant for protection of hypertensive subjects planning physical activity at HA.

P4199 | BEDSIDE
Aerobic interval exercise training improves the apnea-hypopnea index and self-reported sleepiness in obstructive sleep apnea patients

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Purpose: To investigate if 3 months of high intensity aerobic interval training improves the obstructive sleep apnea-hypopnea index (events h^{-1}) in obese patients diagnosed with moderate to severe obstructive sleep apnea.
Methods: In a prospective randomized controlled study 30 Thirty obese (BMI = 37±6 kg/m^2) men and women (51±9 years, height 177±9 cm) diagnosed with obstructive sleep apnea for 5.7±4.6 years (Apnea-hypopnea index (AHI index) = 42±26) was randomized 1:1 to 12 weeks of supervised aerobic interval exercise training (AIT) or control (CON). AIT was performed as 4 x 4 minutes of treadmill running or walking at 90-95% of maximal heart rate two times per week. CON continued with their normal lifestyle. Subjects were investigated at baseline and 12 weeks and sleep evaluation with respiratory polygraphy (blinded data evaluation), cardiopulmonary exercise testing, spirometry, blood biomarkers and self-reported sleepiness was investigated.
Results: Twenty-eight subjects completed the intervention period. Twenty-four subjects were regular CPAP users. The AHI-index was improved from 31.4±21.7 to 23.9±20.4 in the AIT group after 12 weeks of AIT ($p\leq0.05$) and was unchanged in CON (50.3±25.5 at baseline and 46.6±26.3 at 12 weeks). The Epworth self-reported sleepiness scale was improved from 10.0±3.6 to 7.3±3.7 in the AIT ($p\leq0.05$) and was unchanged from baseline (5.9±4.3) after CON. There was no change in body weight (120.5±26.1 kg and 118.6±23.1 kg in AIT/CON), average sleep oxygen saturation (92.4±1.6% and 92.6±1.6% in AIT/CON) or number of sleeping oxygen desaturation events per hour (36.9±18.6 event·h^{1-} and 55.8±28.6 event·h^{1-} in AIT/CON) from baseline to after the intervention period. Maximal oxygen uptake improved from 28.2±7.4 ml·kg^{1-}·min^{1-} to 30.2±7.7 ml·kg^{1-}·min^{1-} in the AIT group ($p\leq0.05$), and was unchanged from baseline (27.0±7.3 ml·kg^{1-}·min^{1-}) in CON. Pulmonary function was unchanged in both groups (Baseline FVC of 4.3±0.9 L and 4.4±0.8 L, and baseline FEV1 of 3.4±0.6 L and 3.4±0.6 L in the AIT and CON respectively). Leptin was significantly reduced after AIT (from 1747±1419 pmol·l^{1-} to 1412±1047 pmol·l^{1-} ($p\leq0.05$), with no change in CON (1656 pmol·l^{-1} at baseline).
Conclusion: Twelve weeks of aerobic interval exercise training two times per week significantly improves the AHI index, self-reported sleepiness and maximal oxygen uptake in obese sleep apnea patients without any change in body weight.

EXERCISE-INDUCED CHANGES

P4201 | BEDSIDE
Regular exercise habits and vascular endothelium function in patients with cardiovascular diseases

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Purpose: Endothelial dysfunction is reported to predict atherosclerotic event and exercise were recommended for patients with cardiovascular diseases. However, the effect of exercise habits on the vascular endothelium function in patients with cardiovascular diseases is uncertain. The purpose of this study was to investigate the relationship between exercise habits and vascular endothelium function
Methods: From December 2012 to December 2013, 145 patients (M/F 110/35, age 65±12) who underwent cardiac rehabilitation in our institution were enrolled in this study. They received flow mediated dilatation testing (FMD) for the evaluation of vascular endothelium function and filled in International Physical Activity Questionnaire for the information of their exercise habits and %FMD 6 and more and walking habits 5 and more per week for exercise habits were defined as normal level of %FMD and regular exercise habits.
Results: Fifty-nine patients (M /F 45/14, age 65±14) had regular exercise habits. Patients with regular exercise habits had significantly better %FMD (6.4±4.0% vs. 5.0±3.4%, p=0.024) and the value of HbA1C (6.2±1.2% vs. 6.6±1.5%, p=0.040). Those patients also showed tendency of less body mass index (BMI, 23.2±3.5kg/m^2 vs. 24.2±4.1 kg/m^2, p=0.057) and smaller prevalence of diabetes mellitus (27% vs. 42%, p=0.069).

Normal level of %FMD was significantly associated with regular walking habits (odds ratio; OR 2.002, confidence interval; CI 1.013-3.357, p=0.045), age (OR 0.963, CI 0.936-0.991, p=0.010), BMI (OR 1.095, CI 1.002-1.196, p=0.002) and the use of insulin (OR 0.250, 0.069-0.902, p=0.034) in univariate analysis. Multiple logistic regression analysis revealed that regular walking habits (OR 2.397, CI1.623-2.397, p=0.022), age (OR 0.963, CI 0.934-0.994, p=0.018) and the use of insulin (OR 0.185, CI 0.048-0.712, p=0.014) were the independent predictors for the normal level of %FMD.
Conclusions: Patients with regular walking habits had better vascular endothelium function and glucose profile. Our data suggested that regular walking habits 5 and more per week preserves vascular endothelium function and may reduce future cardiovascular events in patients with cardiovascular diseases through the preservation of vascular endothelium function.

P4202 | BEDSIDE
The association of moderate and vigorous physical activity on vascular function, bmi and cardiovascular risk factors in teenagers

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Purpose: Physical activity (PA) has been shown to improve cardiovascular (CV) health and 30-60 minutes moderate to vigorous physical activity 3–5 times a week is currently recommended in adults for CV prevention. The impact of similar level of PA in adolescence and its effect on CV risk factors and arterial disease in young adulthood remains largely unknown.
Methods: Our study population consisted of 1,489 subjects from the ALSPAC cohort who had vascular assessment at age 17 years and PA assessment at 15 years. PA was assessed using Actigraph accelerometer. Time spent in moderate to vigorous PA (MVPA) like cycling, swimming, running was calculated, the cut-point being four times resting metabolic rate (equivalent to brisk walking). Minutes of MVPA was calculated as the average minutes of such activity per valid day of measurement. Cardiovascular risk factors (including body mass index and lipids) and carotid distensibility were assessed at age 17 years.
Results: At 15 years, 24% subjects had low MVPA (on average less than 10 minutes each day), 49% engaged in moderate (10–30 minutes) MVPA each day and 27% spent more than 30 minutes in MVPA daily (high MVPA). Male participants were more engaged in high MVPA than females (40% versus 17%, chi2 p-val<0.001). Among males, those who spent more than 30 minutes in MVPA compared to less than 10 minutes had a reduced BMI at age 17 (beta –1.13 (95%CI –2.1, –0.19), p:0.018), reduced total-cholesterol (beta –0.20 (–0.37, –0.03), p:0.021), LDL-Cholesterol (beta –0.074 (–0.12, –0.03), p:0.001), and triglycerides (beta –0.83 (–0.93, –0.75), p:0.001). Carotid distensibility was also higher (beta 2.49 (95%CI 0.64, 4.35), p:0.009) in high MVPA compared to low MPVA in males. The beneficial effect of PA on carotid distensibility remained after adjustment for BMI and Systolic Blood Pressure at 17 years, however, it was reduced after adjustment for total-cholesterol (1.9 (–2.2, 4.0), p:0.078). These effects were not seen in female participants. Moderate to vigorous PA performed at 15 years was not associated with systolic blood pressure at 17 years in both sexes.
Conclusions: This study demonstrates that in adolescence, males seem to engage more in moderate to vigorous physical activity compared to females. PA exposure was associated with improved CV risk factor profile and carotid distensibility in young adult life. Therefore, participation in moderate to vigorous PA for at least 30 minutes can be recommended for optimal CV prevention, particular in young men.

P4203 | BEDSIDE
Six-minute walk distance is a strong determinant for physical activity after hospital discharge in patients with ischemic heart disease

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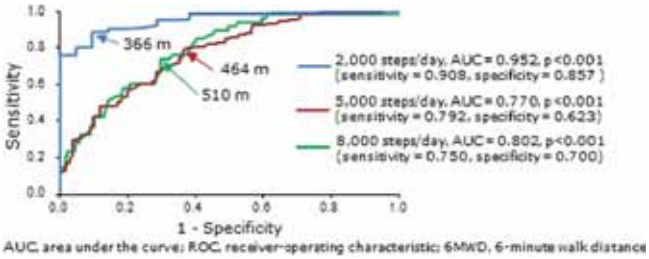
Background: Physical activity (PA) is well known to be an independent determinant for long-term survival in patients with ischemic heart disease (IHD). On the other hand, decreased 6-minute walk distance (6MWD) is associated with poor prognosis in them. In the number of steps as a PA, <2,000, <5,000 and >8,000 steps/day indicate the restriction of physical activities, higher recurrence rate and prevention of cardiovascular events, respectively. The purpose of this study was to investigate whether the 6MWD at hospital discharge predicted PA after discharge, and to clarify its cut-off value for PA assessed with steps/day in IHD patients.
Methods: We studied 271 IHD patients (64.2±10.9 years, 241 males) who underwent cardiac rehabilitation during hospitalization. We measured 6MWD at discharge and steps for 1 month after discharge, and assessed the PA with mean steps per day. To confirm determinants of PA, multivariate logistic regression analysis was performed using parameters of clinical characteristics and 6MWD as predictive variables. Receiver-operating characteristics (ROC) curve was used to determine the cut-off values for >2,000, >5,000 and >8,000 steps/day.
Results: PA showed significant univariate correlations with age (r=-0.395, p<0.001) and 6MWD (r=0.624, p<0.001). The multivariate logistic regression analysis detected the 6MWD as the strongest determinant for PA (p<0.001). Figure shows the cut-off values of 6MWD for >2,000, >5,000 and >8,000 steps/day: 366 m (AUC: 0.952, p<0.001), 464 m (AUC: 0.770, p<0.001) and 510 m (AUC: 0.802, p<0.001), respectively.



AUC, area under the curve; ROC, receiver-operating characteristic; 6MWD, 6-minute walk distance

Conclusions: The 6MWD at discharge was identified as a strong determinant for PA after discharge in IHD patients. The cut-off values of 6MWD for >2,000, >5,000 and >8,000 steps/day as PA were 366 m, 464 m and 510 m, respectively.

P4204 | BEDSIDE
Increased heart rate variability is associated with exercise capacity in patients with syndrome X

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Introduction: Heart rate variability (HRV) reflects the healthiness of autonomic nervous system, which is associated with exercise capacity. We therefore investigated if HRV could predict the exercise capacity in adults with syndrome X.
Methods: A total of 238 subjects (57.0±12.4 years, 67.8% men) presented with chest pain and abnormal treadmill test were enrolled, while they have undergone Holter ECG study and the following coronary angiogram were normal. Power spectrum from 24-hour recording of heart rate (HR) was analyzed in frequency domain to total power (TP) and components in the very low frequency (VLF), low frequency (LF) and high frequency (HF) ranges, which were taken nature logarithm transformation for statistical analyses.
Result: Subjects who achieved 90% maximal predicted HR during treadmill test (n=109) were younger, with less co-morbidities than those who didn't (n=129). Age, body mass index, SBP, VLF, LF and TP correlated with exercise duration during treadmill test, and they were predictors of achieving 90% maximal predicted HR. After accounting for age, BMI, SBP, VLF and TP remained correlated with total exercise duration and peak metabolic equivalents (METs). In multivariate analysis, VLF (OR per 1SD and 95% CI: 1.753, 1.169-2.628), LF (1.425, 1.066-1.906), and TP (1.535, 1.119-2.107), but not HF significantly predicted the achievement of 90% predicted HR, after accounting for age, heart rate, and SBP. In subgroup analysis, all of TP, VLF, LF and HF significantly predicted the achievement of 90% predicted HR in subjects younger than 60 yrs rather than in subjects older than 60 yrs, after accounting for age. (Fig. 1)

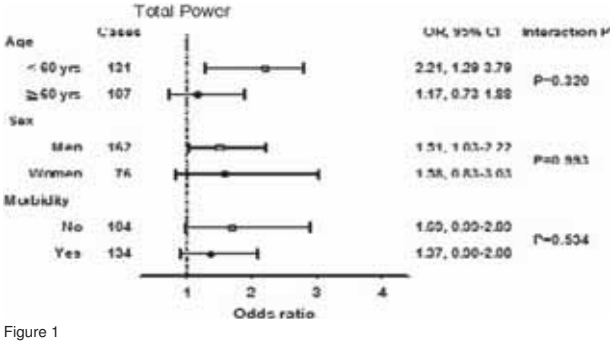

Figure 1

Conclusion: In patients with syndrome X, HRV might predict the exercise capacity, especially in younger population.

P4205 | BEDSIDE
Correlation between left ventricular mass and physical activity in a young asian male population

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Background: Increased Left Ventricular (LV) Mass is known to be a benign find-

ing in athletes. However, this phenomenon has been predominantly studied in the professional or "elite amateur" Caucasian athlete population. Thus far, the relationship between LV mass and participation in amateur sports has not been well delineated. Our study sought to assess the influence of participation in amateur sports on LV mass in a young asymptomatic Asian male population

Methods: From July to December 2011, 16231 male conscripts underwent routine pre-participation screening for military service, out of which, 685 young asymptomatic males were referred for echocardiographic screening due to isolated increase in QRS voltages on Electrocardiogram (ECG). The criteria for increase in QRS voltages on ECG included i) amplitude of R or S wave in a standard lead of ≥2mv, ii) amplitude of S wave in Lead V1 or V2 of ≥3mv or iii) amplitude of the R wave in lead V5 or 6 of ≥3mv. Of these, 630 underwent echocardiographic screening at a single Cardiology Centre and were included in the study. Study subjects were stratified by competitive involvement, intensity of participation and the type of sports (Bethesda Classification) they participated in. Subjects were categorized as "competitive sportsmen" if they competed at an intercollegiate level or higher. Results were expressed as mean±SD unless otherwise specified.

Results: The mean age was 18.65 (range 17 to 25) and the mean Left Ventricular Mass Index (LVMI) was 74.2±15.2 g/m^2 (range 32 to 118). Competitive Sportsmen had a higher LVMI than Non-Competitive Sportsmen (Mean 76.98±15.38 (Range 43 to 117) vs Mean 72.66±14.97 (Range 32 to 118), P=0.001). ANOVA analysis showed that LVMI increased significantly with frequency of participation in sports (P=0.005). Post-hoc analysis (Bonferroni) revealed that Sportsmen who participated in their respective sports ≥4x/week were the main drivers of this increase. No significant difference in LVMI was observed with different types of sports, despite stratification by static or dynamic component.

Conclusion: Increased left ventricular mass was found in amateur Asian male athletes who participated in sports at a competitive level, or at a frequency of ≥4x/week. Consideration of these parameters may be useful in the clinical evaluation of amateur sportsmen with suspected left ventricular hypertrophy.

P4206 | BEDSIDE
The effect of physical exercise and healthy diet on reducing the risk factors ofcardiovascular diseases in diabetic patients; a community based participatory research

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Introduction and objective: This study aimed to investigate whether a community-based participatory intervention program could reduce risk factors of cardiovascular diseases in diabetic patients.

Materials and methods: To induce a participatory approach, a local group (Health Companion) was established in the western suburb of Yasuj (2009-2010) in partnership with academics, local leaders, health providers and public representatives to guide all aspects of the study and intervention. Yasuj which is the capital of Kohgiloyeh and Boyer-Ahmad province is located in the southwestern Iran, with an estimated population of 136,509 in 2005. The target population was comprised of people 30-65 years of age who were usual residents of western suburbs of Yasuj. A total of 2569 individuals were screened for diabetes and cardiovascular risk factors. Through the screening process the high risk participants were recognized. These people were introduced to an assigned laboratory. Blood samples were drawn after 12 h fasting for the measurement of total cholesterol, triglycerides and fasting glucose levels. An intervention program consisting of nutrition education and physical exercise were planned and implemented for diabetic and impaired fasting glucose participants under leadership of the health companion group for 13 weeks period.After this period, the participants were invited to complete the post intervention survey questionnaire, anthropometric measurements and laboratory tests.

Results: Finding of screening program showed; 14.2% of the population had history of hypertension, 36.3% with BMI ≥30 and 44.0% with 25 ≤ BMI <30.Systolic blood pressure ≥140 observed in 12.7%, Diastolic blood pressure ≥90 in 24.8%. Out of 1336 high risk individuals, 17% had Fasting Blood Sugar (FBS) ≥126 and 13.5% with FBS between 110-125. Percentages of participants with Triglyceride (TG) ≥150 and cholesterol ≥200 were 33.8% and 23.5%, respectively.After completion of the intervention, the mean FBS, HbA1C, TG and cholesterol were decreased significantly. Although systolic and diastolic blood pressure and body mass index were decreased, but the differences were not statistically significant. The mean physical activity and exercise increased and consumption of frying foods and saturated oil were decreased significantly in target population.

Conclusion: The results suggest that participatory community based intervention could be a feasible model for reduction and control of risk factors of cardiovascular diseases in diabetic patients.

P4207 | BENCH
The effect of recreational exercise, caloric restriction, and high triglyceride diet in experimental menopause

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Purpose: The incidence of cardiovascular diseases are significantly higher after occurrence of estrogen deficiency in menopausal age. Augmented level of pro-inflammatory cytokines (tumor necrosis factor alpha; TNF-α) and activity of myeloperoxidase (MPO) enzymes and decreased activity and expression of heme-oxygenase (HO) are accompanying factors of heart and coronary diseases. We investigated the effects of hormone deficiency after surgical menopause as well as the recreational physical exercise (RPE) and nutrition on levels of TNF-α and HO-1 and activity of MPO and HO enzyme systems from blood plasma and tissue (heart left ventricle -LV) homogenates.

Methods: Female Wistar rats were divided into 12 groups. The two main groups were the ovariectomized (OVX) and sham-operated (SO) groups. Both of the OVX and SO groups were divided into trained and control (without exercise) groups. We separated high trigliceride (HT), caloric restriction (CR) and normal (CTRL) diet groups within running and control groups. The feeding and training period were monitored over 12 weeks. TNF-α and HO-1 level were measured by ELISA while the activity of HO and MPO enzymes were detected by spectrophotometric assays.

Results: We found that the HO activity and HO-1 expression were significantly decreased in OVX CTRL LV comparing with SO CTRL rats, which could be normalized via CR and running. The HT diet reduced significantly the level of HO-1 in case of SO animals and this changes might be prevented by RPE.

The concentration of plasma TNF-α and MPO activity of heart were significantly higher in OVX females as compared to the SO groups. The level of TNF-α and MPO were reduced by CR diet while the activity of MPO was significantly decreased via RPE. The HT diet caused significant increase in TNF-α and MPO of SO animals and this rising could be improved by RPE.

Conclusion: The OVX and HT diet are responsible for cardiovascular risk which might be associated with inflammatory processes and the decreased function of antioxidant systems, which could be improved by RPE.

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P4208 | BEDSIDE
Relationship between habitual physical activity and arterial stiffness in Himalayan high-altitude dwellers

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Background: High-intensity physical activity has been associated with an increased cardiovascular events. Aim of the study is to investigate the determinants of arterial stiffness in Himalayan high-altitude dwellers, living in the rural village of Chauricharka (Nepal, 2600 m s.l.) considering traditional cardiovascular risk factors and, in particular, habitual physical activity level, as well as acclimatization to high altitude.

Methods: 72 individuals (age 42±15yrs, age range 15-85, 23 men) were enrolled. Carotid-femoral pulse wave velocity (PWV) was assessed by applanation tonometry (Sphygmocor, Atcor). Habitual physical activity was evaluated by International Physical Activity Questionnaire, allowing the calculation of the Total Physical Activity Score (TPAS). Medical history, brachial BP and anthropometric parameters were taken. A blood sample was drawn to evaluate metabolic profile, renal function and hemoglobin.

Results: In the studied population the prevalence of hypertension was 21%, diabetes 7%, hypercholesterolemia 44% (LDL>130mg/dl), smoke 7%, obesity 10%, chronic kidney disease7% (GFR<60ml/min1.73mq), low HDL 49%, hypertriglyceridemia 24%. TPAS was 12807±5443 MET-minutes/week, with 97% of the population performing a high level of physical activity. O2 saturation (SO2) was 94.1±1.6%, and hemoglobin 15.0±1.4g/dl. Mean PWV was 7.2±1.6m/s and, among the abovementioned CV risk factors, only hypertension was associated with higher PWV (p=0.01). At the univariate analysis, PWV was associated with age (r=0.59, p<0.0001), mean blood pressure (r=0.45, p<0.001), and TPAS (r=0.35,p<0.01), but not with SO2 or hemoglobin. In the multiple regression analysis, (including age, gender, SO2, mean blood pressure, TPAS) only age (r2=0.37, p=0.0003) and TPAS (r2=0.11, p=0.001) remained independent predictors of PWV.

Conclusions: Strenuous physical activity shows a positive, independent association with increased arterial stiffness in Himalayan high-altitude dwellers, explaining 11% of its variance. Conversely, PWV was not influenced by traditional CV risk factors (except for age) or acclimatization to high altitude.

P4209 | BENCH

Physical training and ikatp blockade maintain myocardial conduction velocity after acute coronary occlusion in isolated rabbit heart

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Purpose: Authors have published that beneficial effects on ischemic myocardium produced by training can be due to KATP channel opening; nevertheless other findings seem to support that training could operate through KATP channel blockade. On the other hand conduction velocity (CV) is a key factor implicated in the onset of reentrant processes, as it is well known. It has been investigated the effect of physical training and the KATP channel blockade on the CV modifications produced by myocardial acute ischemia: a) to assess both the protective effect of training and KATP channel blockade on this parameter; and b) the possible similarity between these two interventions. Our hypothesis is that the CV evolves similarly in trained hearts and in hearts undergoing KATP channel blockade.
Methods: NZW rabbits were used, 5 were submitted to a six-week endurance exercise training program (trained group), and 6 (glibenclamide group) and 5 (control group) were not trained. After exercise program, rabbits were anaesthetized (ketamine, 10 mg/kg i.v.), euthanized and the hearts excised, isolated and perfused in a Langendorff system. A pacing electrode and a plaque with 256 recording electrodes were positioned on the left ventricle. The blockade of KATP channels was performed by glibenclamide (10 μM). CV was measured during VF (induced by pacing at increasing frequencies), dividing the distance between two electrodes positioned 5 interelectrode spaces apart in a direction perpendicular to the isochrones by the difference between their activation times (average of 5 determinations). The parameters were determined immediately before circumflex coronary artery occlusion and five minutes after. An ANOVA test (two factors) repeated measures on one factor was used to comparisons.
The results are shown in the table.

Ventricular conduction velocity

	Control (5)	Trained (5)	Glibenclamide (6)
Pre-occlusion	49.12±3.12	44.67±2.54	45.03±3.72
Post-occlusion	39.72±1.91†	44.69±4.31‡‡	45.81±3.30‡

CV is expressed in cm/s. †$P<0.05$ vs. pre-occlusion in control group. ‡$P<0.05$ and ‡‡$P=0.10$ vs. post-occlusion in control group.

Conclusion: Physical training maintains the conduction velocity in the early acute myocardial ischemia. This effect could be due, at least in part, to a KATP channel blockade.

P4210 | BEDSIDE

Hypocaloric diet and exercise training improve postexercise sympatho-vagal balance in patients with metabolic syndrome and obstructive sleep apnea

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Purpose: Previous study showed that patients with metabolic syndrome and obstructive sleep apnea (MetS+OSA) have impaired attenuation of heart rate recovery (HRR) after maximal exercise. The increase in sympathetic nerve activity (SNA) is a mechanism involved in this alteration. We tested the hypothesis that hypocaloric diet and exercise training (D+ET) improve the HRR, the heart rate reserve and decrease muscle SNA (MSNA) in MetS patients with and without OSA.
Methods: Never treated patients with MetS (ATP-III) with OSA (n=26) or without OSA (n=19) were assigned into intervention groups, based in D+ET (D,-500 kcal/day; ET, aerobic moderate intensity for 40 min, 3 times/week): 1) MetS+OSA/D+ET (n=16); 2) MetS-OSA/D+ET (n=9); or no treatment groups as control (C): 3) MetS+OSA/C (n=11), and 4) MetS-OSA/C (n=10) for 4 months. We evaluated OSA (AHI >15 events/hour - polysomnography) and the MSNA (microneurography). We calculated the HRR (maximal HR minus HR in the 1st, 2nd and 4th min of recovery) and the heart rate reserve (maximal HR minus resting HR) through the HR registered in maximal exercise reached on cardiopulmonary exercise test.
Results: Both groups D+ET improved metabolic profile, reduced body weight, reduced MSNA and increased functional capacity. Furthermore, the group MetS+OSA/D+ET reduced AHI (38±6 vs. 20±3 events/hr, P=0.02). Interestingly, MetS+OSA/D+ET increased HRR at 2nd min (29±2 vs. 37±2 bpm, P=0.05) and HRR at 4th min (43±2 vs. 52±2 bpm, P=0.03). The same results were observed in MetS-OSA/D+ET with increase of HRR at 2nd min (30±2 vs. 41±2 bpm, $P<0.01$) and of 4th min (50±2 vs. 69±2 bpm, $P<0.01$). The heart rate reserve only increased in the MetS+OSA/D+ET (71±4 vs. 81±5 bpm, P=0.04). No significant change was observed in C groups. In addition there was an inverse correlation between MSNA and HRR at 2nd min (r=-0.45, P=0.003) and between MSNA and DHRR at 4th min (r=-0.39, P=0.009).
Conclusion: Regardless of OSA, intervention by D+ET enhances the sympathovagal balance on heart rate recovery after maximal exercise in patients with MetS. In addition, in patients with MetS and OSA, the D+ET may have a more pronounced effect, since they had also an increase in the chronotropic response during progressive maximal exercise. (FAPESP #2011/17533-6

P4211 | BENCH

Exhaustive physical exercise induces myocardial oxidative damage and left ventricular functional impairment in a rat model

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Purpose: The role of physical exercise in the prevention and treatment of cardiovascular diseases has been well-described, even though elevations in cardionecrotic biomarkers after prolonged exercise (i.e. ultramarathon running) were observed. We aimed to establish and validate a rat model of acute exhaustive exercise and determine the biochemical, molecular biological, structural and functional alterations in the heart.
Methods: Rats of the exercise group were forced to swim for 3h with 5% body weight (workload) attached to the tail, control rats were taken into the water for 5min. 2 hours after completion of swimming we performed left ventricular (LV) pressure-volume analysis using a pressure-conductance microcatheter to investigate LV function and mechanoenergetics. Additionally, blood and myocardium samples were harvested for biochemical and histological examination. Alterations of gene expressions were detected using qRT-PCR.
Results: When compared to controls, elevated plasma levels of cardiac troponin T (0.131±0.022 vs. 0.025±0.006ng/ml, $p<0.001$), creatine kinase, transaminases and lactate dehydrogenase were detected after exhaustive exercise. Histological analysis showed sporadic fragmentation of myocardial structure, tissue edema and leukocyte infiltration. Myocardial gene expression analysis showed a significant increase of endogenous antioxidants (thioredoxin-1: 1.24±0.07 vs. 1.01±0.04, $p<0.05$) and dihydroethidium staining indicated robust generation of superoxide anions after exhaustive exercise. We found a markedly significant augmentation of Bax/Bcl-2 ratio (1.80±0.18 vs. 1.04±0.03, $p<0.01$) and the proapoptotic activity was confirmed by semiquantitative analysis of TUNEL staining. Dysregulation of the matrix metalloproteinase (MMP) system (MMP-2/TIMP-2 (tissue inhibitor of matrix metalloproteinase-2) ratio: 1.46±0.08 vs. 1.05±0.03, $p<0.01$) was observed after exhaustive swimming. We observed increased end-systolic volume, decreased ejection fraction (48±5 vs. 59±3%, $p<0.001$), impaired contractility (end-systolic elastance: 0.70±0.07 vs. 0.95±0.07mmHg/μl, $p<0.05$) and mechanoenergetics (mechanical efficiency: 48±2 vs. 59±2%, $p<0.001$) of LV in the exercise group.
Conclusions: Excessive physical activity has an adverse effect on the heart. Enhanced oxidative stress and apoptotic signalling as well as MMP dysregulation could underly the elevation of myocardial necrotic markers. The characteristic molecular and histological alterations are associated with impairment of LV systolic function, contractility and mechanoenergetics.

P4212 | BENCH

Development and complete morphological and functional reversibility of athletes heart in a rat model

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Purpose: Long-term exercise training is associated with characteristic structural and functional cardiac adaptation termed athlete's heart. However the effect of discontuniation of the training (detraining) on left ventricular (LV) function is still unclear. Our aim was to evaluate the development characteristics of athlete's heart and the reversibility of morphological and functional changes during detraining.
Methods: Rats were divided into trained (n=15) and control (n=17) groups. Trained rats swam 200 min/day for 12 weeks, while control rats were taken into the water for 5 min/day. Detrained rats remained sedentary for 8 weeks after completion of the training protocol. We regularly performed echocardiographic measurements to investigate development and regression of exercise-induced cardiac changes. LV pressure-volume analysis was performed to calculate cardiac functional parameters. LV samples were harvested for histological examination. Myocardial gene expression analysis was performed using qRT-PCR.
Results: Echocardiographic examinations showed rapidly developing LV hypertrophy in the trained group according to wall thickness values (LVmass index after training period: 2.45±0.09 vs. 2.07±0.07g/ttkg, $p<0.05$). This adaptation regressed after detraining (LVmass index: 1.94±0.02 vs. 2.05±0.05g/ttkg, p=0.0634), which was confirmed by post-mortem measured heart weight and histological morphometry. Unchanged myocardial expression of TGF-β and β-MHC and unaltered amount of LV collagen confirmed the physiologic nature of the observed cardiac hypertrophy. Hemodynamic measurements indicated decreased LV end-systolic volume (LVESV: 75±5 vs. 100±7μl, $p<0.05$) along with unchanged end-diastolic volume (EDV), improved systolic function and contractility (slope of the dP/dtmax-EDV relationship: 35.9±2.6 vs. 25.8±2.8Hgmm/s/μl, $p<0.05$), ameliorated active relaxation and mechanoenergetics (mechanical ef-

ficiency: 53±2 vs. 45±2%, p<0.05) after long-term exercise training. After the detraining period regression of exercise-induced cardiac functional changes were observed: LVESV (117±5 vs. 115±6μl, p=0.7846), active relaxation, LV contractility (slope of the dP/dtmax-EDV relationship: 30.5±1.7 vs. 28.4±4.3Hgmm/s/μl, p=0.5871) and mechanoenergetic (mechanical efficiency: 50±2 vs. 48±5%, p=0.7760) enhancement reverted completely to control values. Training and detraining did not affect myocardial stiffness.
Conclusions: Our results confirm that the morphological and functional properties of exercise-induced physiologic LV hypertrophy completely regressed after an eight week detraining period.

NOVEL ASPECTS OF EXERCISE TESTING AND TRAINING

P4214 | BEDSIDE
Cardiopulmonary exercise testing as a diagnostic tool for the detection of pulmonary hypertension and prognostic value in patients with dilated cardiomyopathy

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Purpose: Recently, it has become increasingly recognized that pulmonary hypertension (PH) is a particularly threatening result of left-sided heart disease. However, there are few investigations about the impact of CPX variables on PH in dilated cardiomyopathy (DCM). The purpose of this study was to evaluate the ability of crucial cardiopulmonary exercise testing (CPX) variables to detect elevated pulmonary arterial pressure (PAP) and prognostic value in patients with DCM.
Methods: Ninety subjects with DCM (52±13 years, 69% male) underwent cardiac catheterization and CPX in our hospital. Predicted peak VO2 and the percentages of the predicted values achieved were calculated. Receiver operator characteristic (ROC) analysis was performed to assess the utility of CPX variables to distinguish between the presence and absence of PH. We followed all patients for the incidence of cardiac events for a mean of 4.3 years. Cardiac events were defined as cardiac death and hospitalization due to worsening heart failure.
Results: Overall mean values were: mean PAP (mPAP), 18.0±9.6 mmHg; plasma brain natriuretic peptide, 233±295 pg/mL; and left ventricular ejection fraction, 30.2±11.0%. Patients were divided into 2 groups on the basis of mPAP, namely DCM without PH group (mPAP<25 mmHg; n=75) and DCM with PH group (mPAP ≥25 mmHg; n=15). Peak VO2 and VE/VCO2 slope were significantly lower and higher in DCM with PH than in DCM without PH (11.3±3.6 mL/kg/min, 19.2±4.8 mL/kg/min, P<0.0001, 38.6±9.7, 29.2±7.4, P=0.002, respectively). The incidence of cardiac events were significantly higher in DCM with PH than in DCM without PH by the Kaplan-Meier method (P=0.002). After adjustment including the presence of PH, multivariate Cox proportional hazard analysis revealed that peak VO2 was the only significant independent predictor of cardiac events (odds ratio, 0.876; 95% confidence interval, 0.808 to 0.950). A cut-off value of percentages of predicted peak VO2 of 52.5% was the best predictor of a mPAP ≥25 mmHg by the ROC analysis (area under the curve [AUC: 0.911]; 95%CI: 0.846-0.977, P<0.001). VE/VCO2 slope >31.01 added significant diagnostic value (AUC: 0.800; 95%CI: 0.686-0.913, P=0.001).
Conclusions: Lower peak VO2 and higher VE/VCO2 slope were strongly associated with the presence of PH in patients with DCM. Moreover, peak VO2 was an independent predictor of cardiac events in patients with DCM. Taken together, CPX variables could have an important diagnostic utility for PH and provide prognostic information in patients with DCM.

P4215 | BENCH
Comparison of peak cardiopulmonary performance parameters from a robotics-assisted tilt table, a cycle ergometer and a treadmill

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Purpose: Robotics-assisted tilt table technology (RATT) provides cyclical stepping movement and physiological loading in immobilized patients. This may facilitate the estimation of peak cardiopulmonary performance parameters in patients who have problems that may preclude testing on a treadmill or cycle ergometer. We have augmented a RATT with force sensors in the thigh cuffs, a work rate estimation algorithm and a custom visual feedback system to guide the subject's work rate. The aim of the study was to compare peak performance parameters and to assess test-retest reliability in able-bodied subjects using the RATT, a treadmill and a cycle ergometer.
Methods: Each subject performed 6 maximal exercise tests, with 2 tests on each of the three exercise modalities (the cycle ergometer, the treadmill and the RATT). The main outcome measures were peak oxygen uptake (VO2peak) and peak heart rate (HRpeak). Differences in VO2peak and HRpeak were analysed using repeated measures ANOVA. Linear regression analysis was used retrospectively to investigate the possibility of estimating treadmill and cycle VO2peak using measured RATT VO2peak.The intraclass correlation coefficient (ICC2,1) was used to analyse the test-retest reliability of VO2peak for all three modes.
Results: 18 able-bodied subjects were included (10 male, 8 female; age 28.6±6.3 years, mean ± SD). Average VO2peak was 32.3, 40.2 and 45.9 mL/kg/min for RATT, the cycle ergometer and the treadmill, respectively (p<0.001). The average HRpeak values were, respectively, 168.0, 178.8 and 183.8 beats/min (p<0.001). The regression equations for estimation of cycle and treadmill VO2peak (L/min) were found to be -0.2 + 1.36*(RATT VO2peak) and -0.1 + 1.45*(RATT VO2peak). These models have R^2 of 0.90 and 0.89 (standard error of estimation [SEE] of 0.27 and 0.30 L/min, respectively). The test-retest ICC was 0.97 for RATT (95% confidence interval [CI] = 0.89 – 0.99), 0.98 for the cycle ergometer (95% CI = 0.94 – 1.00) and 0.99 for the treadmill (95% CI = 0.95 – 1.00).
Conclusions: VO2peak obtained from RATT was lower than the treadmill and the cycle ergometer. The high R^2 and acceptable SEE from the predictive equations show that the RATT VO2peak can estimate well the cycle and treadmill VO2peak values. The VO2peak obtained from all 3 devices showed high test-retest reliability. RATT may be an effective exercise testing approach for persons who cannot perform the exercise testing on standard devices.

P4216 | BEDSIDE
Cardiac rehabilitation with exercise training in patients after pulmonary thrombendarterectomy for severe chronic thromboembolic pulmonary hypertension

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Background: The benefit and risk of exercise-based cardiac rehabilitation (CR) in patients after pulmonary thrombendarterectomy (PEA) for chronic thromboembolic pulmonary hypertension (CTEPH) remains unestablished.
Objective: To assess the effects of CR on exercise capacity and to determine the predictors of good response to exercise training in patients after PEA.
Methods and results: We studied 49 patients (mean age 53.1±9.3years, female 61.2%) who participated in our CR program after PEA. Hemodynamic assessment with right heart catheterization was done before and after the PEA surgery. Cardiopulmonary exercise test was performed at the beginning and the end of the 3-month CR. Exercise training consisted of aerobic endurance exercise and supplementary low-intensity resistance training, with duration of 30-60 min and frequency of 3-5 times a week for 3 months. Oxygen saturation (SpO2) was monitored by pulse oximetry and maintained above 85-90% during exercise training. Before surgery, the patients had severe PH with mean pulmonary artery pressure (PAP) of 46±11mmHg, which was ameliorated by PEA to 20±8mmHg (p<0.001). However, their exercise capacity remained severely impaired; age- and body weight-adjusted peak oxygen uptake (PVO2) at the beginning of CR was only 53±11% of the predicted normal value. After the 3-month CR, PVO2 substantially increased by 31±21% on average (p<0.001). When we divided the patients into two groups by the median value of the percent increase in PVO2 (%ΔPVO2), there was no significant difference between the two groups in the baseline values of mean PAP, pulmonary vascular resistance, cardiac index, or right ventricular ejection fraction. However, %ΔPVO2 showed a strong inverse correlation with baseline PVO2 (r=-0.66, p<0.001). There was no major adverse events during exercise training.
Conclusion: These findings suggest that CR with exercise training is effective in safely improving exercise capacity in patients after PEA for CTEPH, regardless of their severity of hemodynamics at baseline.

P4217 | BEDSIDE
Comparative efficacy of different exercise modalities in patients with systolic heart failure

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Exercise has been proven to be of benefit in patients with systolic heart failure (SHF). Most research has been done with moderate intensity aerobic training (AT), data regarding high intensity aerobic intervals (IT) and resistance training (RT) are much less available. We compared these exercise types to determine their influence on LV performance (LVP) and functional status (FS) in patients with SHF.
Methods: 214 pts 63±13 years (78 female) with SHF NYHA III, EF <40% were randomized to three groups to receive AT (n=56), RT (n=53) or IT (n=55) for 4 weeks or passive group (PG, n=50). AT was performed on treadmill four times per week for 30 min and 70% of peak heart rate (PHR). RT was implemented as a weight lifting of 10 predetermined exercises of the upper and the lower body (2 set of 10 repetitions) for the same duration and frequency with the intensity of 50% of the one repetition maximum. IT was performed on treadmill as four cycles of 4 min uphill walking at 95% PHR and 3 min recovery periods at 50% PHR. Patients warm up and cool down for 5 min. EchoCG indexes of LV EDV, ESV, maximal LA volume (LAVI), EF, E/Emseptal, LV global longitudinal 2D strain

(GLS) and NTproBNP were obtained at the onset and the end of the study. FS was assessed as peak VO2 consumption on 9 min self-powered treadmill test. Baseline data were comparable between groups.
Results: All exercise groups improved E/Em and NTproBNP levels compared to baseline and PG end-study unchanged parameters (E/Em: AT14.1±2.4 vs 11.8±1.4, $p<0.05$; RT13.7±2.1 vs 9.3±1.2, $p<0.03$; IT13.5±2.1 vs 9.2±1.1, $p<0.03$; NTproBNP: AT1589±198 vs 937±69 pg/ml, $p<0.05$; RT1576±193 vs 534±35 pg/ml, $p<0.02$; IT1584±195 vs 513±35 pg/ml, $p<0.02$) without changes in EF, EDVI and ESVI. E/Em and NTproBNP reductions were more in the RT and IT groups compared with AT group and comparable in RT and IT groups (E/Em: AT11.8±1.4 vs RT9.3±1.2 vs IT9.2±1.1, $p<0.05$; NTproBNP AT937±69 vs RT534±35 pg/ml vs IT513±35, $p<0.05$). The greater LAVI reduction was in RT and IT (RT27±5 vs IT25±4 vs AT37±7, $p<0.05$) without changes in PG. GLS was greater in all exercise groups with a greater degree in RT and IT (RT-13.8±3.3% vs IT-14.2±3.7% vs AT-10.1±2.1, $p<0.05$) without changes in PG. FS was improved in 37 pts (78%) in RT and 38pts (80%) in AT and 97% in IT compare with baseline (AT13.7±1.4 to 18.3±1.6 ml/kg/min, $p<0.05$; RT13.6±1.4 to 18.6±1.7ml/kg/min, $p<0.05$; IT13.5±1.3 to 23.7±2.2 ml/kg/min, $p<0.02$).
Conclusion: All exercise types are beneficial in SHF. RT and IT better alter LA remodeling and improve LVP. IT appears to be most preferable in terms of FS improvement.

P4218 | BEDSIDE
High exercise capacity and low white blood cell counts are determinants of survival up to 90 year: findings in a community based study of 75-year-olds

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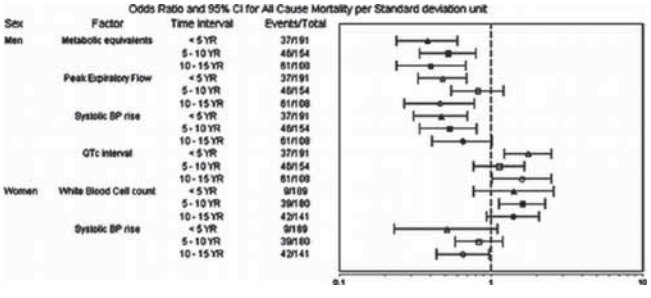
Purpose: The overarching aim was to explore potential predictors of up to 15 year survival in 75-year-olds. A secondary aim was to study if the relative importance of the potential predictors varied over time.
Methods and results: We performed logistic regression analyses by sex to assess the associations between mortality and the variables given below in 191 men and 189 women – 61.5% of the 618 invited 75-year-olds from a Swedish city. The variables comprised prevalent disease (diagnosed myocardial infarction/angina, hypertension, and diabetes), exercise test (exercise capacity measured as Metabolic equivalents (METS) and exercise systolic blood pressure (BP) rise), established cardiovascular risk factors (HDL-cholesterol, triglycerides, systolic and diastolic blood pressure (BP), BMI, waist, and smoking) and other potential risk factors (peak expiratory flow (PEF), QTc and QRS intervals in resting ECG, white blood cell (WBC) counts, and creatinine). The most important factors for 15 year survival in men were METS (Odds ratio (OR); 95% confidence interval for mortality per standard deviation unit:0.35; 023-0.54), PEF (OR: 0.45; 0.29-0.69), exercise systolic BP rise (OR: 0.51; 0.36-0.74), and QTc interval (OR: 1.70; 1.19-2.45). In women the most important factors were WBC counts (OR: 1.60; 1.17-2.18) and exercise systolic BP rise (OR: 0.67; 0.50-0.91). Their relative importance as predictors of <5, 5-10, and 10-15 year survival in men and women are shown below.



Conclusions: In 75-year-old men the most important predictors of survival until 90 year were related to high exercise capacity and they were relatively stable over time. In women the picture was more disparate. The relatively best predictors of survival until 90 year were WBC counts and exercise systolic SP rise.

P4219 | SPOTLIGHT
Skeletal muscle pump may be one of major determinants of exercise capacity in patients with chronic heart failure

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Background and purpose: Decreased skeletal muscle strength in heart failure (HF) patients has been reported to well relate to the reduced peak oxygen consumption (VO2). The underlying mechanism of its relationship, however, has not been fully understood. During incremental exercise, in the normal elderly, stroke volume increases first by augmentation of left ventricular ejection fraction (LVEF) then by increased venous return because of inability to maintain ejection fraction. In HF patients, this phenomenon may occur earlier than the normal subjects, therefore, the ability to maintain preload during exercise could be a vital factor to maintain exercise capacity. However, the contribution of skeletal muscle pump function in lower leg to preload during exercise in HF patients has not been investigated. We, therefore, aimed to examine the contribution of skeletal muscle pump function on the cardiopulmonary exercise testing (CPX) parameters in HF patients.
Methods: Eighty eight patients with HF underwent echocardiography, laboratory measurements, and CPX on the same day. The bicycle ergometer was applied for CPX with initial load of 20 watt for 4 minutes followed by 10 watts/min ramp to patients' volitional fatigue and respiratory gas variables were acquired by breath by breath throughout exercise. We measured venous volume (VV) and ejected volume (EV) of lower extremity by strain-gauge plethysmography during three times of calf raise in standing position. We calculated leg ejection fraction (LEF) (LEF=EV*100/VV) as the marker of skeletal muscle pump function.
Results: A data of 65 out of 88 patients were analyzed (23 patients were excluded by atrial fibrillation). The average values of age, LVEF, hemoglobin level, peak VO2, peak VO2/HR (peak O2 pulse), and LEF were 63.1, 48.6 [%], 13.1 [g/dl], 17.8 [mL/kg/min], 8.8 [ml/beat], and 48.6 [%], respectively. LEF significantly correlated with peak O2 pulse ($r=0.48$, $p<0.001$) and peakVO2 ($r=0.31$, $p=0.007$). Multiple linear regression analysis revealed that LEF ($\beta=0.449$, $p<0.001$) and LVEF ($\beta=0.368$, $p=0.001$) were significant determinants of peak O2 pulse. In HF with reduced ejection fraction (EF<40%), LEF was more strongly correlated with peak O2 pulse ($r=0.60$, $p=0.009$) than in HF with preserved ejection fraction (EF≧50%) ($r=0.31$, $p=0.09$).
Conclusions: The findings of this study demonstrated that the skeletal muscle pump function contributes to achieve stroke volume during exercise in HF patients. This function may be more important factor to maintain exercise capacity especially in HF with reduced ejection fraction.

P4220 | BEDSIDE
A single session of inspiratory muscle training improves autonomic imbalance resulting in the reduction of stress reaction in patients with chronic heart failure

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Background: Inspiratory muscle training (IMT) is well known to increase respiratory muscle strength and exercise capacity in patients with chronic heart failure (CHF). Several studies have shown that increased inspiratory muscle strength augments respiratory tidal volume and consequently reduces sympathetic nervous activity. On the other hand, higher serum level of cortisol has been reported to be a poor prognostic factor in CHF patients. Continual exposure to mental or physical stress stimulates their sympathetic nervous activity and promotes cortisol secretion. The immediate effects of IMT on autonomic nervous system and stress reaction are still unclear, although a long-term IMT reduces sympathetic nervous activity. We investigated the immediate effects of IMT on sympathetic and parasympathetic nervous activities and stress reaction in CHF patients.
Methods: Twenty patients with compensated CHF (67.0±10.8 years, 15 males) were enrolled, who underwent cardiac rehabilitation during hospitalization. The patients who received thoracic surgery within 6 months or had chronic respiratory disease were excluded from this study. We measured maximum inspiratory pressure (PImax) as an inspiratory muscle strength using pressure transducer connected to a spirometry. Patients performed the IMT with inspiratory load of 30% PImax for 10 minutes. Blood pressure, cardiac output (CO) and systemic vascular resistance (SVR) were continuously measured with a non-invasive blood pressure monitoring device as cardiovascular responses. Low-frequency (LF) component in blood pressure variability and high-frequency (HF) component in heart rate variability were analyzed before and after IMT to assess sympathetic and parasympathetic nervous activities, respectively. Salivary cortisol concentration was measured using ELISA method before and after IMT as an index of stress reaction. The Wilcoxon signed rank test was performed to assess the statistical differences in autonomic nervous activity and stress reaction before and after IMT.
Results: HF component increased significantly from 134.7±237.0 before IMT to 217.7±293.0 ms^2 after IMT ($p<0.05$), and LF component decreased from 14.2±26.2 to 3.8±3.8 ms^2 ($p<0.05$). CO increased significantly from 4.2±1.7 to 4.6±1.8 L/min ($p<0.05$), and SVR decreased from 2,162.1±1,339.0 to 1,454.4±524.0 dyn·s/cm5 ($p<0.05$). Salivary cortisol concentration decreased significantly from 2.3±0.7 to 1.7±0.6 ng/mL ($p<0.05$).
Conclusion: A single session of IMT improved autonomic nervous imbalance resulting in the reduction of stress reaction in patients with CHF.

P4221 | BEDSIDE
Cardiopulmonary exercise testing to identify patients with pulmonary hypertension

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Background: The importance of cardiopulmonary exercise testing (CPET) as a cost-efficient, safe and non-invasive method in the functional characterization and treatment-control of patients with confirmed pulmonary hypertension (PH) is undoubted. Less well established is the capability oft CPET to distinguish between patients with and without PH as well as between pre- and postcapillary PH.
Patients and methods: We retrospectively investigated the data of 340 patients who underwent resting right-heart catheterization and treadmill CPET within 30 days. Patients were classified into groups based on hemodynamic criteria: non-PH (PAPmean <25 mmHg; PCWP <15 mmHg) and PH (PAPmean ≥25 mmHg).The PH group was further divided into precapillary PH (PAPmean ≥25 mmHg; PCWP ≤15 mmHg) and postcapillary PH (PAPm ≥25 mmHg; PCWP >15 mmHg). Nominal scaled data were compared by Chi-squared-test and CPET data were compared by Kruskal-Wallis-Test. Values of p<0,017 (pre- vs. postcapillary PH) and p<0,001 (PH vs. non-PH) were considered significant. A receiver operating characteristic (ROC) analysis was performed to evaluate specific cut-off values to differentiate PH from non-PH and pre- from postcapillary PH. An area under the curve (AUC) >75% was classified as clinical relevant.
Results: We identified 230 patients with PH, 60 with precapillary PH and 170 with postcapillary PH. 110 patients were classified as non-PH. PH-patients did differ from non-PH relative to each CPET value (HR, VO2/HR, VO2, pETCO2, EqCO2, respectively at peak exercise and at anaerobic threshold (AT), and the VE/VCO2-slope). ROC analysis showed an AUC >75% for VO2@AT ≤11,8 ml/min/kg and peak VO2 ≤15,9 ml/min/kg to differentiate between PH and non-PH. Patients with precapillary PH showed significant lower VO2/HR and pETCO2 respectively at peak exercise and AT and a higher EqCO2@AT and VE/VCO2-slope as compared to postcapillary PH. ROC analysis for these values did not show an AUC >75%.
Conclusion: Patient with PH have a significant lower exercise capacity and a worse ventilatory efficacy as compared to non-PH. Cut-off values for VO2@AT ≤11,8 ml/min/kg and peakVO2 ≤15,9 ml/min/kg were identified to detect a PH by CPET. It was not possible to differentiate patients with pre- from postcapillary PH by specific cut-off values of CPET parameters.

P4222 | BEDSIDE
Significance of impaired heart rate response to exercise in diabetes

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Background: Diabetes may have neurologic effects including autonomic impairment which turn affects the heart rate (HR) response to exercise. We assessed resting HR, peak HR, percent of age predicted maximal HR and HR recovery (peak HR- HR at 1 minute post peak exercise in active recovery at 1.7 MPH/0% grade) according to diabetes and determined the role of HR in survival in diabetes.
Methods: Non-imaging exercise tests performed on patients 20-91 years of age on the Bruce protocol from 1-1-94 to 1-5-06 were included. Patients with baseline cardiovascular diseases or on drugs that influence heart rate were excluded. Because diabetes and HR responses were not equally distributed by sex, we performed separate analyses for men and women. T-tests for continuous and Chi-square tests for categorical variables were used to compare HR responses by diabetes and sex. We determined total mortality according to diabetes by Cox regression adjusted for age and sex. The influence of HR responses was assessed by adding HR recovery (reflecting parasympathetic tone) and peak HR (reflecting sympathetic tone) into the Cox model.
Results: A total of 29,960 patients (69% men) of whom 1630 diabetics (5.4%) were included. HR responses by diabetes and sex are shown in the Table. Both male and female diabetics had higher rest HR, lower peak HR and lower HR reserve and HR recovery compared to non-diabetics. There were 999 deaths (3.3%) over a median follow-up of 12.3±3.1 years. Diabetes was a significant age-and-sex-adjusted predictor of mortality (hazard ratio = 1.55 with 95% CL 1.27 – 1.81, p<0.0001). Peak HR <85% predicted (hazard ratio = 1.62 with 95% CL1.31 – 1.96, p<0.0001) and abnormal HR recovery <13 bpm (hazard ratio = 1.62 with 95% CL 1.42 – 1.84, p<0.0001) both contributed to risk.

Heart rate responses by diabetes and sex

	Men			Women		
	Normal (N=19,575)	Diabetes (N=1,223)	p	Normal (N=8,755)	Diabetes (N=407)	p
Peak HR (bpm)	167.9±17.3	157.2±18.1	<0.0001	165.2±16.0	158.2±15.4	<0.0001
HR reserve (bpm)	91.5±18.7	76.3±18.9	<0.0001	83.9±17.1	72.2±16.5	<0.0001
HR recovery	17.7±7.8	14.6±7.9	<0.0001	17.2±8.3	14.4±7.9	<0.0001
Abnormal HR recover (%)	24.2	39.6	<0.0001	28.1	41.8	<0.0001

Conclusions: Diabetics have abnormal HR responses to exercise and these abnormalities are independently associated with reduced long-term survival.

P4223 | BEDSIDE
Linear discriminant analysis of heart rate variability differentiates between autonomic modulation induced by acute physical and psychophysiological stress

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Purpose: Heart rate variability (HRV) is increasingly used to study the psychophysiology of stress in laboratory environment. However, in the real life, it can be difficult to differentiate the relative contribution of psychophysiological stress (PS) and physical stress (PhS) when their effects may overlap, such as during military or police tactical operations, or critical incidents. This study aimed to assess the predictive accuracy of HRV parameters in differentiating autonomic modulations induced by maximal PhS and by PS during realistic operational training (OT).
Methods: 12-lead ECG of 40 police officers (POs) was continuously monitored during rest daily activity (control state) and during highly demanding OT scenarios implying high PS without or with minimal PhS. All POs underwent, in a separate session, an exercise test with bicycle ergometer until muscle exhaustion. Baseline clinical and psychological assessment was performed on the days of the OT session. Behavior and tactical outcome were monitored with multiple video cameras. Quantitative estimates of time-domain (TD), frequency-domain (FD), and nonlinear HRV parameters were computed from standard (300-seconds), short-term (120-seconds) and very short-term (60-seconds) intervals. Preliminarily time-varying (TV) spectral HRV analysis was used to visualize transient fluctuations of FD components. Discriminant Analysis (DA) was applied to evaluate which HRV parameters (or their combination) were efficient to provide adequate separation between PhS and PS.
Results: TV HRV analysis provided dynamic imaging of transient autonomic adaptation induced by PS and/or PhS. Quantitative estimation of the majority of TD and FD HRV parameters was not significantly affected by shortening the length of the explored time-segments (from 300 to 60 seconds), as demonstrated by the intraclass correlation coefficient >0.70. DA differentiated PhS from PS with best predictive accuracy of single HRV parameters ranging between 82% and 92% (SD1/SD2 and SDNN/RMSSD, measured from 60-seconds and 120-seconds intervals, respectively). The highest classification accuracy (93%) was obtained with the combination of NL SD1/SD2 (Poincaré plot), rplmean and rpadet (recurrence plot).
Conclusions: TV HRVa is efficient in evidencing transient changes of autonomic modulation of the heart rate during realistic OT. Quantitative estimate of HRV parameters is not significantly affected by shortening the duration of the explored time-window from 300 to 60 seconds. DA of HRV features may be useful to evaluate PS induced by realistic police OT and to distinguish it from overlapping PhS.

DETAILS OF EXERCISE TRAINING AND TESTING

P4225 | BEDSIDE
Clinical validation of fractional flow reserve in aorto-iliac lesion; a comparison with post-exercise ankle brachial index

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Purpose: Post-exercise ankle brachial index (ABI) is an essential testing for symptomatic peripheral artery disease (PAD) patients with normal resting ABI. In many cases, typical claudication may not occur in patients with co-morbidity that prevent sufficient exercise to produce limb symptoms, causing underestimate of limb status. Recently, fractional flow reserve (FFR) has been used as a physiological assessment of stenosis. However, there were no reports regarding use of FFR to evaluate severity of stenosis in aorta-iliac artery. The purpose of this study was to evaluate that FFR may correlate post-exercise ABI and could be an alternative tool for physiological assessment of stenosis.
Methods: Fifteen PAD patients underwent baseline resting and post-exercise ABI using treadmill testing (2.4km/h, 12% grade, 5minutes). All patients had an accelerated peak systolic velocity in duplex ultrasound and underwent catheter angiography for further examination. Pre-interventional FFR was performed during angiography using a 0.014" pressure guidewire and recorded with papaverine. We evaluated the correlation between post-exercise ABI and FFR with papaverine. And then, we assessed cut-off value for detecting aorto-iliac artery ischemia comparing to patients without claudication and obvious stenosis at angiography.
Results: Mean baseline resting ABI and post-exercise ABI were 0.89±0.13 and 0.65±0.22 in overall, respectively. In 15 PAD patients, 6 patients had normal or borderline resting ABI. Three out of these 6 patients had 20% drops in post-exercise ABI compared to resting ABI. In present analysis, a significant linear correlation was observed between the post-exercise ABI and the FFR at hyperemia (r=0.825; p<0.001). A receiver operating characteristic (ROC) analysis of the ability of FFR at hyperemia to predict significant stenosis gave an area under the ROC curve of 0.853 (95%CI 0.687-1.000, p=0.021). The optimal cut-off FFR value at hyperemia was 0.78 with sensitivity of 100% and specificity of 73%.
Conclusions: We could show that a significant linear correlation between post-exercise ABI and FFR in an aorto-iliac lesion for the first time. FFR measurement

could be an alternative tool to post-exercise ABI in physiological assessment of stenosis because FFR isn't influenced by co-morbidity and limb status.

P4226 | BEDSIDE

Clinical significance of a spiral phenomenon in the plot of CO2 output against O2 uptake in heart failure patients with oscillatory breathing

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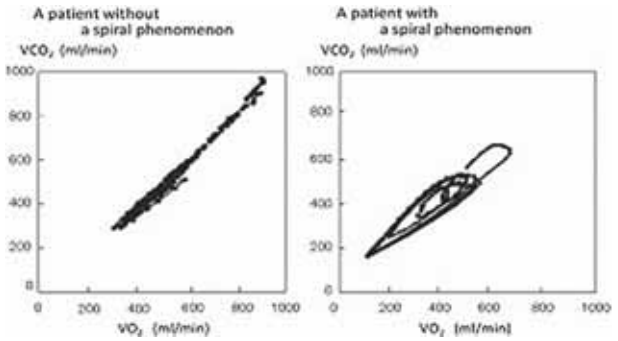
Background: Although some cardiac patients with oscillatory breathing (OB) present a spiral phenomenon (SP) in the plot of VCO2 vs. VO2 during exercise, its clinical significance has not been clarified.
Methods: Consecutive 772 patient who performed cardiopulmonary exercise testing and whose NYHA functional class is $\geq$ II were served as the subjects. Cardiopulmonary indices and total death during the prospective follow-up period of 4.5±2.5 years were compared between patients with OB (n=85) and those without it (n=687), and also between patients with SP (n=22) and those without it (n=63) among the patients with OB.
Results: As compared to the patients without OB, those with OB had significantly lower peak VO2 (13.6±4.7 vs. 15.1±5.1 mL/min/kg, p=0.01) and higher VE-VCO2 slope (40.7±11.1 vs 34.9±8.8, p<0.001), although the presence of OB was not significantly related to the prognosis. Among the patients with OB, patients with SP had lower peak VO2 (10.0±2.9 vs 14.8±4.6 mL/min/kg, p<0.001) and higher VE-VCO2 slope (47.8±11.8 vs. 38.4±9.9, p=0.01), than those without SP. The patients with SP had significantly higher mortality than those without it (p<0.01).



The plot of VCO2 vs. VO2 during exercise

Conclusion: The spiral phenomenon of VCO2 vs. VO2 plot is significantly related to cardiopulmonary dysfunction and poor prognosis in heart failure patients.

P4227 | BEDSIDE

Vascular endothelial dysfunction is an independent predictor for excessive blood pressure elevation during exercise simulating the ordinary activities of daily living in patients with hypertension

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Background: Excessive blood pressure (BP) elevation was frequently observed during exercise at low or moderate workload in patients with hypertension (HT), although their BP at rest was successfully controlled with antihypertensive treatment. Vascular endothelial dysfunction has been reported to cause excessive BP elevation during treadmill exercise test in HT patients. However, it is still unknown whether vascular endothelial dysfunction contributes to excessive BP elevation during exercise simulating the ordinary activities of daily living (ADL) in them. The purpose of this study was to investigate whether vascular endothelial dysfunction induced excessive BP elevation during exercise simulating the ordinary ADL in them.
Methods: We recruited 65 outpatients with HT aged 68±6 years, whose BP at rest was controlled below 140/90 mmHg, and 42 age-matched community-dwelling healthy individuals as control. We measured high-sensitivity C-reactive protein (hs-CRP) and assessed homeostasis model assessment ratio (HOMA-R) as parameters of vascular inflammation and insulin resistance, respectively. We also measured reactive hyperemia index (RHI) as a parameter of vascular endothelial function and evaluated an arteriosclerosis using a brachial-ankle pulse wave velocity and intima-media thickness of the carotid artery. The intensity of exercise simulating the ordinary ADL was defined as 75% of peak heart Rate (HR) that was measured with treadmill exercise test. BP elevation during the exercise was determined as the difference from systolic BP (SBP) at rest to peak SBP during cycle ergometer exercise test that was performed at the exercise intensity of 75% peak HR (ΔSBP). The patients were divided into two groups based on the median of ΔSBP obtained from the age-matched healthy individuals: excessive ΔSBP and normal ΔSBP groups. We compared all parameters between the two groups and analyzed the relationship between RHI and ΔSBP in all patients. Multiple regression analysis was used to detect the predictors for excessive BP elevation during the exercise.
Results: RHI was significantly lower in the excessive ΔSBP group than in the normal ΔSBP group (P<0.05) and negatively correlated with ΔSBP in all patients (r=-0.313, P<0.05). Multiple regression analysis identified RHI (β=-0.297, P<0.05), HOMA-R (β=0.347, P<0.05) and hs-CRP (β=0.412, P<0.01) as significant independent predictors for excessive ΔSBP (R2=0.28).
Conclusion: Vascular endothelial dysfunction was an independent predictor for excessive BP elevation during exercise simulating the ordinary ADL in patients with HT.

P4228 | BEDSIDE

Regular training in patients with advanced heart failure (NYHA III) and implantable cardioverter-defibrillator - a prospective 18-months observation

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Background: Exercise, beside drug therapies and procedures, is one of the heart failure (CHF) treatment options. The aim of the study was to evaluate the impact of individual training on the level of physical capacity and echocardiographic parameters in patients with CHF (NYHA III) and implantable cardioverter-defibrillator (ICD).
Methods: The study included 86 ICD patients hospitalized for worsening CHF, randomly assigned to one of two groups: with regular training (ICD -Ex) and control group (ICD-Control). ICD-Ex group participated in a comprehensive hospital rehabilitation program which after the discharge has been individually continued for 6- months in an outpatient setting. ICD–Control group was trained only during hospitalization, but after discharge did not perform any controlled activities. Prior to discharge, at 6 and 18 months ergospirometry test (CPX) was performed in all patients. Standard echocardiographic examination (2D plus Doppler) and 6-minute walk test (6- MWT) were additionally completed.
Results: ICD-Ex group finally consisted of 37 pts, age 63.6±9.1 and ICD-Control – of 40 pts, age 61.7±10.0. Groups did not differ in terms of demographic and clinical features. Ischemic etiology of CHF was most prevalent (ICD–Ex: 73% vs. ICD-Control: 65%). After training and after 18 months most of the parameters of CPX in the ICD-Ex group improved significantly: peak VO2, p=0.017, peak VO2 (%), p=0.0025, peak VCO 2, p=0.0002, time effort, p=0.0083, Watt, p=0.0057, METs, p=0.047. In the group of ICD-Control there was no significant improvement of any parameter. LV systolic dimension remained significantly lower at 18 months in the group of ICD -Ex, and in ICD-control group did not differ compared to initial examination. LV EF in both groups significantly increased at 6 and 18 months compared to baseline testing. Distance of 6-MWT was significantly improved (377.4±118, after 6 months 491±127 and 18 months 490±137, p<0.0001) in the ICD-Ex group and was longer (p<0,05) than in the ICD-control group (respectively: 378±82, 423±114, 422±111, ns). Number of ICD interventions: 1 in ICD-Ex, 5 in ICD-Control (in 5 pts), ns.
Conclusions: Individual, 6-month exercise program used in patients with severe heart failure after implantation of ICD contributed to a significant improvement in exercise tolerance, exercise capacity and echocardiographic parameters. Individually selected rehabilitation in these patients was safe and should be a crucial part of a complex treatment necessary to maintain their optimal clinical condition.

P4229 | BEDSIDE

CHA2DS2-VASc scores are associated with exercise capacity in patients with AF: Linkage between diastolic dysfunction and thromboembolic risk

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Background: CHA2DS2-VASc score is popular tool for thrombo-embolic risk stratification in patients with atrial fibrillation (AF). Each components of CHA2DS2-VASc score is well-known risk factor for diastolic heart failure. Intra-atrial blood stasis resulting AF might cause unfavorable effect to diastolic filling and exercise capacity, as well as thrombus formation. We tried to evaluate whether CHA2DS2-VASc score is associated with exercise capacity and diastolic dysfunction function in patients with AF.
Methods: Consecutive patients with persistent non-valvular AF and preserved functional capacity (NYHA I-II) were enrolled prospectively. The clinical characteristics, plasma BNP, echocardiography, and exercise capacity (peak oxygen uptake, peak VO2) using cardiopulmonary exercise test were compared with CHADS2-VASc scores.
Results: Among study population (n=57, 31 men, mean age= 61±9 years), female patients were older and had higher CHA2DS2-VASc score than male patients. Peak VO2 value was correlated with age (r= -0.595, p<0.001), CHA2DS2-

VASc score (r= -0.613, p<0.001), estimated glomerular filtration rate (r=0.429, p=0.001), resting BNP level (r= -0.628, p<0.001) and diastolic index of E/E' ratio (r= -0.456, p=0.013). Age (b= -0.366, p=0.004) and CHA2DS2-VASc score (b= -0.427, p=0.004) were independent predictor for peak VO2 value.

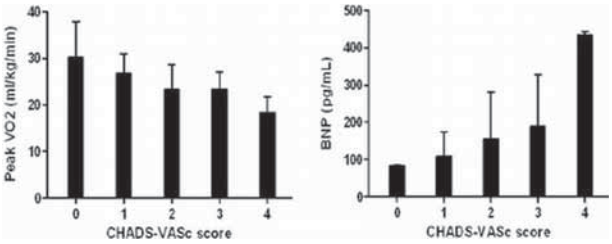

Figure 1

Conclusion: CHA2DS2-VASc score is associated with exercise capacity in patients with chronic AF. Diastolic dysfunction is thought to the major mechanism of both exercise capacity and thromboembolism. Patients with high CHA2DS2-VASc score need to careful monitoring for the development of heart failure.

P4230 | BEDSIDE

Blood pressure recovery after maximal exercise at high altitude in mild hypertensive subjects and effects of antihypertensive combination treatment

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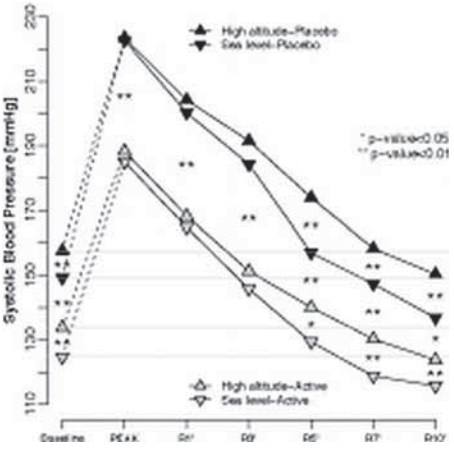
Purpose: Exposure to high-altitude (HA) hypoxia increases resting and ambulatory blood pressures (BP). No data are available on systolic BP (SBP) at peak exercise and during recovery in hypertensive subjects acutely exposed to HA.
Methods: 55 mild-hypertensives from HIGHCARE-ANDES study (age 57.5±8.9; 29M) performed an incremental cardiopulmonary exercise test to exhaustion in 3 conditions: at sea-level (SL) off-treatment (SLbas) and 6-weeks after double-blind randomization (SLtx) to Telmisartan (T)/Nifedipine (N)-GITS (n=27) or placebo (PL, n=28); and on the 1° full day of permanence at 3260m (Huancayo-Perù) under randomized treatment. For all of them SBP values were available at rest, at peak exercise, and at 1-3-5-7-10min recovery.
Results: At SLbas there were no differences among the two treatment groups. HA exposure increased SBP at rest in both groups, although SBP was significantly lower in T/N group. At peak exercise SBP was similar between SLtx and HA, but peak exercise at HA corresponded to a 13% lower (p<0.001) oxygen consumption. T/N-GITS reduced SBP not only at rest, but also at peak exercise and during recovery both at SLtx and at HA.
For the first 3min immediately after exercise, SBP was similar between SLtx and HA, either on T/N-GITS or on PL. Conversely at 5-7-10° min of recovery SBP was higher at HA than at SLtx, either on T/N-GITS or on PL (figure).



Conclusions: In hypertensive subjects:
– recovery of SBP towards resting values after maximal exercise is slower at HA, possibly due to an impairment of the autonomic cardiovascular regulation in hypoxic conditions;
– T/N-GITS effectively reduces SBP both at SL and at HA, at rest, at peak exercise, and throughout recovery.
These findings should be considered when managing hypertensive subjects planning an acute exposure to HA.

P4231 | BEDSIDE

Exercise oscillatory ventilation occurrence in a population at risk without cardiac dysfunction: insights from the EURO(pean) EX(ercise) population-based study

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Background: Among exercise-derived variables that may define cardiovascular risk, oxygen consumption (VO2) is an established indicator of prognosis. Gas exchange analysis allows to define a series of ventilator and metabolic parameters that may add to characterize the level of risk. We aimed at assessing the exercise gas exchange analysis phenotype in the general population at risk for cardiovascular disease enrolled in the EUROEX study.
Methods: 373 asymptomatic subjects (mean age 59±14 years; male 48%; BMI 28±6 kg/m^2)with different cardiovascular risk factors (hypertension 64%, dyslipidemia 48%, smoking 20%, diabetes 14%) underwent a maximal cardiopulmonary exercise testing (CPET) with personalized ramp protocol.
Results: The population was divided into two groups according to the occurrence of EOV (Table). Subjects in the EOV group showed a reduced tolerance to exercise (lower peak VO2, % of predicted VO2, peak O2 pulse and delta VO2/delta WR) and a worse ventilator efficiency (steeper VE/VCO2).

Table 1

Variables	No EOV (n=316)	EOV (n=57)	P value
Age (y)	59±14	61±13	ns
Male (%)	53.8	21	<0.05
BMI (kg/mq)	28±5	28±5	ns
Peak VO2 (ml/min/kg)	20.2±7.4	15.8±3.6	0.0000
% of predicted VO2	74±21	62±15	0.0000
VE/VCO2 slope	25.5±3.8	26.6±4.1	0.08
HRR (bpm)	17±11	15±10	ns
Peak O2 pulse (ml/beat)	11.5±3.9	9.3±2.7	0.0000
Work (Watt)	120±49	120±50	ns
ΔVO2/ΔWork rate	9.5±1.5	9±2	0.07
End-tidal CO2 (mmHg)	39.5±4	37.4±4	<0.05

Conclusions: In the sample population investigated, an oscillatory gas exchange pattern was documented in 15.3% of population. For the same level of risk and demographic characteristics, this group of patients exhibited a lower performance and a worse ventilation efficiency. These findings may provide the bases for a more-in-depth definition of abnormal exercise phenotypes worth of special consideration.

P4232 | BEDSIDE

Effect of combined cognitive-exercise training on vascular and cognitive function in patients with mild cognitive impairment: the Train the Brain study

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Objective: Vascular factors are possibly involved in cognitive decline development, related both to vascular and Alzheimer dementia. Aim of this study was to evaluate the effects on cognitive and vascular function of a combined cognitive-exercise training in mild cognitive impairment (MCI), an initial stage of cognitive decline associated with a higher incidence of dementia.
Methods: 45 individuals with MCI (31 men, age 75±5 years, BMI 27±4 kg/mq, 3 smokers, 24 hypertensives, 9 diabetics, 5 with previous CV events) underwent a combined 7-month cognitive (6h/week) and exercise training (3h/week). Vascular function was evaluated by means of endothelium-dependent (flow-mediated-dilation, FMD) and independent (response to glyceryl trinitrite – GTN) vasodilation of the brachial artery (BA), pulse wave velocity (PWV), hematopoietic (CD34+) and endothelial progenitor cells (EPCs). Cognitive function was evaluated by means of the ADAS-cog scale (higher values indicating worse performance).
Results: Mean blood pressure (MBP) was significantly reduced after 7-month training (95±9 to 91±9, p=0.007). FMD was significantly increased (2.86±1.77 to 3.85±2.03, p=0.04), whereas BA diameter, baseline and hyperemic shear rate and GTN were not modified. PWV was unchanged (10.4±2.3 to 9.9±2.8, p=0.20).

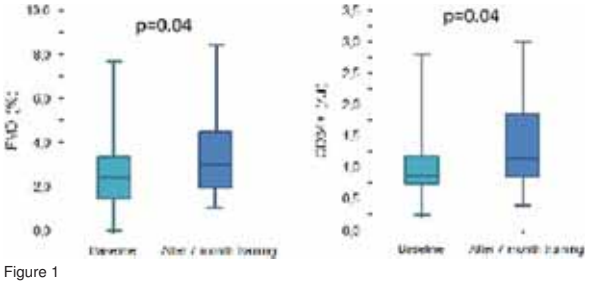

Figure 1

CD34+ cells (0.87±0.43 to 1.13±0.43/μl, p=0.04), but not EPCs, were increased after 7-month training. ADAS-cog was significantly decreased (13.5±5.0 to 11.7±3.8, p=0.04). Training-induced changes in cognitive performance were unrelated to changes in FMD (r=0.05, p=0.77) and CD34+ cells (r=-0.14, p=0.39). **Conclusions:** A combined 7-month cognitive and exercise training is able to improve cognitive function as well as systemic endothelial function and to increase hematopoietic cell mobilization in MCI.

P4233 | BEDSIDE

Utility of cardiopulmonary exercise testing on treadmill and recumbent bycicle in prediction of coronary artery disease severity in comparison to stress echocardiography

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Cardiopulmonary exercise test (CPET) on upright bicycle is superior to ECG-exercise test in detection of myocardial ishaemia. The aim of this study was to examine the utility of CPET on treadmill and recumbent bicycle in relation to stress echocardiography testing, and in between, in prediction of coronary artery disease severity. We studied 30 Caucasian males, mean age 63.10±8.55, with significant lesions of coronary arteries (≥50%), quantified by Syntax score. CPET on recumbent bicycle and treadmill were performed in two visits (2-4 days in between), within two months of coronary angiography. The protocol involved ramp-pattern increase in work rate (WR) on bicycle and standard Bruce protocol on treadmill. Tests were symptom limited, or were stopped when ≥2 mm ST depression occurred in at least two adjacent leads. Myocardial wall motion was recorded by echocardiography at rest and maximal phase of the test, and reported using conventional 16-segment model. The ishaemia was quantified by wall motion score index (WMSI). Basal spirometric parameters were normal. Mean ejection fraction was 59.3±7.63%. Examiners exhibited mean 1.56±0.88 number of stenotic coronary arteries (NSCA) and Syntax score 10.39±7.56. PeakWMSI was 1.18±0.1, and ΔWMSI peak/rest 0.12±0.07. Most CPET data obtained on recumbent bicycle suggested a lower values then on treadmill, as peak oxygen uptake (peakVO2; 1.21±0.23 vs. 1.59±0.40 l/min, p=0.02), peak minute ventilation (peakVE; 37.35±13.14 vs. 49.96±14.39 ml/min, p=0.005), peak O2pulse (11.36±2.61 vs. 13.27±3.03 ml, p=0.027) and ΔVO2/ΔHR (20.03±9.47 vs. 30.15±5.25 l, p=0.007), whereas VE/VCO2 slope and end-tidal pressures of O2 (PETO2) and CO2 (PETCO2) in all phases were similar. Our results revealed significant correlations of peakWMSI; ΔWMSI peak/rest; peakVE; peak and rest PETCO2 and PETO2; as well as the change of HR, O2pulse and VO2 in recovery with Syntax score ($p<0.01$). The best independent predictor of Syntax score was peakPETCO2 (R2=0.86, r=0.93, $p<0.0001$) obtained on recumbent bicycle. NSCA correlated with restWMSI; ΔWMSI peak/rest; peakVO2; O2pulse and PETO2 et peak exercise and in recovery; the change of VO2 and O2pulse in recovery; and VE/VCO2slope, on both treadmill and bicycle ($p<0.01$). The best predictor of NSCA was peak O2pulse (R2=0.86, r=0.93, $p<0.0001$), obtained on recumbent bicycle. Our data suggest that CPET parameters have better predictive value for coronary artery disease quantification scores then WMSI. Furthermore, CPET parameters obtained on bicycle seem to be more reliable in this sense then parameters obtained on treadmill.

P4234 | BEDSIDE

Right ventricular systolic dysfunction can better predict exercise intolerance in patients after myocardial infarction with preserved left ventricular ejection fraction than elevated NT-proBNP

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Background: Patients after acute myocardial infarction (MI) with preserved left ventricular (LV) systolic function, have low exercise capacity (EC). Predictive value of elevated NT-proBNP plasma concentration and right ventricular (RV) dysfunction for low EC in that group is unclear.
Aim: To assess predictive value of elevated NT-proBNP concentration and RV systolic dysfunction for prognosis of exercise intolerance in patients after acute MI with preserved LV EF without history of heart failure.
Methods: We evaluated prospectively patients with first inferior MI with ST segment elevation treated by primary percutaneous coronary intervention (pPCI) and preserved LV systolic function (LV EF ≥45%). ECHO was performed post pPCI within 48 hours from the onset of symptoms. RV function was estimated with Tissue Doppler Echocardiography (TDE) at the basal segment of RV free wall as systolic myocardial velocity (Sm RV). NT-proBNP plasma concentration was measured in the first 48 hours after pPCI with Roche immunoassay. Cardiopulmonary exercise test (CPET) was done on day 14±10 after acute MI. As exercise intolerance we considered EC lower than 70% of maximal predicted values peak VO2 (ml/kg/min). Receiver operating characteristic (ROC) and area under the curve (AUC) were used for assessing sensitivity, specificity and predictive values.
Results: In evaluated patients (n=90, 75,5% males, mean age 60,5±10 years) mean Sm RV was 11,3±2,6 cm/s and mean NT-proBNP - 1197±1729 pg/ml. Mean peak VO2 was 19,9±5,5 ml/kg/min (68±19% VO2 max. predicted). ROC and AUC analysis showed that RV systolic dysfunction more accurate predict exercise intolerance than elevated NT-proBNP plasma concentration (Table).

	Sm RV (cut off value 10,2 cm/s)	NT-proBNP (cut off value 1700 pg/ml)
Sensitivity	55,8%	27,5%
Specificity	84,2%	89,5%
Positive predictive value	82,9%	77,8%
Negative predictive value	58,2%	47,9%
AUC (95% CI)	0,703 (0,594–0,812)*	0,506 (0,384–0,627)*

*P=0.02.

Conclusion: RV systolic dysfunction can better predict exercise intolerance than elevated NT-proBNP in patients after acute inferior MI with preserved LV ejection fraction.

THE BITTER TASTE OF SWEET

P4236 | BEDSIDE

Fasting blood glucose predicts cardiovascular risk in TNT and IDEAL

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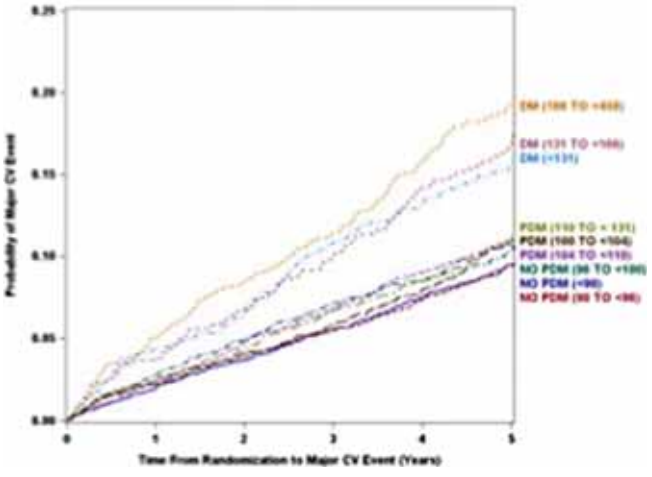
Purpose: In this study, we sought to: (1) characterize risk of CV events by baseline FBG in outpatients with stable coronary disease and (2) investigate how statin therapy, which can affect glucose metabolism, affected this risk relationship over time. We hypothesized that patients who jumped to a higher FBG tertile 6 months after initiating statin therapy might be at higher risk compared with those who remained in the same FBG tertile.
Methods: We compared CV event rates, stratified by FBG at baseline, among 15,941 patients with coronary disease in the pooled TNT and IDEAL cohorts, excluding those who had an endpoint event prior to 6 months. Patients were divided into no pre-diabetes (no PD), pre-diabetes (PDM), diabetes (DM) and further into tertiles within these groups. CV events included coronary heart disease death, myocardial infarction, stroke, and resuscitated cardiac arrest. Cox regression models were constructed to assess event rates and adjusted for a pre-specified set of covariates.
Results: The rate of primary CV events increased in a stepwise fashion from the lowest to the highest tertile of FBG (Figure). CV risk reduction with high versus moderate-intensity statin treatment was independent of baseline FBG (p-interaction=0.85). There was a no difference in the CV event rate in patients on statin therapy who increased their FBG tertile from baseline to 6 months (N=3432) (adjusted HR 0.95, 95% CI 0.80-1.12, p=0.51) compared with those who stayed in the same FBG tertile at 6 months.



Conclusion: The rate of CV events increases with increasing baseline fasting blood glucose in patients with stable coronary disease. Those who jumped to a higher FBG tertile at 6 months with statin therapy did not have a higher CV event risk compared to those who stayed in the same FBG tertile.

P4237 | BEDSIDE
Long-term outcomes in patients with and without diabetes following an incident myocardial infarction: a population-based study

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Purpose: Post myocardial infarction (MI) rates of new cardiovascular events in diabetic patients reflect the effectiveness of treatment and prevention. We examined the risk and predictors of major cardiovascular events in diabetic versus nondiabetic patients following incident MI in a population-based setting.
Methods: 30-day survivors of incident MI aged 35-84 years were identified from whole-population linked hospital morbidity and death data for 2003-2010, using a 13-year lookback period to exclude prevalent MI cases. Validated diabetic status was identified from hospital data. Outcomes were available for all patients up to 30 June 2011. Outcomes included MI/coronary revascularisation, heart failure (HF) and stroke hospitalisation (principal diagnosis), and composite endpoints of CHD (MI, revascularisation or CHD death), and major CVD (MI, HF, stroke, revascularisation or CHD death). Cumulative incidence was estimated from Kaplan-Meier curves, and multivariate adjusted hazard ratios calculated from Cox regression models, adjusted for age, indigenous status, comorbidities, and revascularisation status.
Results: There were 16,537 30-day survivors of incident MI in the study cohort (25.2% diabetic, 70.1% men). Mean age was 65.8 years in diabetics and 63.2 years in nondiabetics. At 1-year, cumulative incidence of a new CHD event was 11% in men and women, double that of nondiabetics, and had increased to 37% by 5 years. Half of the diabetic patients experienced a major CVD event by 5 years, compared with 25% of nondiabetics. In diabetics, this was associated with a 2-3 times higher cumulative incidence of nonfatal events (MI/revascularisation 34%; HF 20%) than CHD death (10%). The multivariate adjusted hazard of a new CVD event in diabetics versus nondiabetics was 1.3 times higher in men (95% CI 1.2, 1.4) and 1.6 times higher in women (95% CI 1.3, 1.8). Most of the excess risk for new CHD and CVD events was accounted for by baseline HF, hypertension and chronic kidney disease, and in women, prior stroke. Indigenous status conferred a higher risk for a CVD event in men (HR 1.6, 95% CI 1.3, 1.9) and women (HR 2.1, 95% CI 1.6, 2.6). CABG at baseline was highly protective of a new CVD event in diabetics relative to nondiabetics (HR 0.2, 95% CI 0.1, 0.3 men; HR 0.4, 95% CI 0.3, 0.6 women).
Conclusion: Very long-term followup highlights the significantly elevated incidence and risk of major CVD events in diabetic patients following incident MI. This demonstrates the imperative for promoting intensive cardiovascular management and secondary prevention in patients with diabetes to improve outcomes.

P4238 | BEDSIDE
Mitochondrial oxidative stress, inflammation and endothelial function in people with type 2 diabetes

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Purpose: Mitochondrial dysfunction and increased oxidative stress are detected in several inflammatory diseases and promote pro-atherosclerotic cytokine production as well as endothelial dysfunction. However, it remains unknown whether these pathways could be reversed by modulation of the host response. Using chronic periodontitis and its treatment as a model of chronic inflammation and vascular dysfunction the aims of this study were: 1) to ascertain if periodontal treatment could change mitochondrial oxidative stress production (MOSP) in peripheral mononuclear cells (PBMC), 2) the association of MOSP with a panel-array of inflammatory/vascular circulating biomarkers and 3) the relationship of these pathways with endothelial function.
Methods: 46 patients with type 2 diabetes and periodontitis where randomly allocated to receive either intensive periodontal treatment (IPT) or control therapy (CPT) and followed over 6 months. PBMC were isolated from peripheral blood using density gradient centrifugation according with standard techniques, whilst MOSP was measured with MitoSOX using flow-cytometry. Specificity of MOSP staining was checked with confocal microscopy. Inflammatory (IFN-γ, IL-1β, IL-10, IL-6, TNF-α) and vascular (E-Selectin, ICAM-3, P-Selectin) circulating markers were assessed by high sensitivity Multiplex assays. Endothelial function was assessed by flow mediated dilation (FMD) of the brachial artery.
Results: 27 patients in the IPT group and 19 patients in the CPT group were included in the study. After 6 months, PBMC of patients in the IPT group had significantly lower levels of MOSP compared to those in the CPT group ($p<0.01$). When analysis was performed by subpopulation of PBMC, the greater reduction in MOSP was observed in lymphocytes ($p<0.05$), whilst no differences were detected in monocytes. Circulating levels of IFN-γ, TNF-α, E-Selecting and P-Selectin reduced in the IPT compared to the CPT group ($p<0.05$ for all biomarkers). FMD improved overtime with significantly greater improvement recorded in the IPT compared to the CPT group ($p=0.005$ for IPT vs CPT at 6 months, $P<0.01$ for % change from baseline between IPT and CPT). These differences were independent of age, gender and BMI differences.
Conclusions: Our results suggest that MOSP could be reduced by periodontal treatment. This change was associated with a reduced production of pro-inflammatory/-atherosclerotic cytokines by lymphocytes and improved endothelial function. MOSP could represent a novel therapeutic target for a more effective cardiovascular disease prevention in people with diabetes.

P4239 | SPOTLIGHT
The effect of incretin-based therapies on metabolic and cardiovascular parameters in diabetic patients: A meta-analysis of 28 randomized control trials with 10171 patients

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There is currently a debate on the positive effects of incretin-based therapies (IBTs) on cardiovascular (CV) parameters. In the meantime, there are studies which have shown opposite results. Therefore, we performed a meta-analysis to investigate whether IBTs influence metabolic and CV parameters in diabetes mellitus (DM) patients.
Data from Scopus, PubMed, Web of Science, and the Cochrane Central Register of randomized controlled trials for years 1966 – August 2013 were searched for appropriate studies.
Twenty eight trials with 10171 DM subjects randomized to receive either IBTs or placebo or other antidiabetic medications were included. Dipeptidyl peptidase-4 inhibitors were associated with weight gains when compared with glucagon-like peptide-1 receptor agonists (Δweight: 1.44 kg, 95%CI: 0.79-2.09; $p<0.0001$). Compared with placebo, IBTs significantly reduced the level of triglyceride (-0.29 mmol/L, 95%CI: -0.48 to -0.11; p=0.002) while in comparison with other antidiabetic medications IBTs increased the level of high density lipoprotein cholesterol (0.03 mmol/L, 95%CI: 0.0003-0.06; p=0.05, respectively). IBT therapy, compared with placebo, were associated with significant reductions in systolic blood pressure (-4.55 mmHg 95%CI: -6.86 to -2.24; p=0.0001) and diastolic blood pressure (-1.75 mmHg 95%CI: -3.12 to -0.37; p=0.01). In addition, IBTs, in comparison to other antidiabetic medications, significantly influenced heart rate (ΔHR: 1.62 beats/min, 95%CI: 0.32-2.93; p=0.0001).
In conclusion, besides the effectiveness of IBTs for lowering blood glucose in type 2 DM, these drugs exert significant positive effects on both lipid profile and blood pressure. More studies are necessary in order to confirm these results.

P4240 | BEDSIDE
Diabetes in relation to incidence of cardiovascular disease in Chinese men and women: a prospective cohort study of 0.5 million adults with 7 years of follow-up

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Purpose: Diabetes is a known risk factor for cardiovascular disease (CVD), but little is known about its association with CVD risk in China, especially with risk of stroke subtypes.
Methods: We analysed 7-year prospective data from 0.5 million men and women recruited into the China Kadoorie Biobank study during 2004-8. Among the 479 405 participants with no prior history of ischaemic heart disease, stroke or transient ischaemic attack at baseline there were 1946 incident myocardial infarction (MI) events, 16 649 ischaemic stroke (IS) and 4076 intracerebral haemorrhage (ICH) events at ages 35–79 years during 3.3 million person years of follow-up.
A self-reported history of doctor-diagnosed diabetes (2.8%) was related to the risks of incident IHD and stroke, using Cox regression analysis, stratifying by age, study area and sex, where appropriate, and adjusting for education, smoking, alcohol, blood pressure and physical activity.
Results: Self-reported diabetes was associated with a highly significant two-fold increased risk of MI (HR 2.41, 95%CI 2.06–2.83), with a HR of 2.32 (95%CI 1.85–2.93) in men and 2.51 (95%CI 2.01–3.14) in women. For incident IS individuals with self-reported diabetes also had 69% excess risk (HR 1.69, 95%CI 1.60–1.79), with more extreme risk at younger, than at older, ages (HR 2.49 at 35–49 years, 1.97 at 50–59 years, 1.73 at 60–69 years and 1.48 at 70–79 years). For ICH, there was a non-significant 15% excess risk (HR 1.15, 95%CI 0.98–1.35), with little difference between men and women.
Conclusions: In Chinese men and women individuals with a prior history of

diabetes experienced a significantly elevated risk of ischaemic cardiovascular events, similar in magnitude to those reported in Western populations.

P4241 | BEDSIDE
Specific deleterious effects of adiponectin on long-term outcome in diabetic patients with advanced coronary artery disease: A case for adiponectin resistance

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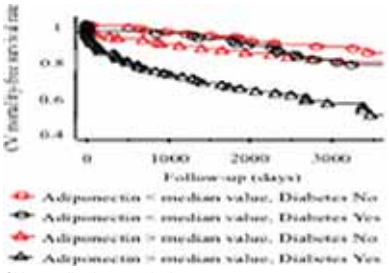
Purpose: Adiponectin, an adipocyte cytokine associated with insulin sensitivity, exerts antiatherogenic effects. However, its association with major cardiovascular events (MACE) bears conflicting results, in particular in patients with insulin resistance.
Methods: We investigated this issue in a population of 408 patients with advanced coronary artery disease (CAD; at least one coronary artery occlusion and a 9-year follow-up).
Results: The population was predominantly male (80.9%) with a mean age of 63±11 years. Baseline plasma concentrations of adiponectin were similar in patients with (6.73 (3.59-10.13) mg/mL) or without (6.31 (3.47-11.48) mg/mL) diabetes (fasting glycaemia>1.1g/L or known history, n=184, 45.1%). We documented cardiovascular (CV) mortality (n=101, 24.8%) and MACE (combined CV mortality, non-fatal myocardial infarction and ischemic stroke, n=197, 48.3%). Using Cox regression proportional analysis, age and sex adjusted adiponectin was an independent predictor of CV mortality (per each 1 mg/mL increase in plasma adiponectin concentration, hazard ratio HR=1.06, 95%CI=1.03-1.09, p<0.0001) and MACE (HR=1.04, 95%CI=1.02-1.07, p=0.0004). Likewise, age and sex adjusted Diabetes was an independent predictor of CV mortality (HR 1.82, 95%CI (1.19-2.70), p=0.0049). In diabetic patients, the presence of a high adiponectin level (above median value) was associated with an increased rate of CV mortality (HR=2.79, 95%CI (1.61-4.83), p=0.0002, Figure). In non-diabetic patients, the effect of a high adiponectin level was marginal on CV mortality (HR=1.69, 95%CI (0.89-3.22), p=0.11, Figure).



CV mortality-free survival rate.

Conclusion: Adiponectin concentrations could help risk-stratify diabetic patients with advanced CAD. The combination of adiponectin and insulin resistance play a specific deleterious role in CAD patients.

P4242 | BEDSIDE
Comparison of treatment outcomes in patients with and without diabetes mellitus attending a multidisciplinary cardiovascular prevention programme (the EUROACTION trial)

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Background: The extent to which diabetics benefit from lifestyle and risk factor interventions when compared to non-diabetics in the same clinical practice settings is not fully established. The objective was to compare the lifestyle and risk factor profiles in patients with and without diabetes mellitus in the intervention arm of EUROACTION study.
Methods: A longitudinal, retrospective analysis of the intervention arm of EUROACTION was performed. Participants (coronary patients and high-risk individuals {HRI}) in the intervention arm were classified as diabetic or non-diabetic based on an existing diagnosis of diabetes and/or fasting plasma glucose above 7 mmol/l. Primary outcome at one year was proportions meeting the European targets lifestyle changes, medical risk factors and cardioprotective drug use. These were compared at initial assessment (IA) and one year. Multiple logistic regression analysis (adjusting for baseline differences) was performed to determine the odds of achieving the targets based on diabetes status.
Results: 179 and 777 coronary patients and 340 and 917 HRIs with and without diabetes respectively were identified. The proportions of diabetic and non-diabetic coronary patients achieving the lifestyle targets improved from the IA except non-smoking, which reduced. At one year, significantly fewer diabetics attained the targets for BMI (13.2% vs 31.3%, p=0.002) and BP <140/90 mmHg (53.5% vs 74.0%, p<0.001) compared to non-diabetics. This was despite a significantly higher proportion of diabetics prescribed angiotensin converting enzyme inhibitors/angiotensin receptor blockers (79.1% vs 65.3%, p=0.021).
Among diabetic and non-diabetic HRIs, there were significant increases in the proportions achieving all the targets from IA. However fewer diabetics compared to non-diabetics achieved targets for oily fish (9.3% vs 11.9%, p=0.043), physical activity (65.8% vs 75.8%, p=0.011), and BMI (9.9% vs 28.1%, p=0.022) at one year. More diabetics compared to non-diabetics achieved the targets for total cholesterol (48.2% vs 22.9%, p<0.001) and LDL (57.9% vs 30.7%, p<0.001).
Conclusions: Multidisciplinary intervention had a beneficial effect on cardiovascular risk factors in both patient groups however, fewer diabetic patients achieved lifestyle targets. This necessitates further research into mechanisms underlying these differences and emphasizes more intensive lifestyle modification and BP management among diabetics for cardiovascular disease prevention.

P4243 | BEDSIDE
Effects of postchallenge hyperglycemia and low-density lipoprotein subclass particles on the risk of aortic stiffness in healthy adults without diabetes

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Purpose: To determine the effects of post-challenge hyperglycemia and LDL cholesterol (LDL-C) subclass particles on the risk of aortic stiffness in subjects without diabetes
Methods: During 2009–2011, we recruited 599 healthy adults without diabetes. All subjects underwent a standard oral glucose tolerance test (OGTT) after fasting; venous blood samples were obtained before and at 30, 60, 90, and 120 min after OGTT. The glucose area under curve (GluAUC) after OGTT was defined as the postchallenge glucose load. LDL-C and small dense LDL-C (sdLDL-C) levels and the brachial–ankle pulse wave velocity (baPWV) were measured.
Results: Postchallenge glucose levels at 1 h and baPWVs in tertile distributions were significantly associated with all conventional cardiovascular risk factors, LDL-C, and sdLDL-C. Multivariate logistic regression analyses revealed that LDL-C (or sdLDL-C) combined with one of the seven glycemic indices (glucose levels at 0, 30, 60, 90, and 120 min; GluAUC; HbA1C) was associated with aortic stiffness after controlling for age, male gender, BMI, hypertension, smoking, and alcohol consumption. All postchallenge glycemic indices, GluAUC, sdLDL-C, and LDL-C were significant risk factors for increased baPWV, whereas fasting glucose and HbA1C combined with LDL-C (or sdLDL-C) were not in the same multivariate models.
Conclusions: The significant synergistic effects of postchallenge hyperglycemia and LDL-C subclass particles on the risk of aortic stiffness indicated the role of postchallenge hyperglycemia in the primary prevention of cardiovascular disease.

P4244 | BEDSIDE
Hypoglycaemia and adverse cardiovascular events: a systematic review and meta-analysis

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Background: Hypoglycemia has been associated with adverse cardiovascular events in patients with diabetes and critical illness. However, such associations in patients with critical conditions and the relation of hypoglycemia severity with poor outcomes haven't been systematically examined.
Methods: We conducted a systematic review and meta-analysis of longitudinal follow-up cohort studies to investigate the associations between hypoglycemia and various adverse cardiovascular events.
Results: After removing duplication and critical appraising the all screened citations, a total of 17 eligible studies were included. Demonstrated by random effects meta-analysis, hypoglycaemia was strongly associated with a higher risk of ad-

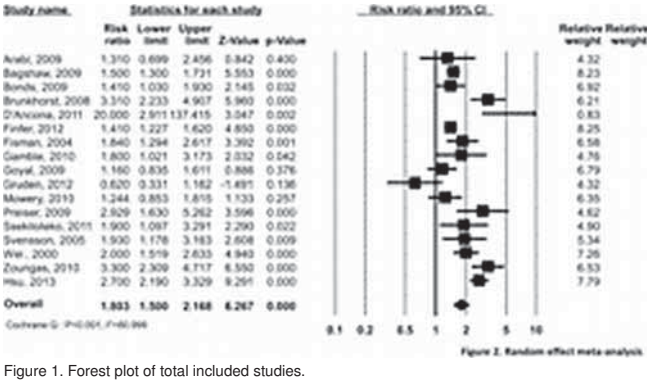

Figure 1. Forest plot of total included studies.

verse cardiovascular events (RR 1.803, 95% confidence interval 1.500 to 2.168; P<0.001). Comparable risk ratios were shown in pre-specified stratified analyses investigating the above association for different study endpoints, in patients with or without critical illness, and patients with or without diabetes (from 1.74 to 2.4; all P for interaction >0.1). Besides, there was a dose response relationship between the severity of hypoglycemia with adverse cardiovascular events (RR for mild hypoglycemia: 1.685, 95% CI 1.268 to 2.239; P<0.001 and RR for severe hypoglycemia: 2.212, 95% CI 1.720 to 2.845; P<0.001). Suggested by a bias-analysis, the above observations were unlikely resulting from unmeasured confounding parameters.
Conclusions: With the dose response relationship linking hypoglycemia with poor cardiovascular outcomes and the comparable risk ratios in different study populations, it may support the speculation that hypoglycemia is a risk factor for cardiovascular diseases.

P4245 | BEDSIDE
Individuals without cardiometabolic risk factors among patients with abdominal obesity

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Objective: To reveal the prevalence of metabolically healthy status the patients with abdominal obesity (AO) and to determine phenotype of these individuals.
Method: 503 patients (71,4% females and 28,6% males) with AO (IDF) without cardiovascular diseases (CVD) 30-55 years old were examined. Anthropometric and metabolic parameters, social-economy status, physical activity, family history of CVD, DM and obesity, smoking and alcohol consumption, birth weight and duration of obesity was assumed by questionnaire. “Metabolically healthy obese” (MHO) were defined as individuals without metabolic syndrome (MetS) according to IDF criteria of MetS and without insulin resistance according HOMA-IR. Patients with MetS or other metabolic disorders identified as “metabolically unhealthy obese” (MUO).
Results: Different components of MetS were revealed in 91,3% patients with AO and 66,5% of them had MetS. Only 8,7% was MHO.The difference between MHO and MUO is presented in table 1. The duration of obesity in MHO was shorter than in MUO patients (p=0,002). Frequency and duration of physical training was greater in MHO than unhealthy one (1,28±0,3 per/week and 0,92±0,1 per/week, respectively; p=0,03; 27,7±6,2 min/w and 15,8±1,4 min/w, respectively; p=0,04). Social-economy status, family history of CVD, DM and obesity, smoking and alcohol consumption, birth weight didn’t differ between groups (p>0,05).

Table 1. Anthropometric and metabolic parameters of metabolically healthy and unhealthy patients with abdominal obesity

Parameters		Healthy AO (n=44)	Unhealthy AO (n=459)	p
Age (yrs)		42,2±1,4	47,0±0,4	0,001
BMI, kg/m^2		29.09±0.51	31.56±0.24	0.01
WC, cm	M	104,66±0,82	108,62±0,95	0.01
	F	93,29±0,76	98,94±0.65	0.01
Leptin, ng/ml	M	29,3±2,4	35,4±3,4	NS
	F	42,4±3,1	57,5±2,1	0.03
Adiponectin, mcg/ml	M	17,3±3,2	16,9±0,9	NS
	F	23,7±0,9	19,0±0,9	0.02

Conclusion: Prevalence of “metabolically healthy obese” among patients with abdominal obesity is low – 8,7%. Benign metabolic status associates with younger age, lower waist circumference, higher physical activity and shorter duration of obesity. Lower leptin and higher adiponectin were revealed in “metabolically healthy obese” females.

BLOOD PRESSURE MEASUREMENT AND PATHOPHYSIOLOGY

P4247 | BEDSIDE
Impaired baseline aortic stiffness predicts pulse wave velocity improvement in recently diagnosed and untreated patients with mild to moderate essential hypertension: a 3-year follow-up study

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Background: Aortic stiffness as an index of subclinical organ damage due to hypertension disease is an important determinant of cardiovascular risk. We aimed to study the long-term influence of successful treatment after a three-year follow up, regarding aortic stiffness improvement from baseline evaluation in recently diagnosed and never treated middle-aged patients with mild to moderate essential hypertension.
Methods: We studied 132 non-diabetic, recently diagnosed and never-treated patients with essential hypertension (mean age 54+11 years, 79 males). At baseline, we performed 24h ambulatory blood pressure monitoring (ABPM) and carotid-femoral artery pulse wave velocity (PWV) in order to evaluate aortic stiffness. After baseline evaluation, all patients started antihypertensive treatment targeting office blood pressure <140/90 mmHg. A second evaluation was performed approximately three years later regarding office blood pressure (BP), ABPM and PWV. We characterized as well controlled patients those patients with 24h mean systolic and diastolic blood pressure after treatment <135/80 mmHg.
Results: PWV after treatment was significantly increased in all hypertensives (p<0.01) and uncontrolled hypertensives (p<0.001) and it was remained unchanged in controlled hypertensives. PWV was decreased only in controlled hypertensives with baseline PWV >12.4 m/sec (p=0.004), independently from the corresponding mean BP decrease.
Conclusions: The present longitudinal study provides substantial evidence that PWV improvement due to successful antihypertensive treatment by RAAS inhibitors, is depending on increased aortic stiffness at baseline while the magnitude of PWV decrease is independent from the observed blood pressure decrease.

P4248 | BEDSIDE
Hypertensive patients with controlled home blood pressure and impaired circadian rhythm

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Purpose: Some patients (Pts) may have controlled to target values home-measured blood pressure (HMBP), but their circadian rhythm may be impaired. Thus they may be exposed to elevated risk than those with optimal circadian blood pressure rhythm. The purpose of this study is to assess what percent of the Pts with controlled HMBP have suboptimal ambulatory blood pressure monitoring (ABPM).
Methods: We included 931 hypertensive Pts in the initial visit [347 (37.27%) males, 584 (62.73%) females] and 263 (28.25%) [178 females (30.48% of the initially recruited), 85 males (24.49% of the initial number)] during the follow-up visit after at least 6 months (6-20, mean 12). The mean age was 65.90±10.00 years. All the Pts were on combination hypertensive treatment. Blood pressure was recorded in the office, at home, 450 of the Pts had ABPM during the inclusion and 213 during the follow-up. All the Pts underwent also basic laboratory and echocardiography evaluation.
Results: Pts with impaired circadian rhythm were nearly twice (64.20% on inclusion and 58.60% during follow-up) as many as the dippers (35.12% on inclusion and 39.53% during follow-up). From all the included Pts, 329 (35.33%) were with controlled to target values HMBP. In 146 was conducted ABPM on inclusion, but in 85 (58.22%) the circadian rhythm was impaired despite the good control of HMBP.
Conclusions: Patients with controlled HMBP may have impaired circadian rhythm. The clinical implication of this finding needs further study, but may be associated with elevated risk for target organ damage.

P4249 | BEDSIDE
Importance of ambulatory blood pressure monitoring in children and adolescents with primary arterial hypertension

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Introduction: Rising incidence of essential hypertension in children and adolescents requires a better screening by measuring blood pressure (BP) at each medical consultation. A better method is ambulatory blood pressure monitoring (ABPM).
The aim of the study was to establish the diagnosis and staging of arterial hypertension in children and adolescents.
Subjects and methods: The study group was represented by 48 children with primary arterial hypertension, aged between 12-18 years (36 males and 12 females), admitted to Cardiology Department, during 2011-2013 for elevated blood pressure values. The children were sent in our department by the general practitioners or by school physicians. The study methods included: anamnesis, clinical examination and laboratory tests for associated risk factors. The secondary causes of arterial hypertension were excluded in all pateints. ABPM consisted in blood pressure measurement each 15-30 minutes, daytime and nighttime (model BTL-08 ABPM). The interpretation of the blood pressure values was done according to the age, height and sex percentiles. Nighttime BP dipping was calculated as the difference between the mean daytime and mean nighttime.
Results: According to the blood pressure values at admission, the subjects were divided in 4 groups: 20 subjects with prehypertension (BP between percentiles 90 and 95), 23 subjects with stage I hypertension (BP between percentiles 95 and 99), 9 subjects with stage II hypertension (BP > percentile 99 + 5mmHg) and 6 subjects with “white coat hypertension”. APBM revealed: prehypertension in 8 children (group A), stage I hypertension in 18 children (group B), stage II hypertension in one child (group C) and “white coat” hypertension in 21 children (group D). The systolic blood pressure load was the following: 39.5% in group A, 49.5% in group B and 10% in group D. All pacients had daytime values more than nighttime values. The nighttime BP dipping was 10.5% in group A, 8.8% in group B and 17.2% in group D. ABPM has changed the staging in 30 patients and influenced the management in 13 patients.

Conclusions: ABPM is a useful modality for the evaluation of BP levels, avoiding the "white coat" reactions in children and adolescents.

P4250 | BEDSIDE
Impact of blood pressure in adolescence on anthropometric indexes, blood pressure, adipokines, and inflammation in brazilian young adults. Rio de Janeiro study

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Background: The impact of blood pressure (BP) during adolescence on other cardiovascular risk factors in young adults is important for primary prevention.
Purpose: To evaluate BP, anthropometric indexes, metabolic and inflammatory profiles in Brazilian young individuals stratified by their BP obtained during adolescence, 18 years earlier.
Methods: A total of 116 individuals, of whom 63 were males, from the Rio de Janeiro study (follow-up of 17.76±1.63 years), were evaluated at two assessments: A1 (12.40±1.49 years old) and A2 (30.09±2.01 years old). Individuals were divided into two groups: GN (n=71), subjects with normal BP at A1; and GH (n=45), subjects with abnormal BP at A1, when BP was ≥95 percentile for age, gender and height percentile. BP, weight, height and body mass index (BMI) were measured at A1 and A2. In A2, abdominal circumference (AC), glucose (G), insulin (Ins), HOMA-IR, lipids, Apolipoprotein A1, Apolipoprotein B 100, Lipoprotein (a), Adiponectin, Leptin, E-selectin, VCAM and ICAM, CRP, and fibrinogen were added.
Results: 1) No difference was observed between the groups regarding age and gender; 2) At A2, GH showed higher weight, BMI, BP, insulin, HOMA-IR ($p<0.001$), leptin ($p<0.02$), apolipoprotein B100 and apolipoprotein A1 ($p<0.02$) means, higher apolipoprotein B100/apolipoprotein A1 ratio ($p<0.010$), and higher prevalences of overweight/obesity ($p<0.001$), of increased AC ($p<0.001$) and of hypertension ($p<0.02$); 3) No difference was observed between the groups regarding the inflammatory variables and adhesion molecules; 4) There was a positive correlation of BP at A1 with BP, BMI, insulin, leptin and HOMA-IR at A2 ($p<0.05$).
Conclusion: In a 18 year-follow-period, BP in adolescence was associated with higher BP, anthropometric and metabolic variables in young adulthood, but not with inflammatory variables.

P4251 | BEDSIDE
Day-to-day repeatability of the new 24 - h parameter, pulse time index of norm

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Objective: The PWV measurement is a method of assessing arterial stiffness and is important in the evaluation of cardiovascular risk. Some systems for PWV measurements are integrated into ABPM systems that not only provide one PWV measurement but also several PWV measurements over a period of 24 to 72 hours. This new 24-h pulse wave analysis led to the development of a new calculation, 'Pulse Time Index of Norm (PTIN)', that is provided by the (...) technology. The aim of the present study is to test the new PTIN for clinical feasibility by using day-to-day repeatability analysis.
Methods: Overall, 85 oscillometrically generated waveform files that had previously been used in ABPM studies lasting more than 2 days (>48 hours) were re-analyzed. The PTIN is defined as the percentage of a period ("24-h", "wake", or "sleep") during which the PWV does not exceed 10 m/s.
Results: Approximately 90% of the monitoring period in normotensive patients and 60% of the monitoring period in hypertensive patients are periods with normal PWV. The PTIN intraclass correlation coefficients of the first and second "24-h", "wake" and "sleep" periods in normotensive and hypertensive patients were ranged from 0.91 to 0.99 (Table 1).

Table 1. A new calculation, "Pulse Time Index of Norm (PTIN)" and its day-to-day repeatability in normotensive and hypertensive patients

Patients	Normotensive			Hypertensive		
Periods	24-h	wake	sleep	24-h	wake	sleep
Day 1 PTIN, Mean (%),	86.5	85.1	89.9	57.5	47.2	62.5
Day 2 PTIN, Mean (%),	87.3	86.4	89.8	57.4	47.6	62.5
Intraclass correlation coefficient	0.98	0,91	0.99	0.95	0.91	0.98
Limits of agreement	4.5	4.8	1.1	4.7	5.1	3.6

Conclusions: The main result of this present study is the excellent day-to-day repeatability, which is important because the conclusions regarding the significant alterations of the aortic function and the inclusion of a patient in a particular risk group is crucially dependent on the accuracy of the PWV measurement. Performing multiple PWV measurements over time for a given patient would be more insightful than performing only a single PWV measurement. Thus, the PTIN assessment with the Vasotens technology appears to be feasible for clinical practice.

P4252 | BEDSIDE
Pulmonary arterial hypertension and sildenafil: a second stage control

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Introduction: We realized a follow-up with 100 patients with pulmonary arterial hypertension whose have clinical symptoms of heart failure, for three months. This group have the next characteristics: presented systolic pressure at pulmonary artery too high; were patient between 60 and 70 years old man and women with a acceptable quality of life before pulmonary failure.
We random them with sildenafil and 60 patients asigned to placebo, with 3- and 6-month assesments fo cardiopulmonary treadmile test, echo-cardiography doppler procedures.
Objectives: As we know right ventricular hypertrophy is a normal phenomen in most of the patients with pulmonary arterial hypertension and is the cause of the heart failure. We gave, in this study, 50mg of sildenafil twice per day in this group of patients. We performed right heart catheterization using a described for other studies method: continuous electrocardiographic monitoring, a Swan-Ganz catheter. Was measured cardiac output by thermodilution and was calculated the pulmonary vascular resistance: PAP- PCW/ cardiac output. (as the difference among mean pulmonary arterial pressure and pulmonary capillary wedge pressure divided by cardiac output).
Results: Sildenafil improved pulmonary capacity and ejection fraction decreasing the high systolic pulmonary arterial pressure, improving pulmonary capacity through the endothelium modulation of the muscle due to exercise.
In the group treated with sildenafil we observed reduction of systolic pulmonary artery pressure (from 50,3 tol 28,6 mmHg and 19,5 mmHg), ergoflex effect on ventilation (from 9,7 to 4,2 l.min-1 and 0.9 l.min-1), ventilation to CO2 production slope (VE/Vco2, from 53.5 to 21,8 and 22.7), and brethlessness (score) (from 41.5 to 19,3 and 15.2), and an increase of FMD (from 7.5% to 19.4% and 16.2%), peak Vo2 (from 11.2 to 25,5 ml.min-1.kg-1 and 19.7 ml.min-1) and ratio of Vo2 to work rate changes (from 4.6 to 12.9 and 13.9) All changes were significant at $p<0.01$.
No adverse effects were observed.
Conclusions: In patients with heart failure as a cause of pulmonary arterial hypertension and high systolic pulmonary arterial pressure, sildenafil decreases significantly all the parameters that leads to heart failure and improves exercise ventilation and aerobic capacity and is sustained and is significantly related with an endothelium-mediated attenuation of exercising muscle oversignaling. We could observed that high systolic arterial pulmonary pressure in patients with atrial fibrillation has a very close relation with right ventricular dysfunction.

P4253 | BEDSIDE
Estimating b-thalassemia trait carrier state on cardiovascular risk factors in patients with newly diagnosed hypertension

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Purpose: Thalassemia minor (Tm), the b-thalassemia carrier state, has been deemed to confer protection against atherosclerotic cardiovascular disease because of the observed lower incidence of cardiovascular and cerebrovascular events.
Methods: We evaluated cardiovascular risk factors, risk-prediction equations along with renal function and selected echocardiographic indices 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: Tm patients had a lower 10-year cardiovascular risk as estimated by the European Society of Cardiology's HeartSCORE ($P<0.001$). Moreover, hypertensive patients with Tm were also less-frequent smokers ($P<0.001$) and had a higher concentration of apolipoprotein A ($P=0.009$) and a lower concentration of apolipoprotein B ($P<0.001$). Thus, Tm patients had a lower estimated INTERHEART score compared with hypertensive patients without Tm ($P<0.001$). Concerning renal function, Tm patients had lower serum creatinine and higher estimated glomerular filtration rate (both $P<0.001$). The prevalence of chronic kidney disease, defined as an estimated glomerular filtration rate <60 ml min per 1.73m^2, was 17.4% in patients with Tm vs 24.1% in those without ($P<0.001$). Additional biochemistry results showed that although plasma renin activity did not differ between the two groups, hypertensive patients with Tm had a lower aldosterone concentration ($P=0.03$). Moreover, Tm patients had lower levels of fibrinogen and plasminogen activator inhibitor (PAI)-1 (both $P<0.001$). Regarding cardiac structure and function as evaluated by transthoracic echocardiography, Tm patients had a lower left ventricular (LV) mass index and consequently a lower prevalence of LV hypertrophy (both $P<0.001$), as well as a higher total and mid-wall fractional shortening ($P=0.03$ and <0.001, respectively). However, left atrial index was similar in the two groups.
Conclusions: Among patients with newly diagnosed hypertension, those with Tm have a better overall cardiovascular risk factors, a lower prevalence of LV hyper-

trophy and LV mass index regarding cardiac structure and function as evaluated by transthoracic echocardiography.

P4254 | BEDSIDE
Increased coagulability in syncopal patients with orthostatic hypotension

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Purpose: While the risk for increased mortality and cardiovascular morbidity has been linked with orthostatic hypotension (OH), there is limited information on its relationship with haemostasis. We aimed to evaluate associations between OH and coagulation factors in patients with unexplained transient loss of consciousness (TLOC).
Methods: A total of 233 consecutive patients above 15 years of age, with episodes of unexplained TLOC underwent head-up tilt test (HUT, Italian protocol). Blood was taken during supine rest before and at 3 min of 70° HUT for determination of coagulation parameters associated with an increased thrombosis risk: fibrinogen (Fbg), von Willebrand factor antigen (vWF:Ag) and vWF:GP1bα activity, factor VIII (FVIII), lupus anticoagulant, and functional APC resistance. Orthostatic hypotension (OH) was defined as persistent decrease in systolic and/or diastolic blood pressure of more than 20/10 mmHg during passive HUT excluding spontaneous vasovagal reflex.
Results: Fifty-five patients were excluded due to lack of blood samples or warfarin treatment. Among remaining 178 patients (81 males), those with OH (n=49) were significantly older (61±18 vs. 47±21 yrs; $p<0.001$), and had a significantly increased FVIII-supine (1.2±0.39 vs. 1.0±0.35, p=0.001), FVIII-standing (1.2±0.36 vs. 1.0±0.34, p=0.001), vWF:Ag-supine (1.5±0.66 vs. 1.1±0.44, $p<0.001$), vWF:Ag-standing (1.5±0.67 vs. 1.1±0.46, $p<0.001$), vWF:GP1bα-supine (1.5±0.73 vs. 1.1±0.42, $p<0.001$), vWF:GP1bα-standing (1.5±0.75 vs. 1.1±0.42 $p<0.001$), Fbg-standing (2.9±0.53 vs. 2.7±0.61, p=0.03) but not Fbg-supine (2.8±0.54 vs. 2.7±0.61, p=0.078) compared with patients without OH. However, after adjusting for age and sex, only vWF:Ag and vWF:GP1bα remained significantly increased in OH patients.
Conclusions: OH has been previously shown to be associated with increased cardiovascular morbidity/mortality. We measured an independently increased VWF antigen concentration and activity, which may be associated with increased cardiovascular risk.

P4255 | BEDSIDE
Reduction in microalbuminuria predicts regression of left ventricular hypertrophy in hypertensive patients

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Purpose: Treatment-related reductions in microalbuminuria (MAU) are associated with a reduced incidence of cardiovascular events and a reduction in progression to end-stage renal disease in hypertensive patients, but if reduction in MAU correlates with regression of left ventricular hypertrophy (LVH) is still insufficiently studied. Our goal was to assess changes in the level of microalbuminuria and its relationship with regression of LVH during antihypertensive treatment.
Methods: 443 patients with microalbuminuria and LVH were treated with losartan 50-100 mg plus hydrochlorothiazide 12.5-25 mg (219 patients) or amlodipine 5-10 mg o.i.d. (224 patients) during follow-up period of 12 months. Albumin-creatinine ratio was measured in the first morning void urine prior to treatment and 4 weeks after treatment. Left ventricular mass index (LVMI) was measured prior to treatment and 1 year after treatment. After 4 weeks of losartan-based combination therapy patients were divided according to reduction in albumin-creatinine ratio on 2 groups: <50% from baseline (1st group) and >50% from baseline (2nd group).
Results: Reduction in albumin-creatinine ratio after 4 weeks of treatment in the 1st group was 28% (from 11.8±7.3 to 8.4±3.8 mg/mmol) ($p>0.05$) and in the 2nd group was 71% (from 10.9±4.2 to 3.2±1.6 mg/mmol, $p<0.05$). In the 1st group office systolic blood pressure (BP) decreased from 166±4/91±3 to 133±3/79±2 mmHg ($p<0.01$) and in the 2nd group from 163±5/93±2 to 131±4/80±1 mmHg ($p<0.05$), respectively. Decrease of LVMI was significantly higher after 1 year of treatment in the 2nd group as compared with the 1st group (-19.4±4.1% vs -6.5±3.2%, respectively ($p<0.01$). In a multiple regression model, significant relationship between reduction in microalbuminuria and decrease of LVMI was found, independent of office systolic and diastolic BP changes, age and sex ($p<0.01$).
Conclusions: There is a strong relationship between reduction in albumin-creatinine ratio and regression of LVH in hypertensive patients. Reduction in microalbuminuria after 4 weeks of treatment predicts further regression of left ventricular hypertrophy in hypertensive patients.

P4256 | BEDSIDE
Effects of aliskiren or a diuretic in addition to an angiotensin II receptor blocker on lowering central aortic pressure in non-diabetic hypertensive patients: Results from the ALEA study

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Purpose: We compared the effects of a direct rennin inhibitor and a diuretic in addition to an angiotensin II receptor blocker on lowering central aortic blood pressure (BP) and augmentation index in non-diabetic patients with hypertension.
Methods: This is a sub-study of the ALEA study, which was a 24-week, prospective, multicenter, randomized, open-label study. THe principle study enrolled hypertensive patients with a clinic BP >140 mm Hg and/or 90 mm Hg and already being treated with valsartan (80mg/day) alone. A total of 103 patients were enrolled from 15 institutions from Jun 2012 to March 2013. In this sub-study, 41 non-diabetic patients in the aliskiren (150-300 mg/day) group and 44 non-diabetic patients in the trichlormethiazide (0.5-2 mg/day) group were analyzed (Mean age, 68 years and 43% of men). Radial augmentation index (AI) and central BP were measured by radial artery tonometory. The primary outcome measure was changes in central aortic blood pressure and radial AI from baseline to the end of follow-up. Secondary primary outcome was change in changes in urine albumin-to-creatinine ratio (UACR) and urinary 8-Hydroxydeoxyguanosine (8-OHdG).
Results: In both the aliskiren group and the diuretic group, brachial systolic and diastolic BP were significantly decreased comparably 24 weeks later. In terms of primary endpoints, The radial AI and central BP were also significantly decreased 24 weeks later; however, there were no difference in the reduction in radial AI and central BP between two groups (the between-group difference in radial AI was 0.6%; 95% CI: -4.3 to 5.5%; p=0.81 and the between-group difference in central BP was 1.7 mm Hg; 95% CI: -7.8 to 11.2 mmHg; p=0.72 by ANCOVA) after adjustment for baseline value, age, and gender. In terms of secondary endpoints, the UACR was significantly reduced 24 weeks later and the reduction tended to be greater in the aliskiren group tan in the trichlormethiazide group (the between-group difference in central BP was 4.9 mg/gCr; 95% CI: -9.9 to 10.8 mg/g Cr; p=0.10). The urinary 8-OHdG after 24 weeks treatment was significantly reduced only in the aliskiren group and there was a significant difference between two groups (the between-group difference was 2.3 ng/g Cr; 95% CI: 0.6 to 3.9 ng/g Cr; p=0.01)
Conclusions: The administration of valsartan and aliskiren for 24 weeks had a comparable effect on lowering central aortic BP and radial AI to the combination of valsartan and a diuretic; however, the anti-oxidative effect of aliskiren in addition to valsartan may exert renal protection in non-diabetic hypertensive patients.

DEVICES IN HYPERTENSION

P4258 | BEDSIDE
Baroreflex activation therapy in resistant hypertension - acute on/off effects and chronic blood pressure reduction

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Background: Baroreflex activation therapy (BAT) by electrical stimulation of the baroreceptors located at the carotid sinus has been shown to reduce blood pressure (BP). However, it is not known whether chronic baroreceptor stimulation influences the acute responsiveness to stimulation. Therefore we determined acute on/off effects after chronic BAT.
Methods: Resistant hypertension patients (n=17) were enrolled in an open-label, single-arm evaluation of unilateral BAT after exclusion of secondary hypertension. Initial eligibility criteria were systolic BP ≥140mmHg despite stable (≥4 weeks) medical therapy consisting of ≥3 antihypertensive drugs including at least one diuretic. For on/off testing, several BP measurements were performed 15.1±8.7 months after initial activation: at rest with activated device, 4-6 min after deactivation of the device and 4-6 min after reactivation of the device.
Results: Before BAT, mean office cuff BP was 178±27 mmHg (systolic BP; SBP) over 98±19 mmHg (diastolic BP; DBP). At the time of on/off testing (before deactivation), BP was reduced to 147±29 mmHg over 84±20 mmHg. On deactivation of the device, BP increased by 11.2±13.9 mmHg (SBP; p=0.004) and 5.3±9.9 mmHg (DBP; p=0.04). BP decreased after reactivation by 14.5±16.0 mmHg (SBP; p=0.002 vs. deactivation) and 6.9±9.6 mmHg (DBP; p=0.009). There was no correlation between duration of chronic BAT and systolic or diastolic acute on/off response (all $p>0.1$).
Conclusions: After long-term follow-up, unilateral BAT reduces BP consistently

in patients with resistant hypertension. There is a significant on/off effect on BP supporting the efficacy of BAT. The acute on/off response to BAT does not depend on treatment duration. Thus, no evidence of tolerance over time to chronic BAT could be found, indicating that this therapy is effective in the long-term treatment of patients with resistant hypertension.

P4259 | BEDSIDE
Beneficial effects of renal sympathetic denervation on cardiovascular inflammation and remodeling in essential hypertension

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Background: Renal sympathetic denervation (RSD) represents an effective treatment option for patients with resistant arterial hypertension (HT). HT is associated with chronic vascular inflammation and remodeling, contributing to progressive vascular damage and atherosclerosis. High-sensitivity C-reactive protein (hsCRP) and Interleukin-6 (IL-6) are related to vascular inflammation in HT and to be a predictive marker for cardiovascular events. HT related cardiovascular remodeling is characterized by an abnormal proteolytic activity of Matrix metalloproteinases. In particular, MMP-9 and MMP-2 levels are decreased in essential HT, which contributes to collagen accumulation in the vascular wall with subsequent increased peripheral resistance. In the present study we aimed to evaluate the influence of RSD on cardiovascular inflammation and remodeling by determining serum levels of IL-6, hsCRP, MMP, and tissue inhibitor of metalloproteinases (TIMP).
Methods: A total of 60 consecutive patients (age: 67.9±[9.6] y) undergoing RSD were included in this study. A therapeutic response was defined as a systolic blood pressure reduction of >10 mmHg in the office blood pressure measurement 6 months after RSD. Venous serum samples for measurement of hsCRP, IL-6, MMP-2, MMP-9, and TIMP-1 were collected prior to (BL) and 6 months after RSD (FU).
Results: A significant reduction in the systolic office blood pressure of 26.4 mmHg (BL RRsys: 169.3 mmHg [SD: 11.3], $p<0.001$) was documented at follow-up, 6 months after RSD. At this time point, the serum levels of hsCRP (BL: 3.6 mg/dL [IQR: 1.9; 6.3] vs. FU: 1.7 mg/dL [IQR: 0.9; 2.4], $p<0.001$) and the pro-inflammatory cytokine IL-6 (BL: 4.04 pg/mL [IQR: 2.7; 6.5] vs. FU: 2.2 pg/mL [IQR: 1.6; 3.2], $p<0.001$) were significantly decreased compared with baseline values. The levels of MMP-9 (BL: 425.2 ng/mL [IQR: 309.3; 573.4] vs. FU: 574.1 ng/mL [IQR: 463.3; 860.2], p=0.024) and MMP-2 (BL: 192.3 pg/mL [IQR: 158.2; 233.1] vs. FU: 231.3 pg/mL [IQR: 190.1; 286.9], $p<0.001$) were significantly increased compared with baseline values. There was no significant change in TIMP-1 levels 6 months after RSD relative to baseline values.
Conclusion: In addition to the effective blood pressure reduction in response to RSD, this study demonstrates a positive effect of RSD on biomarkers reflecting vascular inflammation and remodeling. A significant reduction of pro-inflammatory cytokines and an improvement of the abnormal proteolytic activity, suggest a prognostic benefit of RSD in high-risk patients for endothelial dysfunction and cardiovascular remodeling as well as end-organ damage.

P4260 | BEDSIDE
Impact of heart failure biomarkers on blood pressure response in patients with resistant hypertension undergoing renal denervation

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Background and methods: Catheter-based renal denervation (RDN) reduces office blood pressure (BP) and left ventricular hypertrophy in patients with confirmed resistant hypertension. In hypertensive patients with left-ventricular hypertrophy, heart failure biomarkers are associated with high BP. This multicenter study investigated the effect of RDN on NT-proBNP, ST-2, galectin-3 and high-sensitivity troponin I in 167 patients with resistant hypertension (defined as office SBP >160 mmHg, despite intake of 3 antihypertensive drugs) undergoing RDN. Echocardiography and blood sampling was performed at baseline, 1 and 6 months after RDN. Linear and logistic effect models were used to determine the association of biomarkers with BP response and echocardiographic parameters.
Results: After RDN office BP was reduced from 172±20/92±14 mmHg to 152±26/84±16 mmHg ($p<0,001$) at 1-month and 148±22/83±12 mmHg ($p<0,001$) at 6-month follow-up, respectively. Response to treatment (drop in office systolic BP ≥10mmHg) after 6 months was documented in 123 (74%) patients. Overall no significant association of biomarkers and BP change after 6 months was observed (Table 1). Furthermore, no association with the determined echocardiographic parameters was detected. There was no significant correlation between biomarker level at baseline and BP response after RDN (Table 2).

Linear mixed effect models for biomarkers and blood pressure
Association of biomarkers and BP

	Coefficient	p-value
ST2	0.0007	0.59
NT-proBNP	0.0000	0.99
Galectin 3	–0.0014	0.070
hsTnI	0.0010	0.53
Cystatin C	–0.0005	0.56

Table summarizing the results for the linear mixed effect models for markers and systolic BP (ABP mean) are given. All biomarkers are log-transformed. The covariates in the model are: systolic BP (mean, overall), age, female, BMI, smoker, diabetes, hyperlipidemia, coronary heart disease, months after RD.

Conclusions: In this multicenter analysis RDN did significantly reduce office BP by 24 mmHg. However, NT-proBNP, ST-2, galectin-3 and high-sensitivity troponin I at baseline were not associated with BP reduction 1 and 6 months after RDN.

P4261 | BENCH
Application of electrical nerve stimulation as a target for renal denervation acute procedural efficacy; the dark side of the moon

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Background: Transluminal renal sympathetic denervation (RDN) reduces blood pressure (BP) in patients with treatment-resistant hypertension but it remains a blind procedure in the cath lab. Electrical stimulation of the renal arterial autonomic nerves has been identified as an end point of ensuring renal fiber disruption.We experimentally assessed the effect of electrical stimulation on renal arterial autonomic nerves before and after RDN by using multi-electrode renal ablation system.
Design and methods: A 7F introducer was inserted into each femoral artery in 10 juvenile farm swines under deep general anesthesia. RDN was performed using the EnligHTN ablation catheter (St. Jude Medical, CA, USA) inserted from the right femoral artery. BP was continuously monitored from the left femoral artery. Electrical autonomic nerve stimulation at 20-Hz frequency, 5-ms pulse duration, and 15-mA output was applied for 60 s to 3 minutes via the distal pair of a quadripolar catheterintroduced via the right femoral artery and placed successively in the ostium, proximal, middle and distal part of each renal artery before and after RDN.
Results: Renal angiograms performed before and after RDN were normal in all cases showing no apparent injury. Electrical stimulation was also applied using different settings (frequency of 20 Hz, with an amplitude of 15 V and pulse duration of 10 ms) as well as an open irrigation catheter. BP and heart rate remained unchanged after electrical stimulation of either 1, 2 or 3 minutes duration applied in the ostium, proximal, middle and distal part of each renal artery. There was also no response to electrical stimulation of either renal artery after RDN.
Conclusion: Although electrical stimulation of the renal arterial autonomic nerves has been reported as an end point of effective RDN in dogs, different settings of electrical stimulation of the renal arterial autonomic nerves in farm pigs failed to affect either BP or heart rate.

P4262 | BEDSIDE
Percutaneous renal denervation effectively reduces blood pressure in patients with isolated systolic hypertension

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Renal denervation (RDN) reduces office blood pressure in patients with resistant hypertension. Previous clinical trials have not focused specifically on isolated systolic hypertension. Therefore we investigated the effect of RDN in 107 patients with resistant hypertension: 57 patients with combined (systolic/diastolic) and 50 patients with isolated systolic hypertension. RDN reduced office systolic and diastolic blood pressure at 3-, 6- and 12-months in combined hypertension by 26/25/25 and 13/11/11 mmHg as well as by 19/20/19 and 7/5/6 mmHg in isolated systolic hypertension ($p<0.05$ for all), respectively. Systolic blood pressure decreased numerical slightly lower, but not significant, in patients with isolated systolic hypertension (p=0.309). The drop in diastolic blood pressure in isolated systolic hypertension was lower compared to patients with combined hypertension ($p<0.05$). The non-responder rate (change in office SBP <10 mmHg) after 6-months was 23% in combined hypertension and 31% in isolated systolic hypertension (p=0.334). Pulse pressure was reduced after 3-, 6-, and 12-months in combined hypertension patients from 75 mmHg at baseline to 62, 64 and 67 mmHg and from 90 to 78, 75 and 79 mmHg ($p<0.001$ for all) in isolated systolic hypertension, respectively. Mean 24-hour ambulatory systolic/diastolic blood pressure was reduced from 153/88±16/10 mmHg to 141/81±15/11mmHg in combined hypertension and from 147/75±15/9 to 139/71±15/7 mmHg ($p<0.05$ for all) in isolated systolic hypertension 6-months after RDN, respectively. Our findings support the efficacy of RDN in patients with isolated hypertension.

MITRAL REGURGITATION: IMAGING AND OUTCOME

P4264 | BEDSIDE
Flattening of annulus saddle-shape in patients with mitral valve prolapse: comparison between posterior and anterior leaflet prolapse

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Background: Flattening of mitral annulus saddle-shape was shown to be associated with severity of mitral regurgitation (MR) in mitral valve prolapse (MVP) and saddle-shaped annuloplasty was proposed to enhance repair durability. We sought to evaluate the difference in annular geometry between patients with isolated posterior leaflet (PL) prolapse and those with anterior leaflet (AL) involvement, which may have implication for the choice of annuloplasty ring.
Methods: Mitral annular geometry was assessed by 3-dimensional (3D) transesophageal echocardiography (iE33, Philips) in 119 subjects including 64 patients undergoing annuloplasty for severe MR due to isolated PL prolapse (48 men, age=59±10y), 24 patients due to AL/bi-leaflet prolapse (15 men, age=55±12y), and 31 age/sex-matched normal subjects (18 men, age=58±15y). Using dedicated software the end-systolic 3D geometry of mitral annulus including annular area, circumference, commissural width, anteroposterior diameter, and height were measured. The annular height to commissural width ratio (AHCWR) was calculated as surrogate of the annular saddle-shape.
Results: The normal AHCWR ranged from 15~33%. Height and AHCWR were significantly lower in patients with AL/bi-leaflet prolapse than those with isolated PL prolapse, despite similar annular area, circumference, and diameters (Table). Annular flattening, defined as AHCWR<15% (the lower limit of normal), was evident in 17 (71%) patients in AL/bi-leaflet prolapse and 34 (53%) in isolated PL prolapse (P=0.13).

Table 1. 3D annulus geometry

Variables	Normal subjects (n=31)	Isolated PL prolapse (n=64)	AL/bi-leaflet prolapse (n=24)	P
Circumference, mm	106±9	123±16*	123±20	<0.0001
Area, mm^2	738±54	1085±308*	1157±409*	<0.0001
Commissural width, mm	33.3±3.7	37.8±5.1*	38.6±7.0*	<0.0001
Anteroposterior diameter, mm	28.0±2.5	36.4±4.9*	37.5±6.3*	<0.0001
Height, mm	7.9±1.9	5.5±1.3*	4.8±0.9*†	<0.0001
AHCWR, %	24±5	15±4*	13±2*†	<0.0001

*P<0.05 vs. normal subjects. †P<0.05 vs. patients with isolated PL prolapse.

Conclusion: Annular flattening is common both in MVP patients with isolated PL and anterior/bi-leaflet prolapse but the degree of flattening appears to be more severe in the latter, for which saddle-shaped annuloplasty may be more important.

P4265 | BEDSIDE
In patients with ischemic cardiomyopathy and secondary mitral regurgitation, mitral annulus contractile dysfunction is related more to left atrial than to left ventricular contractile dysfunction

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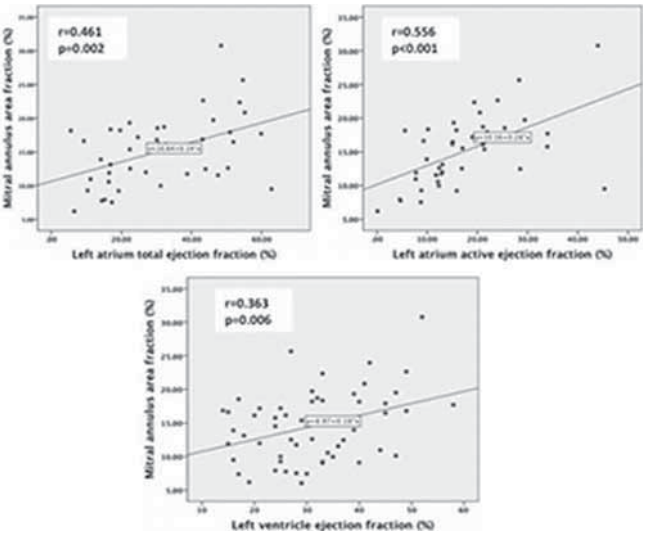
Background: 3D echo revealed dysfunctional mitral annulus (MA) in secondary mitral regurgitation (SMR), and suggested it as a consequence of left ventricular (LV) systolic dysfunction and remodelling. However, the relation between the MA and left heart chamber dysfunction remained to be explored in these pts.
Methods: 56 pts (59±16 yrs, 43 men) with mild to severe SMR due to ischemic cardiomyopathy and regular rhythm underwent 3D full-volume acquisition of the MA, left atrium (LA) and LV.
Using dedicated software package (MV assessment 2.3, TomTec) able to track the MA frame-by-frame during systole, we measured MA area and anterior-posterior (AP) diameter fractional changes, and MA displacement. We assessed LA maximum (LAvol), minimum and pre-P volumes, and total and active LA emptying fractions (EF) (LA analysis 2.3, TomTec). LV end-diastolic volumes (LVEDV) and LVEF were measured with AutoLVQ (Echopac BT 12, GE Vingmed).
Results: Subjects had LVEDV of 116±29 ml/m^2, LVEF of 31±10%, LAvol of 60±42 ml/m^2 and MA mid-systolic area of 12±3 cm^2. Even though MA area had good and similar correlations to LVEDV and LAvol (r=0.55 and r=0.51, both p<0.001), MA area fraction showed closer correlations to total and active LAEF than LVEF (Fig. 1). AP diameter fractional change showed closer relation to total and active LAEF (r=0.55 and r=0.61, p<0.001) than LVEF (r=0.27, p=0.04), too. Conversely, MA displacement showed the highest correlation to LVEF (r=0.63, p<0.001), and none with active LAEF.
Conclusion: In SMR, MA contractile dysfunction relates closer to LA dysfunction, while the MA translation is decreased due to LV systolic dysfunction. Our data suggest that the loss of atrial contraction might have an additional impact on the severity of SMR in pts with ischemic cardiomyopathy.



Abstract P4265 –Figure 1. Relationship of MA to LA and LV function.

P4266 | BEDSIDE
Effect of heart rate, rhythm, and net atrioventrciular compliance on echocardiographic assessment of mitral stenosis anatomic severity: proximal isovelocity surface area versus pressure half time

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Background: We reported that mitral valve area by proximal isovelocity surface area (MVA-PISA), unlike pressure half time (MVA-PHT) is not affected by changes in net-atrioventrciular compliance (Cn) in patients with mitral stenosis (MS). Aim: Compare the effect of Cn in the light of changes in heart rate (HR), rhythm, and diastolic filling time (DFT) on MVA-PISA and MVA-PHT, and study effects of MS severities on the radius of PISA (PISA-r).
Methods: For 84 consecutive patients, MVA was calculated by 2-D planimetry (MVA-PLN, reference), PHT, and PISA, after fixing valve angle to 100° and aliasing velocity to 33 cm/s, a previously tested method that allows studying MS effects on PISA-r and maximal mitral early diastolic velocity (Vmax). Differences from MVA-PLN were calculated in mm^2 for MVA-PHT (d-PHT), and MVA-PISA (d-PISA). Cn was calculated as: 1270×MVA-PLN/E-wave deceleration slope.
Results: Mean age was 42.5±17.8 years, (51 (58%) females and 32 (38%) Af). HR, DFT, and Cn were 76.9±14 b/m 485±128 ms, and 4.53±1.9 mL/mmHg. HR was<70 and >70 b/m in 27 and 57 patients, respectively. MVA-PISA correlated with MVA-PLN stronger than MVA-PHT (r=0.948, 0.379, all p<0.001), and PISA-r correlated with MVA-PLN stronger than Vmax (r=0.758, –0.471, p<0.001). d-PHT correlated with Cn, HR, and DFT (r=0.74, 0.24, 0.3, p<0.001, 0.02, 0.006, respectively), while d-PISA did not (r=0.07, 0.1, 0.03, p=0.53, 0.35, 0.79, respectively). PISA-r significantly decreased with each increase in MS severity, while Vmax, and pressure gradient (PG) only were different between moderate and severe but not mild and moderate MS. ROC-curve revealed that PISA-r can effectively differentiate MS severities. MVA by different methods, PISA-r, and d-PISA were similar when HR<70 vs. >70 b/m, or in sinus vs. Af, while patients with HR>70 b/m had higher d-PHT (1.03±4.1 vs. -1.07±3.5 mm^2, p=0.02), higher Vmax (219±46 vs. 205±35 cm/s, p<0.001), higher PG (12.6±6.6, 8.3±3.8 mmHg, p=0.003), and lower Cn (4.3±1.7 vs. 5.6±2.2 mL/mmHg, p=0.003) compared to HR<70 b/m, and patients with Af had lower d-PHT (-0.7±3.6 vs. 1±3.6 mm^2, p=0.06), lower Vmax (202±35 vs. 222±45 cm/s, p<0.049), lower PG (8.1±4.1, 13.1±6.3 mmHg, p<0.001), and higher Cn (5.3±2.1 vs. 4.03±1.7 mL/mmHg, p=0.002) compared to sinus. HR was higher and DFT was lower in patients with HR>70 vs. <70 b/m, but were similar between sinus and Af.
Conclusions: MVA-PISA and PISA-r unlike MVA-PHT and Vmax are not affected by Cn changes, irrespective of the the effect of HR, DFT, or the presence of Af rhythm. Given its simplicity, PISA-r can be an alternative to MVA in assessment of MS anatomic severity.

P4267 | BEDSIDE
Mitral annulus remodeling and dysfunction in patients with mild to severe organic mitral regurgitation

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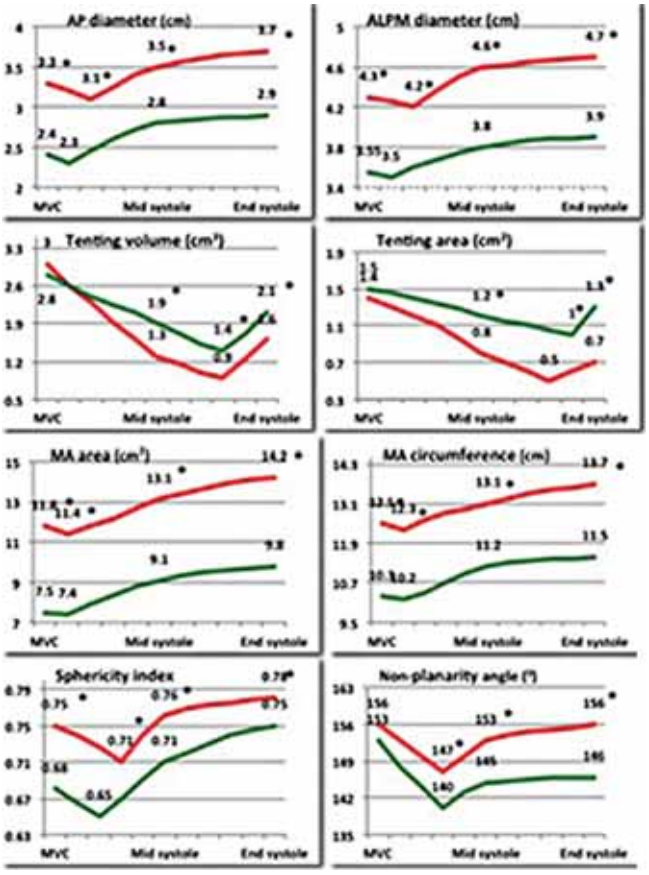
Background: Assessment of mitral annulus (MA) geometry and dynamics

changes according to mitral regurgitation (MR) etiology is key to tailor mitral valve (MV) repair procedures.
Objectives: To analyse the extent of MA remodelling and changes in dynamics using 3D echo in mild to severe organic MR (OMR).
Methods: We compared MA geometry and function between 50 pts (57±15 yrs, 30 men) with OMR (posterior MV prolapse-38 pts, Barlow disease-12 pts) and 52 controls (C) who underwent 3D full-volume MV acquisition. MA geometry was analysed using prototype software package (MV assessment 2.3, TomTec). MA parameters were recorded at 4 reference frames: mitral valve closure (MVC), mid (MS) and endsystole (ES), and minimum value frame. Time to minimum was recorded as % of systole duration.
Results: OMR pts had larger antero-posterior (AP) and anterolateral-posteromedial (ALPM) diameters, MA area (MAA) and circumference (MAC), and higher sphericity index (SI) at all reference frames (*p<0.001) (Figure). Non-planarity MA angle (NPA), tenting area and volume were similar in OMR and C at MVC. MA shape became progressively flatter, and tenting area and volume smaller in OMR than in C from MS to ES (*p<0.001).
OMR pts had significant delays of minimum AP (17±8% vs 11±9%) and ALPM diameters (18±10% vs 13±8%), MAA (16%±8 vs 11±6%) and MAC (16±7 vs 11±6%) and SI (38±28% vs 22±18%) than N, for all p<0.01.
MA area fraction was reduced in OMR (22±5% vs 28±5%, p<0.001), while MA displacement was similar to N (10±3 vs 10±1 mm).



Mitral annulus dynamics in OMR vs C.

Conclusion: OMR pts have larger and more spherical MA during entire cardiac systole, with decreased contraction but preserved translation. Even though MA saddle-shape is preserved at early systole, MA progressively flattens from MS to ES, concurring to prolapse severity and late-systolic MR.

P4268 | BEDSIDE
The impact of functional mitral regurgitation on right ventricular function and clinical outcome in patients with right ventricular infarction

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Introduction: Right ventricle (RV) infarction is associated with increased mortality. Functional mitral regurgitation (FMR) may complicate inferoposterior infarction with RV involvement leading to pulmonary hypertension and increased RV afterload, potentially exacerbating RV remodeling and dysfunction.
Methods: We studied 178 patients with inferior STEMI and right ventricular infarction. The presence and severity of FMR and RV function were assessed by echocardiography. Hemodynamically significant FMR was considered when the severity of regurgitation was moderate or severe.
Results: Eighteen patients (10.0%) had hemodynamically significant FMR. Estimated pulmonary artery systolic pressure was higher in patients with FMR than in patients without FMR (43±10 vs. 34±10; P=0.002). RV systolic dysfunction was present in 76 patients (42.5%). In a multivariable logistic regression model, FMR was a strong predictor of RV dysfunction (odds ratio 5.35, 95% CI 1.65-17.48, P=0.005) independent of reperfusion therapy (Table). During a median follow-up of 4.1 years, 20 (12.4%) and 10 (55.6%) deaths occurred in patients with and without significant FMR (P<0.001). In a multivariable Cox regression model, compared with patients without FMR and with normal RV function, the adjusted hazard ratio for mortality was 1.02 in patients without FMR and with RV dysfunction (95% CI, 0.39-2.69, P=0.97) and 3.62 in patients with FMR with RV dysfunction (95% CI, 1.33-9.85, P=0.01).

Logistic regression for RV dysfunction

Characteristic	Odds Ratio (95% CI)	P value
Reperfusion therapy	0.18 (0.07–0.51)	0.001
Moderate/severe FMR	5.35 (1.65–17.48)	0.005
Basal posterior WMA	2.84 (1.32–6.10)	0.008

Conclusion: In patients with RV infarction the development of concomitant hemodynamically significant FMR is strongly associated with RV dysfunction, presumably by producing pulmonary hypertension and increasing RV forward impedance during acute ischemia. The risk for mortality is increased predominantly in patients with both RV dysfunction and FMR.

P4269 | BEDSIDE
The underestimated burden of mitral regurgitation: morbidity, mortality, and risk factors

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Purpose: The management of mitral regurgitation (MR) is challenging. Patients with MR may present as asymptomatic, oligosymptomatic, older with comorbidities, or clinically symptomatic and not appropriate candidates for surgery. Understanding morbidity and mortality risks in patients with MR is therefore important as the consequences, such as pulmonary hypertension and left ventricular dysfunction, are often irreversible. The current review considers the medical/conservative management of MR and was designed to assess mortality, morbidity, and risk factors associated with functional and organic MR, particularly severe MR.
Methods: A structured literature review was conducted in MEDLINE, Embase, the Cochrane Library, and via hand-searching of conference proceedings. Structured search strings were adapted for each database as appropriate and included free text and Medical Subject heading (MeSH) terms. Studies were screened on the basis of title/abstract against the eligibility criteria. Prospective randomised controlled trials and observational studies including adult patients with MR which reported on treatment response rates, survival, time to treatment failure, quality of life, and adverse events were eligible for inclusion.
Results: A total of 32 publications met the inclusion criteria of the review (9 in functional, 18 in organic, and 5 in a mixed population [functional/organic]). Despite the heterogeneity of the identified studies, particularly regarding classification of severity, asymptomatic organic MR had an important impact on 5 and 10 year overall survival and symptomatic functional MR was associated with a severely impaired prognosis. There was a clear association between MR of increased severity and a greater risk of morbidity and mortality. Advancing age, presence of atrial fibrillation, increasing effective regurgitant orifice, ejection fraction, left ventricle end systolic diameter, diabetes, and increasing New York Heart Association Class were identified as risk factors associated with mortality and morbidity.
Conclusions: The burden of MR for patients is considerable and there is a need to raise awareness for earlier and dedicated management of MR. The current review found that patients presenting with severe symptomatic MR and a high surgical risk have a poor prognosis and limited treatment options. There is a clear unmet need in the management of patients with severe MR not indicated for surgery. Further research into alternative medical strategies and patient management is needed to improve prognoses and reduce morbidity and mortality.

P4270 | BEDSIDE
Feasibility of doppler hemodynamic evaluation of primary and secondary mitral regurgitation during exercise echocardiography

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Purpose: Exercise transthoracic echocardiography (ExTTE) was recently proposed to evaluate exercise tolerance and to help risk stratification in Mitral Regurgitation (MR). Extensive monitoring during exercise of hemodynamic parameters including quantification of MR by the Proximal Isovelocity Surface Area (PISA) method appeared reliable in secondary MR in clinical studies. Nevertheless, few

data are available on the feasibility of Doppler echocardiographic recordings at exercise in daily practice, in both secondary and primary MR.
Methods: Comprehensive resting and Ex TTE were performed in 72 unselected consecutive patients (age 59±15 years, 62% men), asymptomatic or with equivocal symptoms, with at least moderate (mean effective regurgitant orifice area (ERO) = 36±14 mm^2) primary or secondary MR in two french university hospitals.
Results: Variation of left ventricular ejection fraction (LVEF) between rest and peak exercise (Pex) was estimated in all patients. LV contractile reserve (CR) at exercise, defined by an increase of LVEF more than 5% was found in 51/72 patients (71%). Systolic pulmonary artery pressure (SPAP) was obtained in all patients at rest and in 83% (n=60) patients at Pex. Mean SPAP at Pex was 57±14 mmHg. At rest, quantification of ERO using the PISA method was more challenging in semi-supine position than in classic left lateral decubitus position (ERO measured in 55/72; 76% vs 66/72; 92%; p=0.012), essentially in mitral valve (MV) prolapse (35/47; 74%). During exercise, ERO was only obtained in 30/55 (55%) patients and was more difficult to assess in MV prolapse than in rheumatic MR or ischemic MR (respectively in 43%, 67% and 88%, p=0.05). ERO was less frequently measured in posterior than in anterior or in bileaflet prolapse (respectively in 29%, 40% and 78%, p=0.04). When available at Pex, ERO remained stable in 1/30 (3%) patient, decreased in 8/30 (27%). and increased in 21/30 (70%). Mean increase in ERO was 10.3±4.7 mm^2. At Pex, ERO was more frequently obtained in symptomatic (NYHA IIb) than asymptomatic patients (NYHA I) (10/13, 77% vs 6/16, 37.5%, p=0.034) because peak heart rate was lower (113±20bpm vs 133±23bpm, p=0.026).
Conclusion: In daily exercise echocardiography, monitoring of the CR and SPAP appeared less challenging than MR quantification using the PISA method. Monitoring of ERO was more feasible in ischemic MR than in asymptomatic primary MR

P4271 | BEDSIDE
Mechanisms of carpentier 1 mitral regurgitation: insights using multi-detector computed tomography

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Background: The underlying mechanism of Carpentier I mitral regurgitation (MR) remains controversial. The present study evaluated changes in mitral valve geometry of patients with atrial fibrillation (AF) and structurally and functionally normal left ventricles and mitral leaflets. The multi-detector row computed tomography (MDCT) evaluations prior to radiofrequency catheter ablation for AF were evaluated.
Methods: From a cohort of 480 patients with drug-refractory AF referred for catheter ablation, 170 patients (mean age 58±10 years, 67.1% men) with structural and functional normal left ventricles and mitral leaflets were included. The intercommissural and anteroposterior diameter, perimeter and area of the mitral annulus and left atrial volume were assessed with MDCT and correlated with the grade of MR as assessed with echocardiography.
Results: 49 patients (28.8%) had MR≥2+. These patients had larger mitral annulus area compared with patients with MR<2+ (665.0±100.6 mm^2/m^2 vs. 530.5±66.6 mm^2/m^2, p<0.001) while left ventricular size and function (ejection fraction 64.9±6.3% vs. 63.1±5.7%, p=0.08) were similar. After adjusting for age, hypertension, left atrial volume and left ventricular end-systolic volume and ejection fraction, the mitral annulus dimensions remained independently correlated with MR≥2+ (Table).

Baseline model	Multivariate	
	Odds ratio (95% CI)	P-value
Age (years)	1.08 (1.02–1.14)	0.008
Hypertension	1.37 (0.57–3.28)	0.479
Left ventricular ejection fraction (%)	0.97 (0.89–1.06)	0.466
Left ventricular end-systolic volume (ml/m^2)	1.07 (0.96–1.20)	0.210
Left atrial volume (ml/m^2)	1.10 (1.05–1.14)	<0.001
Baseline model + mitral annular intercommissural diameter (mm/m^2)	1.50 (1.20–1.87)	<0.001
Baseline model + mitral annular anteroposterior diameter (mm/m^2)	1.79 (1.35–2.39)	<0.001
Baseline model + mitral annular perimeter (mm/m^2)	1.17 (1.08–1.27)	<0.001
Baseline model + mitral annular area (mm^2/m^2)	1.02 (1.01–1.02)	<0.001

Conclusion: In AF patients with structural and functional normal left ventricles and mitral leaflets, MDCT demonstrated that mitral annulus dilatation is independently associated with type I MR.

P4272 | BEDSIDE
Frank Starling law of left atrium in patients with mitral valve regurgitation

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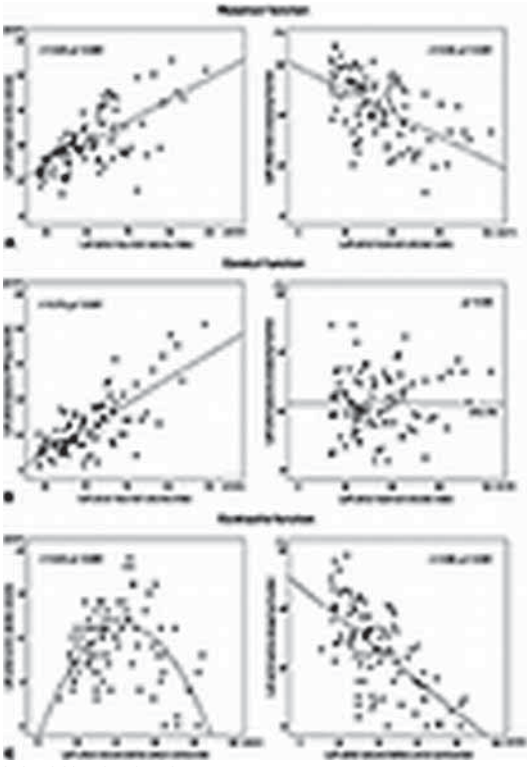
Objective: The Frank–Starling behaviour of the LA, evidenced by an increase of the contraction force after increase of the stretch level in patients with degenerative MR has not been evaluated before.The purpose of this study was to describe the Frank–Starling law and myocardial mechanics of the left atrium (LA) in patients with degenerative mitral regurgitation (MR).
Methods: Eighty patients with degenerative MR and 20 controls were included. LA volume was measured with three-dimensional transthoracic echocardiography at three phases of the cardiac cycle as maximal volume (LAVmax), minimal volume (LAVmin) and the volume before atrial contraction (LAVpre-A). From these volumes, active stroke volume (SV), and emptying fraction (EF) were calculated. LA strain and strain rate were measured with vector velocity imaging on 4-chamber and 2-chamber views.
Results: LAVmax, LAVmin and LAVpre-A all increased with increasing MR volume. LA active SV increased with LAVpre-A up to a certain point upon which it decreased despite further increased LAVpre-A (r=0.53, p<0.001). The LA active EF correlated negatively with the LAVpre-A index (r=0.65, p<0.001). LA late negative strain decreased with increasing MR volume. A positive correlation existed between LA late negative strain and the LA active EF (r=0.55, p<0.001).



Left atrial functions by volumes

Conclusion: The Frank–Starling Law exists in the LA of patients with degenerative MR, evidenced by an increase in LA contractility (SV) in response to an increase in LA preload (LAVpre-A) up to a point, beyond which the LA contractility (SV) decreased.

P4273 | BEDSIDE
Presence and significance of delayed enhancement on CMR in primary mitral regurgitation

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Purpose: The appropriate timing for surgery in severe asymptomatic primary mitral regurgitation (MR) remains controversial. It has been shown that late gadolinium enhancement on cardiovascular magnetic resonance (LGE CMR), which may identify myocardial fibrosis, is associated with a worse outcome in various cardiomyopathies. We sought to investigate the prevalence and significance of delayed enhancement in primary MR.
Methods: We prospectively included 41 patients with at least moderate primary MR and without overt signs of left ventricular (LV) dysfunction. Patients with evidence of coronary artery disease, arrhythmias or significant concomitant valvular disease were excluded. All patients were scheduled for transthoracic echocardiography and LGE CMR.
Results: 39 patients had interpretable LGE CMR images. Among them, 12 (31%) had late contrast uptake of the LV wall. LGE CMR showed an infarct pattern in 3 patients, a pattern of mid-wall fibrosis in 7 patients and 2 patients had a combined pattern. Patients with delayed enhancement on CMR had significant higher LV diameters (LV end-systolic diameter 39±4 vs. 34±5mm, p=0.002; LV end-diastolic

diameter 57±5 vs. 50±5mm, p=0.001). There was a trend towards a higher indexed left atrial volume (55±21 vs. 44±13ml/m^2, p=0.06). By contrast, there was no significant association between myocardial contrast uptake and age, LV ejection fraction and MR severity. 17 patients underwent mitral valve surgery within a follow-up period of 2 years. There was a trend towards more post-operative LV dysfunction, defined as a LVEF < or =50% at 6 months, in patients with late contrast uptake on LGE CMR (50% vs. 9%, p=0.1).
Conclusions: LV remodeling seems to be associated with the presence of delayed enhancement on CMR in primary MR. Further data are needed to determine whether LGE CMR can predict a less favourable outcome or could improve risk stratification in asymptomatic primary MR.

P4274 | BEDSIDE
High incidence of new-onset atrial fibrillation among patients with mitral valve disease - a nationwide cohort study

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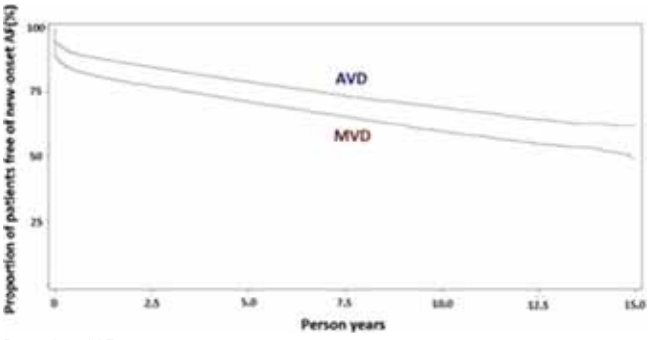
Background: Aortic valve disease (AVD) and mitral valve disease (MVD) are due to the aging population increasingly prevalent illnesses. Atrial fibrillation (AF) has in previous studies shown to be associated with valve disease, but has not previously been examined in a nationwide setting. This study investigates the differential risk of new-onset AF in a nationwide cohort of patients suffering with AVD or MVD.
Methods: Patients admitted with first-time AVD or MVD from 1997 to 2011 with no pre-existing AF were identified from nationwide registers. Information on comorbidity and concomitant medication was identified by individual-level linkage of administrative registers. Incidence rates of new-onset AF were calculated and risk assessed in multivariable adjusted Cox-proportional–hazard models.
Results: A total of 64,442 patients with either AVD or MVD were included; mean age 70 (SD±15) years and 49% males. Mean follow-up for occurrence of AF was 687 days (SD±1009). A total of 9150 (19.2%) with AVD and 5436 (28.9%) with MVD developed new-onset AF. Incidence rates for new-onset AF was 52 and 74 events per 1000 person-years for AVD and MVD, respectively. In Cox regression analysis the risk of new-onset AF was significantly higher in patients suffering MVD (HR 1.69; CI (1.63-1.75)).



Proportion of AF per person-years.

Conclusions: New onset AF is a very common complication for patients with AVD or MVD. Risk was particularly high in patients with MVD. Focus on risk of AF in patients with valve disease is warranted.

P4275 | BEDSIDE
Measurement of type-B natriuretic peptide in organic mitral regurgitation: normalization by age and sex predicts survival after diagnosis

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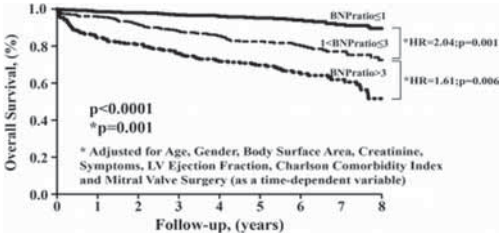
Background: Plasma level of type-B natriuretic peptide (BNP) is highly influenced by age and sex however it has never been normalized for these variables as a predictor of mortality in organic mitral regurgitation (OMR). The objective of this study was to assess the impact of an increase in BNP compared to normal upon mortality in a large population of OMR patients.
Methods: In 1015 patients with flail and/or prolapse of mitral valve, plasma level of BNP was measured at the time of Doppler-Echocardiography and divided by the normal value of BNP according to age and sex to evaluate the level of BNP increase for each patient (BNPratio).
Results: OMR patients had a mean age of 65±15 years and 634 were (62%) men. Mean left ventricular ejection fraction (LVEF) was 63±9%, the incidence of coronary artery disease was 19% (n=189), heart failure 24% (n=241) and mild chronic kidney disease was 9% (n=83). Median BNP level was 103 (interquartile: 39-285) and BNPratio was 1.2 (0.5-2.8). After adjustment age, gender, body surface area, Charlson comorbidity index, creatinine, symptoms, LVEF and mitral valve surgery (as a time dependent variable), BNPratio (log transformed) was a powerful predictor of mortality (p<0.0001) with a hazard ratio of 1.42 (1.22-1.66). Moreover, when dividing elevated BNPratio in groups, each groups had an increases in risk of death compared to the precedent one (Figure).



Overall survival according to BNPratio.

Conclusion: Abnormal BNP levels normalized for age and sex of patients with OMR is a powerful independent predictor of long-term mortality. Each doubling of observed/normal BNP ratio predicts higher likelihood of poor mortality outcomes. Thus, BNP level interpretation should be quantitative and integrated into the clinical decision-making process to potentially improve late patient survival.

INTERVENTIONS IN MITRAL VALVE DISEASE

P4277 | BEDSIDE
Mitral valve surgery in asymptomatic or mildly symptomatic patients with preserved left ventricular function: follow-up to 20 years

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Objectives: Mitral valve (MV) surgery is recommended in symptomatic patients with severe mitral regurgitation or in asymptomatic patients with signs of left ventricular function deterioration (class I, ESC guidelines). There are few reports in the literature analyzing, in a long-term basis, the outcomes of those patients who are "off-class I" indications. We aimed at analyzing the immediate results of mitral valve surgery, especially mitral valve repair, and the long-term survival and freedom from mitral reoperation.
Methods: From January 1992 to December 2012, 467 patients with degenerative severe mitral valve regurgitation (MR) and no symptoms or mildly symptomatic were submitted to mitral valve surgery. Exclusion criteria were moderate or severe LV dysfunction and associated surgeries, other than tricuspid valve repair for functional tricuspid regurgitation. Patients were followed up to 22 years (total 3,983.5 patient-years) and follow-up was complete for 92.3% of patients.
Results: Mean age was 55.3±14.5, male gender predominated (75.4%) and atrial fibrillation was present in only 19.5%. Myxomatous disease was present in 69.6% (Barlow's disease, 17.1%), fibroelastic deficiency in 25.7% and others causes, such as isolated annular dilatation, in 4.7%. Preoperative echocardiographic findings revealed a mean ejection fraction of 67.7±8.6%, LV (s/d) 39.3±6.0mm/63.5±7.3mm and SPAP 44.5±15.6mmHg. Posterior leaflet prolapse was found in 79%, anterior prolapse in 40.5%, and bileaflet prolapse in 25.1%. MV repair was performed in 98.3% of cases and only 8 patients required valve replacement. Concomitant tricuspid repair was done in 7.7%. Hospital mortality was 0.6% (3 patients) and only one patient required mechanical LV assisting device. There were 43 late deaths (10.1%) and 14 patients (3%) required reoperation, at a mean of 8.6 years after repair. Overall survival at 5y, 10y and 20y was 95±1.5%, 90±2.1% and 73.2±5.8%, respectively. Freedom from mitral reoperation at 5y, 10y and 20y was 98.9±0.5%, 96.5±1.2% and 93.1±2.1%, respectively.
Conclusion: Mitral valve repair can be accomplished in the great majority of patients with degenerative MV regurgitation, independently of the type of disease or the leaflets involved. MV surgery carries a very low mortality and long-term survival and freedom from MV reoperation is excellent. These results reinforce the rationale for operating on patients with severe MR in an early phase of the disease.

P4278 | BEDSIDE
Functional mitral stenosis after restrictive annuloplasty for secondary mitral regurgitation: does size really matter?

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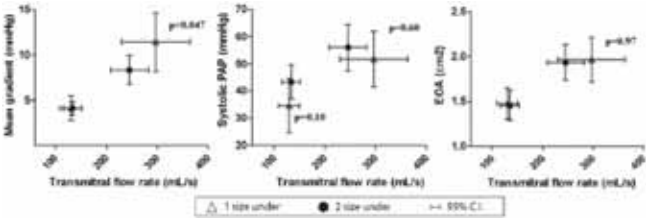
Purpose: Functional mitral valve stenosis due to undersizing may complicate restrictive mitral annuloplasty (RMA) for secondary mitral regurgitation (MR), although underlying mechanisms remain debated. This study evaluated whether the degree of undersizing (2-size versus 1-size under) affects postoperative hemodynamics at rest and during exercise in patients in whom a coaptation length of 8mm is pursued to ensure durable repair.
Methods: Consecutive secondary MR patients, treated with a 2-size (n=26) or 1-size under (n=13) RMA – to achieve a coaptation length of 8mm – were studied. Anterior leaflet size was similar in both groups. At 33±17 months af-

ter surgery, patients underwent a symptom-limited supine bicycle exercise test with Doppler echocardiography. Transmitral gradients, systolic pulmonary artery pressures (PAP) and effective orifice area (EOA) were compared in 2-size under versus 1-size under patients at rest and during exercise.
Results: At rest, the mean transmitral gradient was similar in 2-size versus 1-size under patients (4.1±1.8 versus 4.1±2.2 mmHg, p=0.99), with a similar cardiac output (4.0±0.8 versus 4.2±0.8 L/min, p=0.50) and EOA (1.4±0.4 versus 1.5±0.3cm^2, p=0.85). At maximal exercise, mean transmitral gradient, EOA, and systolic PAP changed with similar proportions in both patient groups depending on transmitral flow rate (Figure).



Evolution of gradient, sPAP and EOA.

Conclusion: In RMA patients with a similar postoperative coaptation length, inflow obstruction at rest and during exercise is not dependent of the degree of undersizing. This suggests that postoperative functional stenosis does not exclusively occur at the annular level, but is influenced by subannular alterations as well.

P4279 | BEDSIDE
Surgical treatment of posterior mitral valve prolapse

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Objectives: Mitral valve repair is the procedure of choice whenever it is expected to be durable (ESC guidelines class I). We intended to evaluate the surgical results of isolated posterior mitral valve prolapse.
Methods: From January 1998 to December 2012, 932 consecutive patients were submitted for the first time to mitral surgery for degenerative regurgitation. Among these, 492 (52.8%) had isolated posterior leaflet prolapse. Myxomatous degeneration was present in 304 (61.8%) and fibroelastic deficiency in 188 (38.2%). Mean age was 61.8±12.1 years (13-86 years) and 375 (76.2%) were male. The majority of patients were in functional class NYHA II (41.9%) and III (39.8%). A previous stroke was documented in 22 (4.5%); COPD in 26 (5.3%); atrial fibrillation in 102 (20.7%). Mean left ventricular end-systolic diameter was 39.3±7.0mm and mean SPAP 48.0±16.7 mmHg. Left ventricle dysfunction (EF<60%) was present in 52 (10.6%).
Results: Chordae rupture occurred in 330 (67.1%) and elongation in 131 (26.6%). In 79 (16.1%) more than one scallop was involved. Mitral valve repair was achieved in 484 patients (98.4%), only 8 (1.6%) had their valve replaced. Prosthetic ring annuloplasty was used in 436 (88.6%) and posterior suture annuloplasty in 46 (9.3%). Resection was performed in 419 (85.2%), implantation of artificial chordae in 40 (8.1%) and sliding plasty in 19 (3.9%) patients. Additional repair techniques were used in 85 (17.3%) cases. Associated surgeries were performed in 153 (31.1%), including tricuspid valve repair in 50 (10.0%), aortic valve surgery in 34 (6.9%), CABG in 64 (13%) and ascending aorta replacement in 5 (1%). Mean CPB and aortic clamp times were 71.9±18.9 and 43.0±13.5 minutes, respectively. Hospital mortality was 0.2% (1 patient). Mean hospital stay was 7.7±5.4 days. There were 71 late deaths (14.4%) and 7 (1.4%) patients required reoperation to the mitral valve. Mean follow-up time was 7.2±3.8 years. Overall survival at 2, 5, and 10 years was 96.1±0.9%; 91.9±1.3%, and 81.9±2.3%, respectively. Freedom from reoperation at 2, 5, and 10 years was 99.8±0.2%, 99.2±0.5, and 98.2±0.9%, respectively.
Conclusions: Mitral valve repair in patients with isolated posterior leaflet prolapse can be done in the vast majority of cases with very low operative risk and excellent long term survival. Surgery should address all lesions found intraoperatively (leaflets, chordae and annulus) using a vast armamentarium. These techniques are difficult to achieve by percutaneous approach. Hence, these patients should be referred to centers with great experience in mitral valve repair.

P4280 | BEDSIDE
Clinical predictors for long term outcome of percutaneous mitral vavlvuloplasty in patients with rheumatic mitral stenosis

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Purpose: We aimed to investigate long term clinical predictors for results of percutaneous mitral valvuloplasty (PMV) in patients with rheumatic mitral stenosis (MS).
Methods: We analyzed clinical data of 1182 patients who underwent PMV from Aug, 1980 to May 2013. Among them, we selected patients who had regular follow up visits more than 10 years [n=578, female 450 (78%), mean age 41.2±10.1 year]. Mean follow up period was 214±50 months.
Results: Procedural success was obtained in 469 (81%) patients. Fifty-one (8.8%) patients underwent redo-PMV, and 3 (0.5%) underwent trido-PMV. Mitral valve replacement was performed in 240 (41.5%) patients. Twenty-five (4.3%) had stroke. Cardiovascular death was occurred in 19 (3.3%) patients. From univariate analysis, male gender [p=0.03, HR 0.63 (95% CI=0.41-0.91)], pre-procedure atrial fibrillation (AFib) [p<0.01, HR 2.02 (95% CI=1.12-2.89)], post procedural severe MR [p=0.02, HR 2.29 (95% CI=1.17-4.43)] and post PMV mean diastolic pressure gradient (MDPG) [p=0.01, HR 1.15 (95% CI=1.04-1.27)] were statistically significant. From multivariate analysis, post procedure severe MR [p<0.01, HR 10.4 (95% CI=3.01-35.9)] and post PMV MDPG [p=0.02, HR 1.11 (95% CI=1.01-1.17] were independent predictors of poor prognosis. However, moderate MR after PMV showed similar long term outcomes compared with non or mild post PMV MR (Fig. 1). From subgroup analysis, moderate MS showed better prognosis (p=0.02) than severe MS in younger patient group (age<50, Fig. 2). Furthermore, patients with sinus rhythm showed better prognosis (p=0.01) than AF in younger patients.

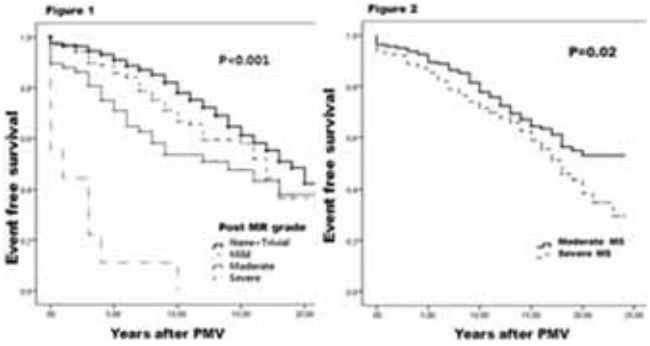

Figure 1. Event free survival curves.

Conclusions: Severe MR and higher MDPG after PMV were independent predictors of poor long term outcome. In younger patients (Age<50), moderate MS and sinus rhythm showed better long term prognosis.

P4281 | BEDSIDE
Failing left atrial remodeling leads to poorer outcome after MitraClip-implantation

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Background: MitraClip (MC) implantation is a new therapeutic option in patients with servere MR and high surgical risk. The long-term outcome and the effects of cardiac left atrial remodeling are not clarified.
Methods: This study enrolled 135 consecutive patients ((72±10 years, ♂ 62%, weight 77±15kg, 30% Diabetes mellitus, CKI 18%, NTproBNP 7054 [180-35000] pg/ml, LVEF 38±15%, CRT 30%, logEURO-Score 26±17%, 100% NYHA III/IV), who underwent MC implantation at our heart center between 2009-2013 due to severe MR and high surgical risk. Patients were followed up regurlarly at our outpatient clinic. Survival analysis was performed using a combined endpoint (all cause mortality, LVAD, MVR).
Results: The volume of the LA reduced from initial 98 (74-132)ml prior MC significantly to 93 (68-111)ml after 6 month (p<0.001) and 83 (68-104)ml after 12 month (p<0.001). Failing atrial volume reduction was a significant outcome predictor for the combined endpoint. The volume of the RA is not significantly changing after MC implantation.
Conclusion: There is a significant remodeling of the LA after MC implantation with significant volume reduction. Failing remodeling predicts poor longterm outcome of patients. The RA shows smaller remodeling than the LA.
Conclusion: There is a significant remodeling of the LA after MC implantation with significant volume reduction. Failing remodeling predicts poor longterm outcome of patients. The RA shows smaller remodeling than the LA.

P4282 | BEDSIDE
Acute decrease in NT-proBNP serum levels after successful MitraClip implantation is associated with lower long-term mortality in surgical high-risk patients

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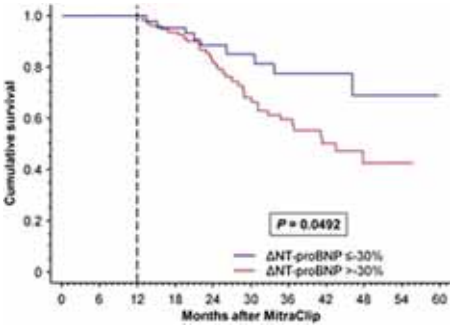
Purpose: In patients with grade 3+/4+ mitral regurgitation (MR) not amenable to surgery, MitraClip (MC) implantation is increasingly being used as a therapeutic option for both degenerative (DMR) and functional (FMR) aetiologies. To date, lit-

tle is known about survival benefits in the long term. N-terminal B-type natriuretic peptide (NT-proBNP) is a routinely used biomarker to evaluate ventricular wall stress in the setting of acute and chronic heart failure.
Methods: In successfully treated patients (MR ≤2+ at discharge), FU information was obtained at clinical visits 6 and 12 months after the procedure and annually thereafter. NT-proBNP serum concentrations were measured before (1-3d) and after successful MitraClip implantation (2-5d).
Results: Of 350 consecutive patients who underwent MitraClip therapy at our centre, 315 (90%; mean age 75 years; 96 DMR, 219 FMR) were treated successfully. Pairs of NT-proBNP values before and after treatment were obtained from 243 individuals (77%). Post-hoc, patients were dichotomized according to acute changes in NT-proBNP (ΔproBNP), with a cut-off at -30% (Group A: ΔproBNP ≤ -30%, Group B ΔproBNP > -30%). Group A comprised 67 patients (28%), leaving 176 patients (72%) in Group B. Kaplan-Meier 12-month landmark analysis showed a survival benefit after 1 year (p=0.049) in patients with ΔproBNP ≤ -30% (Figure). Interestingly, cumulative freedom from rehospitalisation due to heart failure was statistically not different in both groups.



Cumulative survival (landmark analysis).

Conclusions: An acute decrease in NT-proBNP by at least -30% after successful MC therapy apparently improves survival after 12 months; however, freedom from heart-failure rehospitalisation is not impacted. Presumably this reflects the multi-morbidity of individuals not amenable to surgery who undergo MitraClip therapy.

P4283 | BEDSIDE
The impact of residual mitral regurgitation after MitraClip implantation as a predictor of 2-year-mortality

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Purpose: MitraClip (MC) procedure is a new tool for treatment for patients with severe mitral regurgitation (MR) and high surgical risk. The long-term outcome these patients is still a topic of research. We investigated the influence of persisting residual MR on the long-term outcome after MC-implantation.
Method: This study included consecutive 211 patients (72±10 years, ♂ 62%, 77±15kg, 30% Diabetes mellitus, CKI 18%, NTproBNP 7054 [180-35000] pg/ml, LVEF 38±15%, CRT30%, logEURO-Score 26±17%, 100% NYHA III/IV), between March 2009 and August 2013, who underwent MC-implantation in our heart center. Patients were regularly followed up every 6 months at our outpatient clinic. Survival analysis was performed using Kaplan-Meier- Analysis. We investigated the influence of residual MR at discharge as a predictor of freedom from a combined endpoint (all-cause mortality, LVAD, surgery, unsuccessful implantation). The MR at discharge was retrospectively analyzed by an experienced echocardiographer.
Results: At discharge 79 patients had small residual MR grad 1+, 107 patients had mild-moderate MR grad 2+ and 20 patients had moderate-severe residual MR grad 3+. The outcome of patients with severe residual MR grad 3+ was significantly worse. Patients with moderate residual MR had a comparable outcome after one year to patients with only small resual MR grad 1+, but the outcome became worse after two years.
Conclusion: Residual MR just after the MC implantation at discharge of the hospital may have predictive power for the long-term outcome of patients. Mild or more MR leads to poorer long-term outcome compared to trivial MR. During MC procedure, we therefore should try to minimize the residual MR as small as possible.

P4284 | BEDSIDE
Percutaneous mitral valve repair with the mitraclip system in patients aged less than 75 versus grater than or equal to 75 years: one-year outcomes from the GRASP registry

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Purpose: The aim of this study was to compare one-year outcomes of percutaneous mitral valve repair with the MitraClip System in high surgical risk patients with moderate-to-severe or severe mitral regurgitation (MR) aged <75 versus ≥75 years.
Methods: Patients enrolled in the prospective Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation (GRASP) who were eligible at one-year follow-up were evaluated in the present analysis. The primary efficacy endpoint was the composite of death, surgery for mitral valve dysfunction and grade 3+ or 4+ MR at one-year follow-up. Secondary endpoints were the components of the primary endpoint, re-hospitalization rates and functional NYHA class.
Results: A total of 139 patients were included: 65 (46.7%) were aged <75 years and 74 (53.3%) ≥75 years. Thirty patients (21.5%) presented with degenerative MR and 109 patients (78.5%) with functional MR. Comparable clinical and echocardiographic baseline characteristics were observed between the two groups except for STS score, NYHA functional class 4 (worst in the older group) and poor ejection fraction (more common in the younger group). All patients had a post-procedural residual MR≤2+. At one-year follow-up, no significant differences were reported in terms of primary end-point (18.5% in younger patients versus 24.3% in older patients, p=0.40). Secondary endpoints rates concerning the two groups are reported in Table 1. No statistically significant differences were observed.

Table 1. One-year outcomes in patients aged <75 years versus ≥ 75 years undergoing percutaneous mitral valve repair with the mitraclip system

	<75 years	≥75 years	p
Death	9.2%	9.5%	0.96
Surgery for mitral valve	–	–	–
MR grade ≥3+	11.8%	19.6%	0.26
Re-hospitalization	10.8%	10.8%	0.99
NYHA class ≤2	83.6%	81.5%	0.76

Conclusions: The MitraClip procedure was associated with low rates of adverse events in elderly patients, reporting one-year outcomes comparable to younger patients.

P4285 | BEDSIDE
Acute changes of mitral valve geometry during interventional edge-to-edge repair with the MitraClip system impacts on mid-term functional outcomes

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Background: Transcatheter mitral valve repair (TMVR) is a treatment option in patients with symptomatic functional (FMR) or degenerative mitral regurgitation (DMR) at high surgical risk. The acute impact of MitraClip procedure on mitral valve (MV) annular geometry, and its relation to functional outcomes is unclear. We sought to assess immediate effect of TMVR on MV annular geometry with 3D transesophageal echocardiography (TEE) and the association of MV diameter reduction with functional response after 6 months.
Methods and results: Consecutive patients (n=111; age 78.3±8.1years) at high surgical risk (logistic EuroSCORE 29.8±21.5%) underwent TMVR. The procedure was completed successfully in 107 patients (96%) with 3D reconstruction of MV annular geometry immediately before and after clip implantation. Only patients with FMR (n=71) experienced an acute reduction of anterior-posterior-MV (AP) diameters (4.0±0.6cm, 3.6±0.6cm, p<0.0001), MV-annulus-areas (2D-annulus-area: 13.9±3.8cm^2, 12.8±3.4cm^2, p<0.0001; 3D-annulus-area: 14.4±3.9cm^2, 12.9±3.4cm^2, p<0.0001) and MV annular geometry (MV-sphericity-index: 0.9±0.1, 0.8±0.1, p<0.0001); the lateral-medial-MV (LM) diameters remained unchanged (4.3±0.7cm, 4.4±0.6cm, p=0.13). In subjects with DMR all MV annular geometry-defining values were not significantly altered after TMVR (n=36, p>0.05).
Acute AP-diameter reduction was significantly associated with clinical response to TMVR after 6 months of FU (cut-off value≥6.4%, AUC=0.81, p=0.002; sensitivity=81.6%, specificity=81.8%), which was confirmed by additional regression analysis (p=0.007).
Conclusion: 3DTEE enables assessment of acute changes of MV geometry in patients undergoing the MitraClip procedure. Only patients with FMR experienced significant reduction of MV annular dimensions, which was associated with clinical response to TMVR.

P4286 | BEDSIDE
Largest series of completely percutaneous antegrade transseptal-transapical mitral valve-in-valve implantation for bioprosthetic dysfunction

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Purpose: Reoperation for mitral valve bioprosthetic deterioration is associated with significant morbidity and mortality. With improvements in technology and imaging capabilities, transcatheter techniques are now utilized as an alternative strategy in high-risk individuals. We report our experience of completely percutaneous transseptal-transapical mitral valve-in-valve (ViV) implantation using fusion imaging.

Methods: Between February 2012 and 2014, 14 patients (age 71±14 years, 7 female, 5 male) presented to our institution with severe mitral bioprosthetic (range 25 to 33 mm) dysfunction at a median of 3302 days [IQR: 2503 to 3565] following surgery. Mode of prosthesis failure was severe regurgitation in 7.1%, stenosis in 57.1%, and combined in 21.4%. Risk scores predicted a 30-day mortality of were 13.1±11.0% (EuroSCORE II) and 14.1±11.7% (STS). All individuals had preoperative transthoracic echocardiography and cardiac computed tomography performed and were evaluated by our multidisciplinary heart team. Percutaneous transseptal and transapical access were performed with creation of an arteriovenous rail for percutaneous delivery via transfemoral approach. At the time of the intervention, fusion imaging using the HeartNavigator and EchoNavigator systems (Philips Healthcare, Best, the Netherlands) were employed.
Results: Complete percutaneous mitral ViV implantation was successfully performed in 12/14 (85.7%) patients. In 10 patients, a Medtronic Melody valve was implanted while the remaining 4 patients received an Edwards Sapien (23mm, 2; 26mm, 2) valve. There were two intra-operative complications: a valve embolization and a tension pneumothorax, both leading to hemodynamic collapse and subsequent intra-procedural and post-operative (day 8) mortality, respectively. The mean NYHA functional class improved from 3.2±0.6 to 1.1±0.8 (p=<0.01) over a median follow of 173 days (IQR: 13.5 to 330). The mean transvalvular gradient improved from 11.6±4.3 to 5.1±2.7 (p<0.01) after implantation with all patients having mild or no residual regurgitation.
Conclusions: In high-risk patients, completely percutaneous transseptal-transapical mitral ViV implantation is a promising therapeutic option in individuals with degenerated bioprostheses that is associated with a favorable outcome.

P4287 | BEDSIDE
Functional parameters to assess clinical benefit after transcatheter edge-to-edge mitral valve repair

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Purpose: We assessed the role of NYHA functional class, six-minutes-walking distance (6MWD), N-terminal pro-brain natriuretic peptide (NT-proBNP) plasma level and quality of life (QoL) as integrative parameters to evaluate efficacy and clinical impact of transcatheter edge-to-edge repair in patients with severe mitral regurgitation (MR).
Methods: In patients who underwent clip repair, we evaluated NYHA functional class and 6MWD before the procedure, at the discharge and after 30-days. During the hospitalization, before the procedure and the day of discharge, BNP serum levels have been collected. Furthermore we calculated QoL using a self-administration questionnaire. Acute procedural success was defined as stable implant of one (or more) clip(s) resulting in MR 2+.
Results: The study includes 60 consecutive patients (mean age 73±9 years old, males 86%), who underwent transcatheter edge-to-edge repair with one (38%), 2 (60%) or 3 clips (2%). The mean left ventricle ejection fraction was 35±13%. Functional MR and degenerative MR were present in 78% and 22%, respectively. Acute procedural success was obtained in all patients. At discharge 82% of patients had MR1+; 18% MR2+. At 30 days 75% of patients had MR1+; 23% MR2+ and 2% MR 3+. During in-hospital stay one patient died for pneumonia at the 13 day after the procedure. Overall NYHA improved from 3.3±0.7 at baseline to 1.8±0.5 at discharge (p<0.0001), and 1.8±0.7 after 30 days (p<0.0001 when compared with baseline; p=ns when compared with discharge). 6MWD improved significantly from a median of 95 m (IQR 67,50-170) at baseline to 174 m (IQR 103-202,50) at discharge (p<0.002) and 180 m (IQR 135-220) at follow-up (p=0.005 when compared with baseline; p=0.066 when compared with discharge). NTproBNP plasma levels decreased from a median of 6347 pg/mL (IQR 2534,75-10315,75) at baseline to a median of 1657,5 pg/mL (IQR 1003,25-4274, p=0.002) at discharge. On the other hand QoL compromising improved from a score of 8.6±1.6 at baseline to 7.8±1.7 after 30 days (p=0.034).
Conclusions: Transcatheter edge-to-edge repair leads to a significant short-term improvement in symptoms, functional status and quality of life in patients considered at high risk for conventional cardiac surgery. These are useful measurements of functional capacity easily performed, not expensive and repeatable. In addition in the subset of heart failure patients NT-proBNP can be very useful not only in diagnosis but also in monitoring the results after clip implantation.

P4288 | BEDSIDE
Closure of the residual interatrial communication after transcatheter mitral edge-to-edge repair

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Purpose: Aim of our study was to assess the hemodynamic impact of the intracardiac shunt due to the residual interatrial communication (IAC) after mitra clip procedure.
Methods: From January 2012 to December 2013, 60 consecutive patients (70% males; mean age 73±9 y.o.; mean logistic EuroSCORE 22±18%), have been treated with mitra clip device. Forty-seven patients (78%) had secondary mitral regurgitation (MR) with a mean left ventricle ejection fraction (LVEF) of 30±10%; 13 patients suffered from primary MR with a LVEF of 56±8% (p<0.00001). The residual IAC was immediately evaluated with transesophageal echo after the guiding-catheter was withdrawn; additionally the right cardiac catheterization was performed before and after the procedure.
Results: Procedures were performed in deep-sedation and spontaneous breathing in 36 patients (60%), whereas 24 (40%) were intubated under general anesthesia; one, two and three clips were implanted in 23 (38%), 36 (60%), 1 (2%) patients, respectively. The mean device time was 41±26 minutes and no intraprocedural deaths occurred. The IAC measured 0,6±0,4 cm and Qp/Qs was estimated 1,4±0,2. Six patients (10%) needed percutaneous closure of the residual defect, using devices for patent foramen ovale, because the shunt was judged to have significant hemodynamic impact. In 4 patients the closure was performed acutely during the same session. Among these the shunt was bidirectional in 3 cases, whereas one patient had acute right ventricle overload with severe acute cardiac failure. Sequentially two patients, who developed chronic right cardiac failure, have been treated treated after one month and eight months, respectively.
Conclusions: In patients with very low LVEF and right ventricle dysfunction who underwent transcatheter mitra clip repair even small IAC with Qp/Qs <1,4 can cause signs of cardiac failure. A careful monitoring and hemodynamic assessment are mandatory to select patients who need percutaneous closure of the defect.

BASICS IN VALVE DISEASE

P4290 | BENCH
Characterization of human valvular interstitial cells isolated from normal and fibrocalcified aortic valves

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Purpose: Aortic Valve Stenosis (AVS) affects 2% to 6% of population over 65 years in industrialized countries. AVS involves Valve Interstitial Cells (VIC) proliferation and commitment to osteoblast-like cells. This prevalent cell type of the valve is heterogeneous and presents five identifiable phenotypes: embryonic progenitor endothelial/mesenchymal cells, progenitor, quiescent, activated and osteoblastic VIC. To study the pathophysiology of AVS, their in vitro cultures are often used. Our purpose is to characterize the phenotype of VIC isolated from normal and fibrocalcified human aortic valves at different cell culture passages.
Methods: VIC were isolated by collagenase digestion from normal and fibrocalcific human tricuspid aortic valves (n=5 each). One cusp was conserved for immunohistological analyses. Characterization was assessed at different passages (P2 to P5) by immunofluorescence and flow cytometry. We analyzed markers of progenitor cells (SSEA4 and ABCG2), fibroblasts (vimentin and HSP47), smooth muscle cells (SMC) (α-actin) and osteoblasts (OsteoBlast CaDHerin (OBCDH)). Viability and proliferation of VIC, in standard and starvation medium at 48h, were analyzed by blue trypan and Cell Titer MTS.
Results: Immunohistology showed the presence of all VIC phenotypes, independently of the valve nature but in specific layer distribution. At the third passage, no statistical difference was found in progenitor markers (SSEA4: 68±10.2% vs 47±14.5% and ABCG2: 91±4.5% vs 81.7±6.4%; positive normal VIC percent vs pathological ones ± SEM). No difference was observed for fibroblast and SMC markers (vimentin: 73.7±34.5% vs 84.7±17.8%; α-actin 5.7±5.4% vs 29.1±27.9%) except for HSP47 (21.9±3.7% vs 46.8±4.7%, p=0.05). Osteoblast markers are more expressed by pathological VIC (OBCDH 0.6±0.5% vs 3.1±0.9%, p=0.05). However, there are changes in VIC subpopulations from cell isolation through culture passages (eg. 0.6 fold higher of SSEA4 positive pathological VIC between P0 and P3). Moreover, pathological VIC had lower viability (89.6±7.9% vs 76.5±5.3%, p=0.02) but a higher proliferation index (1.4 fold normal VIC, p=0.02).
Conclusion: There is a fluctuation in the distribution of VIC subpopulations from the explanted valve through the progression of cell culture. Although all phenotypes persist through different passages, the prevalence of one or another depends on the nature of the aortic valve. These novel findings are of the utmost importance to analyze the responses of the mixed VIC population in vitro to understand their participation and the mechanisms of AVS.

P4291 | BENCH
Histological and molecular fingerprints of low-gradient aortic stenosis

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Purpose: We investigated histological and molecular correlations of impaired left ventricular (LV) function in low-gradient aortic stenosis (LGAS) compared to aortic stenosis (AS) with normal ejection fraction (EF).
Methods: Intraoperative biopsies were obtained from 5 consecutive patients (pt) with LGAS, 7 pt with AS and from 4 donor healthy hearts. The fraction of cardiac interstitial tissue, the intracellular volume fraction of myofibrils and my-

ofiber diameters were determined by light microscopic morphometry. Expression of sarcoplasmic-endoplasmic reticulum calcium ATPase SERCA-2a and of natrium/calcium exchanger NCX-1 were assessed by immunohistochemical staining.
Results: Histologically, a significant increase in interstitial volume fraction distinguished LGAS from AS, without differences in myofiber diameters and myofibrillar volume fraction. At protein level, a decrease in SERCA-2a and a marked increase in NCX-1 were found in LGAS (Table 1, Fig. 1).

Table 1

Parameters	LGAS (n=5)	AS (n=7)	Controls (n=4)
Interstitial volume fraction (%)	28.6±19.7*	10.1±7.7	N/A
Myofiber diameter (μm)	21.5±3.9	23.4±2.4	N/A
Myofibrils volume fraction (%)	55.6±5.4	59.3±2.3	N/A
SERCA-2a (units)	1.7±0.45*°	2.79±0.27	2.88±0.25
NCX-1 (units)	2.6±0.22*°	0.36±0.38°	1.13±0.48

*p<0.05 vs. AS, °p<0.05 vs. controls.

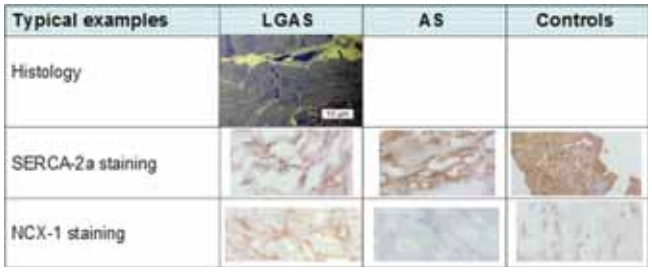

Figure 1

Conclusions: LGAS is typically associated with increased interstitial volume, decreased SERCA-2a and strong overexpression of NCX-1, compared to AS with normal EF.

P4292 | BEDSIDE
Angiogenic and angiostatic factors in patients with coronary artery disease and mitral annulus and/or aortic valve calcification

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Background: The balance between angiostatic factors (endostatin (ES), angiostatin (AS)) and angiogenic factors (vascular endothelial growth factor (VEGF), osteopontin (OPN)) is essential in physiological and pathological angiogenesis and may also play a role in valve calcification in patients with coronary artery disease (CAD).
Methods and results: In total 224 non-or ex-smoking patients (161 male, mean age: 61,09±11,02 years; 63 female: mean age: 67,49±7,87 years) with angiographycally verified CAD were recruited. Serum ES, AS, VEGF and proBNP (brain natriuretic peptide) levels and plasma OPN levels were measured and mitral or aortic valve calcification were evaluated by echocardiography. Mitral valve was calcified in 35,3%, aortic valve in 26,3%. ES, OPN and proBNP were significantly higher in patients with moderate or severe mitral (p=0,003/<0,001/0,001) and aortic valve calcification (p=0,001/0,006/0,022) compared to patients with non-calcified valves.
Conclusions: Mitral annulus and aortic valve calcifications (MAC, AVC) are frequent pathologies in CAD-patients. ES, OPN and proBNP which were shown to be elevated in CAD, were even higher in CAD-patients with MAC and AVC and seem to be of distinct interest when trying to understand the process of heart valve calcification. However, in particular concerning the role of ES in connection to calcification this might be the first clinical study which attends to that topic and much more molecular research is needed.

P4293 | BEDSIDE
Circulating bone turnover markers in patients with severe aortic stenosis

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Background: The abnormalities of calcium metabolism have been observed recently in patients with aortic stenosis. We propose that calcification of aortic valve increases due to inflammation and disruption in calcium homeostasis. The aim of the study was to determine circulating osteoprotegerin (OPG), soluble ligand receptor activator of transcription factor kappa B (sRANKL) and collagen metabolites concentrations in patients with bicuspid and tricuspid calcific aortic stenosis (AS).
Materials and methods: Patients with peak aortic jet velocity (Vmax) more than 4.0 m/s were included. 61 pts with aortic valve stenosis (AS): 31 pts with bicuspid aortic valve (BAV) (57.3±1.0 yrs; m:f 1.8:1) and 30 pts with tricuspid aortic valve (TAV) (59.7±0.7 yrs; m:f 1:1) and 31 healthy persons as a control (57.6±0.8 yrs; m:f 1.1:1) were examined. Pts with infective endocarditis and rheumatic disease were excluded. Serum OPG, sRANKL, vitamin D, cholestherol (Chl), C-terminal telopeptide of collagen I (CTx), C-terminal propeptide of procollagen type I (PICP) were performed in all pts by enzyme-linked immunosorbent assay. Bone mineral density of lumbal spines (BMD) was investigated with dual energy x-ray absorptiometry.
Results: Patients with BAV and TAV were comparable for age, gender and ECHO parameters. Increased level of circulating OPG was revealed in pts with AS compared to healthy controls (ANOVA, p=0,008). Serum level of vitamin D was normal in all groups. There wasn't correlation between OPG/sRANKL and BMD. Despite of normal T–criterion negative relationship between aortic valve pressure gradient and T-criterion and BMD was detected in all pts (r=-0.309, p=0.01 and r=-0.275, p=0.03, respectively). There was positive correlation between CTx and Vmax (r=0.352, p=0.01), especially in BAV pts (r=0,521; p=0,004). Increased ratio PICP/CTx was associated with thickening of the interventricular septum.
Conclusion: Elevated circulating collagen metabolites concentrations were associated not only with the severity of aortic stenosis, but also with left ventricular hypertrophy. Possible bone resorption and remodeling may increase the availability of calcium and its deposition in the aortic valve especially in patients with BAV.

P4294 | BENCH
Leptin is expressed in human calcific aortic valves and promotes osteoblastic differentiation of aortic valvular interstitial cells: a new regulatory mechanism of valvular calcification

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Purpose: Calcific aortic valve disease (CAVD) affects 2% to 6% of the population over 65 years in industrialized countries. CAVD, assimilated to an "atherosclerosis-like" disease, results from dysregulated processes such as calcification, supported in part by the osteoblastic differentiation of valvular interstitial cells (VIC), the most prevalent cell type in the human aortic valves. Leptin, known as the product of obesity gene and as an important regulator of food intake and energy balance, has recently been linked to aortic valve calcification in ApoE –/– mice. Our hypothesis is that leptin could play an important role in the calcifying processes implicated in CAVD via direct effects on VIC phenotype in humans.
Methods: Expression of leptin and its receptor was analysed by RT-qPCR, immunohistochemistry and ELISA in 74 human calcific aortic valves and in 10 normal valves. VIC isolated from calcific and normal aortic valves were also analysed. The effects of leptin on osteoblastic differentiation of cultured VIC were investigated by alizarin red staining and by RT-qPCR analysis of the osteoblastic markers osteopontin, SPARC/osteonectin, alkaline phosphatase, bone morphogenetic protein (BMP)-2 and BMP-7.
Results: The presence of leptin and its long functional receptor isoform (ObR-L) was observed in human calcific and normal aortic valves with an overexpression of leptin in calcified vs non-calcified valvular zones (114.52 pg/mg (47.96-234.55) vs 66.95 pg/mg (42.76-137.15), p<0.05). Moreover, ObR-L and leptin were constitutively expressed in VIC with a higher ObR-L expression in VIC isolated from pathological vs normal valves (0.83 vs 3.44, p<0.05). Furthermore, acute leptin stimulation (24h) of VIC increased the expression of the pro-calcifying protein SPARC/osteonectin (p<0.05) and decreased the expression of the anti-calcifying

Abstract P4292 – Table 1. ES, AS, VEGF, OPN (ng/ml) and proBNP (pg/ml) in dependence of aortic valve calcification (AVC) and mitral annulus calcification (MAC)

	ES	AS	VEGF	OPN	proBNP
MAC					
– No MAC (n=145)	180,9 (143,9–229,8)	267,8 (225,8–328,9)	439,0 (276,7–667,8)	102,9 (79,1–139,4)	475,6 (140,4–1591,3)
– Mild MAC (n=47)	212,9 (165,4–254,5)	267,4 (221,5–303,3)	444,7 (309,6–629,5)	122,7 (86,6–184,5)	966,2 (215,3–2495,3)
– Moderate/severe MAC (n=32)	231,2 (175,5–290,2)	292,9 (235,0–345,0)	351,8 (239,7–641,5)	187,0 (104,9–234,1)	2005,5 (268,3–9719,0)
AVC					
– No AVC (n=165)	176,7 (146,7–228,1)	268,0 (221,1–323,8)	449,7 (287,2–701,4)	104,4 (79,3–149,1)	474,3 (164,5–1753,0)
– Mild AVC (n=15)	211,6 (188,6–256,1)	267,3 (256,8–310,0)	318,7 (243,1–616,0)	130,2 (79,83–201,1)	898,4 (246,7–1259,0)
– Moderate/severe AVC (n=44)	233,3 (180,8–299,7)	280,2 (234,5–347,1)	374,1 (249,0–602,2)	119,5 (94,7–205,1)	1033,0 (320,5–3949,3)

Data is given as median (1st–3rd quartile).

protein BMP-7 ($p<0.05$). Osteopontin, alkaline phosphatase and BMP-2 expressions were not affected by leptin. On the other hand, chronic leptin stimulation (21 days) led to an increased calcium deposition in VIC.
Conclusions: Taken together, these novel findings underline the potential role of leptin in the process of human valve calcification by promoting osteoblastic differentiation of human aortic VIC.

P4295 | BENCH
Extracellular pyrophosphate accumulation is reduced in aortic interstitial valve cells acquiring a calcifying profile: implications for aortic valve calcification

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Purpose: Pyrophosphate (PPi) is a potent inhibitor of ectopic mineralization but its role during aortic valve calcification is not known.
Methods: Anti-calcific effect of PPi was investigated by using an in vitro model of serum-driven calcification of type I collagen matrix. Primary bovine aortic VIC clonal subpopulations were obtained by using a limiting dilution technique. VIC pro-calcific potential of the different clones was tested through the measurement of alkaline phosphatase activity (ALP) and calcium deposition (mg/mg collagen) after 12 days of treatment with a combination of endotoxin (500 ng/ml) and phosphate (2.0 mmol/L). VIC, were also seeded within the type I collagen sponges or in transwell chambers to test the cell's ability to inhibit serum-induced calcification. PPi extracellular accumulation was quantified through a luciferase-based assay (expressed as nM/mg protein).
Results: High serum levels induced a dose-dependent calcification of type I collagen matrices that was blocked by PPi (calcium FBS50%: 1.583±0.137; FBS50% + PPi 1 mM: 0.008±0.008, $p<0.05$). This potent inhibitory effect was preserved even when the matrices were pre-treated with PPi just for three days before exposure to the serum (calcium FBS50% 1.669±0.399; FBS50% + PPi 1 mM: 0.010±0.006, $p<0.05$). A similar protective effect was observed when VIC were either statically seeded into the collagen matrices or co-coltured by using a transwell system (calcium FBS 50%: 1.116±0,091, VIC within matrix: 0.203±0.021, $p<0.05$ vs FBS 50%; VIC in transwell: 0.448±0.069, $p<0.05$ vs FBS50%). However, when we performed co-colture experiments by using clonal VIC harbouring different calcifying potential, we observed that the subset of cells expressing high levels of ALP (clone 1) lost the ability to protect the collagen from serum-driven calcification (calcium clone 1 in transwell: 0.942±0.124, p=n.s. vs FBS50%) as compared to other clones expressing low ALP levels (calcium clone 2 in transwell 0.315±0.122, $p<0.05$ vs FBS50%). Pro-calcific differentiation of the clonal VIC was also accompanied by reduced extracellular accumulation of PPi (PPi clone 1: untreated 59.04±18.13, LPS: 10.42±7.52, $p<0.05$). This reduction was not observed in the clone unable to acquire a calcifying profile (PPi clone 2: untreated 106.45±30.0, LPS: 97.60±9,62, p=n.s.).
Conclusions: We showed that PPi is a potent inhibitor of serum-driven calcification of collagen matrix and that its extracellular accumulation is reduced in calcifying VIC. Modulation of PPi metabolism may represent a novel treatment strategy for the treatment of calcific valve degeneration.

P4296 | BEDSIDE
Angiotensinogen plasma levels and progression of LV hypertrophy in patients with aortic stenosis - the PROGRESSA study

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Background: The renin-angiotensin system (RAS) has been involved in the development of LV hypertrophy (LVH) and severe LVH has been associated with worse outcomes in patients with aortic stenosis (AS). Experimental and clinical studies reported a link between some angiotensinogen (AGN) gene polymorphisms and LVH in healthy subjects and hypertensive patients. The objective of this prospective study was to examine the relationship between AGN plasma levels and the progression of LVH in AS patients.
Methods: 139 consecutive patients with AS were prospectively recruited in the PROGRESSA study and underwent a comprehensive Doppler-echocardiography annually (mean follow-up: 2.6±1.4years). LV mass was calculated with the modified ASE formula and was indexed to 2.7 power of height (LVMi).
Results: Among the 139 patients included in this study, mean age was 65±14 years and there were 29% of women. Forty three (31%) patients were under angiotensin-converting enzyme inhibitors (ACEi), 42 (30%) under angiotensin receptor blockers (ARB) and the remaining 54 (39%) patients had no medication targeting RAS. There was a significant interaction between AGN plasma levels and ARB (p=0.003) but not ACEi (p=0.59) with regards to LVMi progression rate. There was a non-significant trend for negative association between AGN plasma levels and LVMi progression in patients under ARB (β=-0.23±6.2; p=0.15), whereas a significant positive association in patients without this medication (β=+0.32±3.6; p=0.001). In patients without ARB, AGN plasma levels remained independently associated with progression of LVMi (β=+0.31±3.8; p=0.004) after adjustment for age, gender, hypertension, mean gradient, LV ejection fraction, valvulo-arterial impedance (Zva), baseline LVMi and creatinine. Further adjustment for the progression rate of mean gradient and Zva provided similar results.
Conclusion: This prospective study shows that plasma AGN is independently correlated with the progression of LVH, even after adjustment for LV afterload. This association appears to be blunted by the use of ARBs, therefore suggesting a potential benefit of this medication to prevent progression of LVH in AS patients.

P4297 | BEDSIDE
Lipoprotein(a) levels are associated with aortic valve calcification in asymptomatic patients with familial hypercholesterolemia

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Aim: To determine the association of plasma lipoprotein (Lp) (a) levels, LPA SNPs and apolipoprotein(a) kringle IV repeat polymorphisms with aortic valve calcification (AVC) in asymptomatic patients with heterozygous familial hypercholesterolemia (FH)
Methods and results: A total of 129 asymptomatic heterozygous FH patients (age 40-69 years) were included in this study. AVC was detected using computed tomography (CT) scanning. Lp(a) concentration, LPA SNPs and apolipoprotein(a) kringle size were measured using immunoturbidimetry, allelic discrimination and immunoblotting assays, respectively. AVC prevalence in the patients was 38.2% with 3 patients displaying extensive AVC (>400 Agatston Unit). Lp(a) concentrations were significantly correlated with gender, number of apo(a) kringle IV repeats, LPA SNP rs10455872 minor allele, the presence and the severity of AVC. Using univariate logistic regression, plasma Lp(a) levels, age, BMI, blood pressure, duration of statin use, cholesterol-year score (CYS) and coronary artery calcium (CAC) score were significantly associated with AVC. No significant association between LPA SNP rs10455872 and AVC was found. After adjustment for significant predictors selected from the univariate model, plasma Lp(a) levels remained a significant predictor for AVC (odds ratio (95%CI) (per 10 mg/dL increment of Lp(a) concentration) = 1.11 (1.01-1.20), p=0.03).
Conclusion: Plasma Lp(a) is an independent predictor for AVC but not CAC in asymptomatic patients with FH.

P4298 | BEDSIDE
Difference in eNOS expression and oxidative stress between fibrotic and calcified aortic stenosis

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Introduction: Aortic stenosis (AS) is one of the life threatening problem facing aging societies and the progression of AS is appeared to be closely associated with endothelial dysfunction. Degeneration of aortic valve in AS is mainly consisted of two pathologic phenotypes: calcified and fibrotic changes. However, the association between each type of valvular degeneration and clinical characteristics in AS have not been clarified concisely.
Objective: To investigate the relationship between pathologic phenotype of aortic valve in AS and clinical variables.
Materials and methods: From 2006 to 2013, consecutive 54 patients (male 29) with AS, who were underwent aortic valve replacement (AVR) in our hospital (mean age 70.0±10.5 years) were included. Tissue sample was taken vertically from each aortic valve cusps near its center and then stained hematoxylin-eosin and elastica-Van Gieson. Immunohistochemical analysis was done by endothelial nitric oxide synthase (eNOS) and 3-nitrotyrosine. Echocardiographic parameters and fasting blood samples were analyzed before AVR.
Results: We divided patients into two by the ratio of calcified/total area of extracted valve samples and we defined subjects with aortic valve of calcified area over 25% of total area as a calcified type (n=35), whereas others were defined as a fibrotic type (n=19). There were no significant differences in coronary risk factors, clinical symptoms and echocardiographic parameters including peak aortic valve flow (4.5±0.8 m/s vs 4.3±0.6 m/s, p=0.2198). By contrast, brain natriuretic peptide was significantly increased in patients with calcified type (400.1±528.9 vs 135.6±117.9 pg/ml, p=0.018). The expression of eNOS was more pronounced in valve leaflets with calcified type than fibrotic one (calcified: n=9 (25.7%) vs fibrotic: n=1 (5.3%), p=0.0452). Oxidative stress 3-nitrotyrosine was similarly detected more intensively in calcified type (36.2±17.3 per high power field (HPF) vs 27.1±14.1 /HPF, p=0.0271). In patients with calcified type, there was a strong correlation between the count of 3-nitrotyrosine positive cells/HPF and fraction of calcified area in valve leaflets (R = 0.3924, p=0.0197).
Conclusion: The eNOS and oxidative stress in the valve are markedly different between two types, and calcified type was closely associated with reactive oxygen species produced in diseased valve, whereas fibrotic type was related to the decrease of eNOS expression in the valvular endothelium.

P4299 | **BEDSIDE**
Notch-1 gene mutations and biomarkers of calcification in patients with aortic stenosis

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Calcific aortic valve disease (CAVD) is the most common acquired valvular disorder. Although the genetic basis of CAVD is unknown for most patients, several disease-associated genes have been identified in humans.
Purpose: The aim of our study was to estimate the frequency of NOTCH1 gene mutations and to investigate the potential relationship between mutations and biomarkers in patients with aortic stenosis (AS).
Methods: Pts with peak aortic jet velocity (Vmax) more than 4.0 m/s were included. 61 pts with aortic valve stenosis (AS): 31 pts with bicuspid aortic valve (BAV) (57.3±1.0 yrs; m:f 1.8:1) and 30 pts with tricuspid aortic valve (TAV) were examined (59.7±0.7 yrs; m:f 1:1). Pts with infective endocarditis and rheumatic disease were excluded. 32 controls pts without heart diseases were also examined (57.6±0.8 yrs; m:f 1.1:1). Serum levels of C-reactive protein, osteoprotegerin (OPG), soluble ligand receptor activator of transcription factor kappa B (RANKL) and lipid profile were made in all the pts. We applied a strategy of targeted mutation screening for 10 out of 34 exons of the NOTCH1 gene by direct Sanger sequencing.
Results: Our analyses revealed 22 NOTCH1 heterozygous variants in AS pts. Ten are located within exons and 12 within introns. Nine variants were described previously as polymorphisms. Mutations in the NOTCH1 gene were identified in 23% of analyzed pts. Out of 14 pts, 8 had BAV and 6 had TAV. Two novel nucleotide changes, one mutation P2097P located in exon 34 and one mutation D1267N located in exon 23 were found. Also, previously described mutations in exon 23 - R1279H and 24 exon - Q1305K were identified. Four out of six patients with TAV had R1279H variant in NOTCH1. Besides, 8 novel polymorphisms were detected. Higher concentrations of OPG 7.64±0.8 pmol/L (compared to 6.06±0.3 pmol / L in patients without mutations, $p<0.05$) and higher ratios osteoprotegerin / RANKL (22.8±3.8 and 15.5±1.6, respectively, $p<0.05$) were revealed in pts with NOTCH1 mutations. Sudden death in relatives was identified in two pts out of five with a mutation in exon 24 - Q1305K.
Conclusion: NOTCH1 mutations are associated with CAVD and increased levels of serum osteoprotegerin.

P4300 | **BENCH**
Plasma YKL-40 levels are elevated and predict mortality in patients with aortic stenosis

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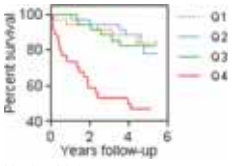
Purpose: Valve calcification and inflammation play key roles in the development of aortic stenosis (AS). A microarray study recently demonstrated that YKL-40, mainly produced by macrophages, neutrophils and vascular smooth muscle cells, was one of the most up-regulated mRNA transcripts in aortic calcified vs. non-calcified valves. We hypothesized that circulating levels of YKL-40 would be upregulated and could predict all-cause mortality in patients with severe symptomatic AS.
Methods: We measured plasma levels of YKL-40 in 136 patients with symptomatic severe AS and 46 healthy controls and its relation with transvalvular gradients, valve area, valve calcification (as estimated by ultrasound backscatter) and indices of heart failure as assessed by echocardiography and its relations to all-cause mortality (n=35) during long-term follow-up (median 4.6 years).
Results: Plasma YKL-40 levels were markedly increased in patients with AS (median [25th, 75th percentile]: 34 ng/ml [21,61] vs. 8 ng/ml [6,11], p=0.003). The strongest determinants of plasma YKL-40 in symptomatic AS were CRP (Beta=0.46, $p<0.001$), age (Beta=0.34, $p<0.001$) and ultrasound back scatter (Beta=0.28, p=0.002). Univariate analysis on quartiles of YKL-40 divided into quartiles demonstrated a non-linear association with all-cause mortality with a particularly enhanced risk in quartile 4 (HR 5.09 [95%CI: 1.88-13.73] p=0.001) compared to quartile 1. Increased YKL-40 (i.e. quartile 4) was associated with all-cause mortality also after adjustment for conventional risk factors (i.e. age, type 2 diabetes, eGFR, LVEF, valve area, atrial fibrillation, troponin T and NT-proBNP) (HR 2.48 [1.15-5.34] p=0.020).



Kaplan-Meier.

Conclusion: Circulating YKL-40 is increased in severe symptomatic AS and enhanced levels are associated with decreased long-term survival.

THE SPECTRUM OF INFECTIVE ENDOCARDITIS

P4302 | **BEDSIDE**
Risk factors for embolic events in left-sided infective endocarditis

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Embolic complications (EC) occur in about 30% to 40% of left-sided infective endocarditis (LSIE) and are associated with a poor prognosis.
Aim: To determine risk factors for embolic events in the systematic analysis of a large cohort of consecutive patients treated for infective endocarditis (IE).
Methods: 533 consecutive patients admitted in an academic hospital for definite or probable LSIE between 1990 and 2012 were included in this study.
Results: Mean age was 64.3±14.9 years, 75% of the patients were male and 26% had a prosthetic valve. The location of IE was aortic in 68% of the cases. Causative microorganisms were Streptococcaceae in 40% of the cases, Staphylococcaceae in 27% of the cases; no microorganism was identified in 11% of the cases. Rate of valve surgery and mortality during the initial hospital stay were 26% and 11%, respectively. The mean follow up was 4.8±5.8 years. Embolic events occur in 164 patients (30%), neurologic complications in 114 patients (21%) and stroke in 90 patients (17%). In multivariate analysis (Cox model), presence of vegetation was an independent risk factor for embolic event (hazard ratio HR=1.96, 95%CI 1.31-2.91, $p<0.001$), neurologic complication (HR=1.88, 95%CI 1.21-2.94, p=0.005) and stroke (HR=1.70, 95%CI 1.04-2.77, p=0.04). Older age and Streptococcus infection were independently associated with a lower risk of embolic events (HR=0.99, 95%CI 0.98-1.00, p=0.02 and HR=0.64, 95%CI 0.44-0.93, p=0.02 respectively) and neurologic complications (HR=0.99, 95%CI 0.97-1.00, p=0.04 and HR=0.51, 95%CI 0.32-0.80, p=0.004 respectively). Streptococcus infection was independently associated with a lower risk of stroke (HR=0.57, 95%CI 0.34-0.93, p=0.03). There were no other predictors of embolic events.
Conclusions: Patients with streptococcal infection have a lower risk of embolic events than patients infected by other microorganisms. The presence of vegetations was independently associated with an increased risk of embolic events.

P4303 | **BEDSIDE**
Staphylococcus aureus and thrombocytopenia, a high risk partnership

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Purpose: In a previous work, we found thrombocytopenia as a risk marker of bad prognosis in infective endocarditis (IE). Several works have pointed out the potential role of S.aureus in the genesis of thrombocytopenia. Our aim was to get an insight into the interaction between thrombocytopenia and S.aureus infection.
Methods: From 855 episodes of left sided IE prospectively recruited between 1996 and 2013, we studied 251 episodes who had thrombocytopenia (platelet count below 150000/μl) in blood analysis at admission. They were classified in two groups: Group I (n=68) caused by S.aureus; and Group II (n=183) caused by another microorganism. Finally, we performed two multivariable analyses for prediction of mortality over the whole population of left sided IE.
Results: The age and gender distribution were similar in both groups (p=0.348, p=0.175, respectively). There were no differences in comorbidities between the groups. The presence of a previous valvulopathy was more common in Group II (66.7% vs 47.7%, p=0.007). Intravascular catheter as the portal of entry was more frequent in Group I (29.8% vs 15%, p=0.029). Clinical presentation with cutaneous (23.9% vs 5.5%, $p<0.001$) and febrile symptoms (92.4% vs 74.7%) predominated in Group I. Acute onset (<15days) prevailed in Group I (82.4% vs 47%, $p<0.001$). At admission, heart failure occurred more frequently in patients from Group II (20.6% vs 45.6%, $p<0.001$) while fever (0.047), arthritis (p=0.002), hemorraghic stroke (p=0.002) and hemorrhagic skin lesions (p=0.044) were more common in Group I. The echocardiogram found vegetations more frequently in Group I (p=0.009), although the presence of periannular complications and severe valvular insufficiency were similar in both groups. During hospitalization, patients from Group I developed more frequently heart failure (p=0.032) and septic shock ($p<0.001$). The need of surgery was similar in both groups (58.8% vs. 50.8%, p=0.259). Two separate multivariable analyses to predict mortality were done in S.aureus and non-S.aureus episodes. In non-S.aureus infection, thrombocytopenia at admission had 1.76 times increased risk of mortality (95% CI: 1.11-2.81), and in S.aureus episodes, thrombocytopenia increased the odds of in-hospital mortality 2.21-fold (95% CI: 1.13-5.79), p=0.04.
Conclusions: A synergistic interaction among thrombocytopenia and S.aureus infection has been observed. Thrombocytopenia independently increased the risk of mortality in non-S.aureus episodes. When the effect of thrombocytopenia was assessed in S.aureus infections the mortality risk strikingly increased.

P4304 | BEDSIDE
Infective endocarditis in intravenous drug users: the prognosis relevance of the valves involved

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Introduction and objective: : Intravenous drug use (IDU) is a well known predisposing condition for infective endocarditis (IE), although their incidence has decreased during the last decade. Even though IDUs has been classically related to right-sided IE (RSIE), left-sided IE (LSIE) has been reported with similar frequency. Nonetheless the profile of LSIED in IDUs is unknown. The aim of this work is to describe and compare the clinical profile and outcome between RSIE and LSIE in IDUs group.
Methods: Among 1.234 episodes of IE consecutively diagnosed in three tertiary centres from March 1995 to January 2014, 66 were in IDUs (5%). Of them, 40 were RSIE (61%) and 26 LSIE (39%). An analysis of 85 epidemiological, clinical, microbiological, echocardiographic and outcome variables has been performed.
Results: Mean age (±SD) was 35±8 years, 86% males and 98% not nosocomial. Comorbidities were common (64%), being HIV-positive (61%) and chronic anaemia (22%) the most frequently associated. HIV-positive serology was significantly higher in RSIE group (72% vs. 42%). The most frequent symptoms at admission were fever (90%), pulmonary embolism (36%) and heart failure (30%). Pulmonary embolisms only appeared in RSIE group (59%). Staphylococcus aureus (53%) and Streptococcus viridians (12%) were the main causative microorganisms, being Staphylococcus aureus significantly more frequent in RSIE group (67% vs. 31%) and Streptococcus viridians in LSIE (2% vs. 27%). Polymicrobial and fungi aetiology were responsible for 8% and 4% respectively. Tricuspid valve was affected in 87% and pulmonary valve in 10% of RSIE group, while aortic valve was affected in 61% and mitral valve in 50% of LSIE group. Multivalvular episodes, perianular complications and need for cardiac surgery were significantly more frequent in LSIE group (3% vs. 10%; 5% vs. 27% and 7% vs. 50% respectively). In-hospital mortality was significantly higher in LSIE group (15% vs. 38%). There were no other significant differences between both groups.
Conclusion: Almost 40% of IE episodes in IDUs are left-sided. Patients with this condition have a poorer prognosis with in-hospital mortality two-fold higher than patients with RSIE and similar to that in non-IDUs with LSIE.

P4305 | BEDSIDE
Short antibiotic regimen is as effective as classic antibiotic therapy for pacemaker related infective endocarditis

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Purpose: Pacemaker-related infective indocarditis (PIE) is a relatively common condition with particularly good prognosis. Recently, shorter antibiotic treatment has been proposed. Our purpose was to analyze in-hospital evolution and prognosis of PIE patients treated with different antibiotic regimens.
Methods: We analyzed 99 consecutive episodes of PIE prospectively recruited in three referral hospitals between 1996 and 2013. They were classified in two groups according to the antibiotic regimen: Group I (n=68) episodes of PIE classically treated during 4 weeks or more; and group II (n=31) who were treated during 1 to 3 weeks.
Results: Patients from Group II were older (mean 62.4 years vs. 70.8 years, p=0.009). Gender distribution was similar between the two groups. There were no differences regarding to clinical presentation, symptoms at admittance and antibiotic treatment within the 15 days previous to admission (47.5% vs. 65.4%, p=0.127). No differences were observed in previous cardiac disease between the two groups. Malignant neoplasia was more prevalent in patients from Group I (16.2% vs. 0%, p=0.016). Vegetations' detection (81.7% vs. 74.1%, p=0.419) and size (p=0.574) by echocardiography were similar in both groups. Involvement of tricuspid valve by the infection was similar in both groups (17.6% vs. 16.1%, p=0.853). S. aureus (27.9% vs. 32.3%, p=0.662) and coagulase-negative staphylococci (39.7% vs. 35.5%, p=0.689) were the most common isolated microorganisms in both groups, without significant differences between them. There were also no differences in the rest of isolated microorganisms between the groups. In-hospital evolution was similar in both groups. Patients from Group II had a shorter in-hospital stay (median 27.5 days IR (22.0-36.0) vs. 45 days (IR 33.3-59.8), p=0.010).There were no differences in the development of septic shock, heart and renal insufficiency, and emboli. The pacemaker system was removed in most of patients (80.9% vs. 80.6%, p=0.978) and the mortality rate was low in both groups (4.4% vs. 12.9%, p=0.201).
Conclusions: In most patients with PIE, a short antibiotic regimen (1-3 weeks) is not inferior to classical antibiotic therapy. This new therapeutic regimen permits a shorter hospitalization.

P4306 | BEDSIDE
Valve surgery in active infective endocarditis: a simple score to predict in-hospital prognosis

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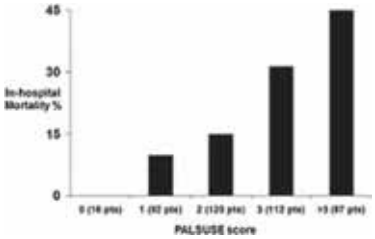
Aims: Surgery for infective endocarditis (IE) is associated with high mortality. Our objectives were to describe the experience with surgical treatment for IE, and to identify predictors of in-hospital mortality.
Methods: Prospective cohort of 1000 consecutive patients with IE. Data were collected in 26 hospitals.
Results: Surgery was performed in 437 patients (43.7%). Patients treated with surgery were younger and predominantly male. They presented fewer comorbid conditions and more often had negative blood cultures and heart failure. In-hospital mortality after surgery was lower than in the medical therapy group (24.3 vs 30.7%, p=0.02). In patients treated with surgery, endocarditis involved a native valve in 267 patients (61.1%), a prosthetic valve in 122 (27.9%), and a pacemaker lead with no clear further valve involvement in 48 (11.0%). The most common aetiologies were Staphylococcus (186, 42.6%), Streptococcus (97, 22.2%), and Enterococcus (49, 11.2%). The main indications for surgery were heart failure and severe valve regurgitation. A risk score for in-hospital mortality was developed using 7 prognostic variables with a similar predictive value (OR between 1.7 and 2.3): PALSUSE: Prosthetic valve, Age≥70, Large intracardiac destruction, Staphylococcus spp, Urgent surgery, Sex [female], EuroSCORE≥10. In-hospital mortality ranged from 0% in patients with a PALSUSE score of 0 to 45.4% in patients with PALSUSE score >3.



Hospital mortality according to PALSUSE.

Conclusions: The prognosis of IE surgery is highly variable. The PALSUSE score could help to identify patients with higher in-hospital mortality.

P4307 | BEDSIDE
Effect of valve surgery on infective endocarditis mortality: a systematic review and meta-analysis

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Background: Infective endocarditis (IE) is associated with significant mortality. Valve surgery is recommended in several groups of patients. Although previous adjusted data from observational cohorts supported its use, they were flawed by survivor bias. We systematically reviewed the literature and performed a meta-analysis of studies that examined the role of valve surgery on mortality of IE and adjusted for survivor bias.
Method: Several databases were searched from inception through December 2013 for studies that adjusted for selection bias and survivor bias. Two reviewers extracted the required data. The inverse variance method meta-analysis was used to pool studies odds or hazard ratios using a random effect model meta-analysis. Publication bias and heterogeneity were assessed by contour funnel plot and the I2 test, respectively.
Results: There were six cohort studies and one randomized controlled trial that enrolled a total of 6668 patients. The proportion of patients who underwent surgery ranged from 23.8% to 61.7%. Valve surgery combined with antimicrobial therapy, as compared to antimicrobial therapy alone, was associated with a significant reduction in the short term mortality of IE (pooled odds ratio of 0.76, [95% confidence interval (CI) 0.59-0.97], I2 = 71% (Figure). There was visual asymmetry of funnel plot indicating the possible presence of publication bias.


Meta-analysis

Conclusion: To our knowledge, this is the first meta-analysis of the impact of valve surgery on the outcome of IE from studies that accounted for survivor bias. Our findings suggest a possible survival benefit of valve surgery in IE. Nevertheless, the evidence is limited by the observational nature of most included studies, between-studies heterogeneity, and publication bias.

P4308 | BEDSIDE
Polymicrobial infective endocarditis: clinical features and prognosis

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Background: The incidence and characteristics of polymicrobial endocarditis remains unknown, as there is no study focused on this topic. Whether the presence of more than one microorganism worsens the prognosis of infective endocarditis has not been elucidated so far. Our goal is to describe the profile of left-sided polymicrobial endocarditis and to compare it with that of patients with unimicrobial endocarditis.
Methods: Among 942 episodes of left-sided infective endocarditis consecutively diagnosed in three tertiary centres from March 1995 to January 2014, 73 were polymicrobial (7,8%), 748 unimicrobial (79,4%) and 118 had negative blood cultures (12,5%). We described the main clinical, microbiological, echocardiographic and evolutive profile of patients with polymicrobial and compared it with unimicrobial endocarditis.
Results: Mean age of polymicrobial endocarditis patients was 62±15 years, 60% were males and 62% community acquired. Diabetes mellitus (32%), chronic anaemia (30%) and chronic renal failure (17%) were the most frequently comorbidities and fever (65%), heart failure (42%) and renal failure (25%) the most frequent symptoms at admission. Prosthetic mitral valve (34%) was the most frequent location, followed by mitral (30%) and aortic (24%) native valves. Coagulase-negative Staphylococci (65%), Enterococci (39%), Gram-negative bacilli (35%) and Staphylococcus aureus (23%) were the most frequent implicated microorganisms. The most repeated combination were coagulase-negative Staphylococci with Enterococci (n=14), and coagulase-negative Staphylococci with Gram-negative bacilli (n=13).
Polymicrobial endocarditis was more frequently nosocomial (38% vs 26%; p=0.029) and prosthetic (54% vs 37%, p=0.007) than unimicrobial endocarditis. In addition, antecedents of indwelling catheters (23% vs 13%, p=0.032) and previous cardiac surgery (16% vs 7%, p=0.016) were more frequently too. On the contrary, echocardiographic detection of vegetations (77% vs 87%, p=0.024) and periannular complications (28% vs 16%, p=0.024) was more frequent in unimicrobial endocarditis. No differences on age (62±16 vs 63±14), sex (males 59% vs 63%), symptoms, need of surgery (66% vs 60%), and in-hospital mortality (31% vs 30%), were detected between both groups.
Conclusion: Polymicrobial endocarditis represents almost 8% of episodes of left-sided endocarditis in our series. Coagulase-negative Staphylococci are the leading cause of polymicrobial endocarditis. Although there are important demographic and echocardiographic differences between polymicrobial and unimicrobial endocarditis, short-term outcome is similar.

P4309 | BEDSIDE
The portal of entry determines the prognosis of patients with infective endocarditis. The special case of catheter related infective endocarditis

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Purpose: To describe the importance of the portal of entry in the prognosis of patients with infective endocarditis (IE) and to put emphasis in a special risk group: intravascular catheter (iv cath) related IE.
Methods: We analyzed 898 consecutive episodes of left-sided IE prospectively recruited in 3 referral hospitals between 1996 and 2013. For the first analysis we selected the cases related with the most frequent portals of entry and classified them in 4 groups: Group I (n=451): unknown; Group II (n=55): dental procedures; Group III (n=27): genitourinary procedures; Group IV (n=113): iv cath. For the second analysis we classified them in two groups: Group A (n=113): iv cath related IE; Group B (n=503): the rest of episodes.
Results: Age, gender distribution, and previous cardiopathy were similar between groups. Nosocomial origin predominates in groups III and IV ($p<0.001$). Chronic renal failure (CRF) and cancer were significantly more frequent in Group III and IV ($p<0.001$). Enterococcus was more frequently isolated in Group III (40.7%, $p<0.001$) and S. aureus and coagulase-negative staphylococci (CNS) predominated in Group IV (28.6% and 35.7%, respectively, $p<0.001$). Patients from Group II showed better in-hospital evolution, with less frequency of septic shock (p=0.05), need for surgery (p=0.015) and mortality ($p<0.001$). There were no differences in prognosis between the others groups. In the second analysis we did not observe any differences in previous cardiopathy (p=0.312) between the two groups. Patients from Group A had higher prevalence of comorbidities: diabetes ($p<0.001$), immunosuppression (p=0.002), chronic anemia ($p<0.001$), CRF ($p<0.001$), and cancer ($p<0.001$). Acute onset of IE was more frequent in group A (68.8% vs 42.4%, $p<0.001$) and they presented acute renal failure (p=0.025) and septic shock (p=0.003) more frequently at admission. Staphylococci (S.aureus and CNS, $p<0.001$ respectively) and fungi (0.020) were more frequently isolated in Group A, while Streptococci ($p<0.001$) were more common in Group B ($p<0.001$). During hospitalization, valve insufficiency (60.0% vs 71.2%, p=0.02) and periannular complications (p=0.037) were more common in Group B. The need for surgery was similar in both groups (p=0.093) but mortality was higher in Group A (40.7% vs. 30.1%, p=0.032).
Conclusions: Portal of entry largely determines the prognosis of IE. Patients with catheter related IE constitute a highly vulnerable group with a clear-cut worse prognosis. Therefore, placement of intravenous catheters should be made under strict aseptic conditions and should be removed early.

NEW INSIGHTS IN INFECTIVE ENDOCARDITIS

P4311 | BEDSIDE
Performance of systematic search for present and potential portals of entry of infective endocarditis

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Infective endocarditis (IE) is a severe disease, with an in-hospital mortality around 20%. Ten percent of the patients will have another episode of IE. Thus, looking for and treating the portal of entry of IE is particularly important. Yet, literature on this topic is nonexistent.
Since January 2005, we have been prospectively enrolling patients hospitalized for certain IE (Duke-Li criteria) in the International Collaboration on Endocarditis database. Since then, we have been systematically looking for and treating the portal of entry of the present IE episode and potential portals of entry of a new IE episode.
Among 444 patients hospitalized in our institution between 2005 and 2011, 318 were included in the present study (exclusion of patients who died during hospitalization; some medical charts unavailable for technical reasons).
Portal of entry of the present IE episode was identified in 238 patients (74%). Distribution of identified portals of entry was: cutaneous: 44% (healthcare-associated: 21%; community-acquired: 13%; IV drug use: 9%); oral / dental: 29%; gastrointestinal: 22%; genitourinary: 3%; ENT: 2%; respiratory: 1%.
Potential portals of entry were: continuation of IV drug use in 21 patients and a cutaneous disease in 2 patients; oral/dental infective foci in 66/125 patients with stomatologic examination; colonic lesions (polyps, diverticulosis, adenocarcinoma) in 32/80 patients in whom colonoscopy was performed because they were ≥50 years old or they had a familial history of colonic polyposis; genitourinary lesions (prostatic cancer or hyperplasia, urethral stenosis...) in 32 / 52 patients with genitourinary examination; ENT lesions (sinusitis, otomastoidosis...) in 6/180 examinations.
In conclusion, systematic search for the portal of entry of infective endocarditis was successful in as many as ¾ of patients. Systematically searching for a potential oral / dental, gastrointestinal or genitourinary portal of entry of a new IE episode was also successful in a lot of patients.

P4312 | BEDSIDE
Infective endocarditis in patients with ventricular septal defect

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In the context of recent change in guidelines for prophylaxis of infective endocarditis (IE), the objective of this study was to assess the features and outcomes of IE in children and adults with non-significant ventricular septal defect (VSD).
Methods: A retrospective analysis of records of patients with non-significant VSD. Clinical, echocardiographic and microbiological data, and outcomes were assessed.
Results: From 1980 to 2013, 57 IE occurred (1 to 4 per year), in patients aged 14.2±11.3y (med12.1), 29males (51%) and 39 were <18y of age. VSD was membranous in all cases, isolated (39=68.5%) or associated with mild aortic regurgitation or pulmonary stenosis. VSD was native in 39 (68.5%) and not diagnosed before IE occurred in 4cases (7%). The cause of infection was unknown in 36% of the cases, while 23% were from dental, 13% from cutaneous, 9% from ENT or digestive origin, and 19% occurred in the early postoperative course of patch closure, i.e. 81% of the cases occurred in native mild VSD. Streptococcus from dental origin was the most frequent causal agent (54.5%), staphylococcus was found in 35% of cases, Gram-negative bacillus in 3.5%. Hemocultures were negative in 7% of the cases. Vegetation was the most frequent echographic lesion, and located either on VSD, and/or tricuspid valve and/or RV free wall and/or pulmonary valve. Aortic valve location occurred in 8cases. Embolic event occurred in 28cases (49%): multiple pulmonary embolia in 21 (37%), systemic embolia in 6. Eighteen patients were operated (31.6%): early surgery in 11 (19.3%), delayed patch closure in 7. Six patients died (10.5%). Death was not related to early surgery. FU was 13.4±11.2y (med 10.2y).
Conclusion: Infective endocarditis can severely impair prognosis of mild membranous VSD and dental events are the most frequent origin of infection. Despite recent recommendations, preventive surveillance and management of any dental lesions are probably to be emphasized in these patients.

P4313 | BEDSIDE

Infective endocarditis in congenital heart diseases: description of main features in a cohort from 1997 to 2013

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Introduction: Due to the improved life expectancy of patients with congenital heart disease, is increasingly seen more frequently acquired various diseases such as infective endocarditis (IE). We describe the main features of IE in this group and their differences with the overall population.
Methods: We collected all cases of IE diagnosed according to the Duke criteria between 1996 and 2013 in three tertiary hospitals. 1173 episodes of IE, 56 associated congenital heart diseases (5%) were found and constitute our interest group. Epidemiological, microbiological, echocardiography, clinical, treatment and outcome variables were collected. We compared a total of 15 variables between patients with IE and congenital heart disease with other patients.
Results: The most common congenital heart defects were bicuspid aortic valve (n=38, 68%) and atrial septal defect (n=5, 9%). The location of IE was more common in the aortic valve (n=28, 50%) and in the aortic and mitral valves (n=8, 14%). These patients are younger than the overall population (44 vs 62, p=0.0002). IE was more common in men in both cases, with a greater difference in congenital heart disease (76% vs 65%, p=0.0211). Surgical treatment was most commonly used (77% vs 57% p<0.0001) in 18 cases of urgent (42%) and the most frequent causes were heart failure (n=9, 50%) and periannular complication (n=7, 39%). Their mortality was lower (7% vs 28%, p<0.0001). The most common pathogens were Streptococcus viridans (n=13, 23%) and coagulase-negative staphylococci (n=13, 23%).

Patients with IE + CHD vs EI

	Congenital	Total	p
Age (years)	44	62	0.0002
Men	76%	65%	0.0211
S. viridans	23%	10.8%	<0.001
S. aureus	9%	18%	0.0191
Aortic	50%	30%	<0.001
Surgical treatment	77%	57%	<0.001
Hospital mortality	7%	28%	<0.0001

Conclusions: Patients with congenital heart disease represent a small subgroup of patients with IE are young patients, often requiring surgery, and the prognosis is better than in other cases of IE.

P4314 | BEDSIDE

Could the risk of developing systemic embolism be predicted up front in patients with infective endocarditis?

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Purpose: Quantification of embolism risk (ER) in infective endocarditis (IE) is of critical importance since early surgery had demonstrated to reduce it. We aimed to assess the validity of a new clinical risk model developed from a multicentre study to predict the ER in patients with IE.
Methods: Retrospectively, between 2009 and 2013, we studied 137 consecutive patients with the final diagnosis of IE. We computed the risk score from the variables: age ≥75 years, diabetes mellitus, vegetation ≥10 mm, embolism prior to initiation of antibiotic, atrial fibrillation and staphylococcus aureus, assigning one point to each. The primary endpoint was the first systematic embolism during the 6 month of follow-up after initiation of antibiotic therapy. At least one imaging test was requested for the documentation of each embolic episode. All patients underwent transthoracic and transophageal echocardiographic studies within 24 hours of admission. The performance of the risk score was evaluated using a binary logistic regression model with the risk score as a continuous variable as the independent variable and the occurrence of systematic embolism before antibiotic initiation as the dependent variable. Discrimination and calibration were expressed by the c-index and the p-value of Hosmer-Lemeshow goodness-of-fit test.
Results: 39.4% of patients were ≥75 years. 9.5% were diabetic and 23.4% were in atrial fibrillation at hospital presentation. The rate of systemic embolism prior to antibiotic initiation was of 9.5%. 48.9% had vegetation size ≥10 mm. Staphylococcus aureus was the cause of endocarditis in the 22.6%. 12.4% of patients presented embolism after initiation of antibiotic therapy. The majority of embolic events occurred in brain (65%). The risk score ranged from 0 to 5 points. 54% of patients had a score ≥2. The predictive model discriminated well those patients who suffered systemic embolism as was shown by the c-statistic: 0.70 (95%CI 0.59-0.78, p=0.01). The observed rate of embolic events approximated closely to that predicted by the risk score (p-value of Hosmer-Lemeshow test=0.3). The in-hospital mortality rate in the group patients who suffered systemic embolic was 22%, as compared to 8.3% in the patients subgroup not suffered systemic embolism (p=0.02).
Conclusions: The ER in patients with IE can be predicted using a simple clinical tool which may help clinicians in the decision-making process. In this study, the majority of embolism occurred in the brain, and the mortality in patients with embolism complications was about 3-times higher than in patients without embolic events.

P4315 | BEDSIDE

Should positron emission tomography/computed tomography results be considered a mayor criterion of infective endocarditis?

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Purpose: The diagnosis of infective endocarditis (IE) and cardiac devices (pacemaker and implantable cardioverter defibrillator) remains challenging. The aim of this study was to assess the usefulness of positron emission tomography/computed tomography (PET/CT) with 18F-FDG in these type of patients.
Methods: A prospective study with PET/CT on 23 patients suspected of having IE or cardiac device infection was performed. PET/CT was considered positive when 18F-FDG uptake was present and persisted in the non-corrected images. Anatomy was the gold standard in patients who underwent cardiac surgery and in those who died and necropsy was performed. In those cases without the anatomical counterpart, Duke criteria were applied.
Results: We studied a total of 41 possible foci of infection: 10 native valves, 17 mechanical valves, 4 biological prosthetic valves and 10 cardiac devices. PET/CT was positive in 22 foci, negative in 17 and non-conclusive in 2. Its accuracy was 71% (29/41). The technique was able to confirm infection in 17 foci and to rule it out in 12. Ten foci were misclassified (5 false positive and 5 false negative). Twenty-five sites of infection occurred in the patients with definite IE, in which PET/CT accuracy was 80% (20/25). In the 12 sites of seven patients with possible IE, PET/CT had an accuracy of 50% according to echocardiography. It is interesting that in the device group patients, the test was right in all but 2 (1 false negative and 1 non-conclusive)
Conclusion: This preliminary data suggest that PET-CT can be useful in some patients with IE, but it does not seem to have enough accuracy to be considered a major criterion.

P4316 | BEDSIDE

Incidence and predictors of infective endocarditis in asymptomatic patients with mild-to-moderate aortic stenosis

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Purpose: The incidence and predictors of infective endocarditis (IE) in asymptomatic patients with mild-to-moderate aortic stenosis (AS) and without substantial comorbidity are not well known.
Methods: Data from the prospective "Simvastatin and Ezetimibe in Aortic Stenosis study" including 1,873 patients were used. The endpoints were IE and a composite of IE or death due to any cause.
Results: IE occurred in 22 (1.2%) patients during a mean follow-up of 4.4 years, including 17 patients with a native aortic valve stenosis and five patients after aortic valve replacement. The IE incidence rate was 2.7/1,000 person-years of follow-up without a gender difference (p=0.47). Patients with IE were more often active smokers (45.5 vs. 18.9%, p=0.004), had a larger aortic valve area (1.5 vs. 1.28 cm^2, p=0.03), higher left ventricular mass index (LVMI) (119.4 vs. 101.6 g/m^2, p=0.02) and higher white blood cells (6.7 vs. 6.0 x109/L, p=0.037) at baseline. However, age (64.1 vs. 67.6 years), gender (68.2 vs. 61.3% men), and the prevalence of bicuspid aortic valves (5.6 vs. 5.7%) were not predictive (all p>0.05). Predictors of IE included active smoking (HR 3.7, 95%CI 1.6-8.5, p=0.003) and higher LVMI (HR 1.02, 95%CI 1.005-1.03, p=0.004). The composite endpoint of IE or death occurred in 223 (11.9%) patients with an incidence rate of 27.2/1,000 person-years of follow-up. Predictors included older age (HR 1.07, 95%CI 1.05-1.09, p<0.001), active smoking (HR 2.01, 95%CI 1.42-2.85, p<0.001), atrial fibrillation (HR 1.63, 95%CI 1.11-2.41, p=0.014), higher high-sensitivity c-reactive protein (HR 1.5, 95%CI 1.11-2.04, p=0.009), higher mean aortic gradient (HR 1.02, 95%CI 1.003-1.04, p=0.023) and higher LVMI (HR 1.009, 95%CI 1.005-1.01, p<0.001). The IE incidence was too small to detect any differences in all-cause mortality (HR 1.59, 95%CI 0.59-4.27, p=0.361), however, two (9.1%) patients died as a direct consequence of IE.
Conclusions: Asymptomatic patients with mild-to-moderate AS and no substantial comorbidity had a total IE incidence rate of 2.7/1,000 person-years of follow-up. Active smoking and higher LVMI were predictors of IE in these patients.

P4317 | BEDSIDE
D-dimer level predicts in-hospital mortality in patients with infective endocarditis: a prospective single-centre study

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Background: Increased circulating D-dimer levels have been correlated with adverse outcomes in various clinical conditions. To our knowledge, the association of on-admission D-dimer and in-hospital mortality in infective endocarditis (IE) has not been investigated. We hypothesized that increased on-admission D-dimer levels would correlate with adverse outcomes when prospectively studied in patients with IE.
Methods: In this prospective study, a total of 157 consecutive patients with the definite IE diagnosis met the inclusion criteria and underwent testing for on-admission D-dimer and CRP assays. The outcome measure was in-hospital death from any cause.
Results: In-hospital mortality occurred in 40 (26%) patients. Increased levels of plasma D-dimer (5.1±1.7 vs 1.9±0.8, p<0.001), CRP [45 (13-98) vs 12 (5-28), p<0.001] were found in dead patients compared with those survived. In addition to S. aureus infection, increased leukocyte count, end-stage renal disease, LVEF<50%, vegetation size of >10mm, perivalvular abscess, on-admission D-dimer (HR: 1.32; 95% CI: 1.24-1.40; p<0.001) and CRP (HR: 1.18; 95% CI: 1.09-1.36; p=0.001) levels were significantly associated with in-hospital mortality. Furthermore, the sensitivity and specificity of D-dimer ≥4.2 mg/L in predicting in-hospital death in IE were 86% and 85%, respectively. Moreover, the sensitivity and specificity of CRP levels ≥13.6 mg/L were 72% and 69%, respectively.

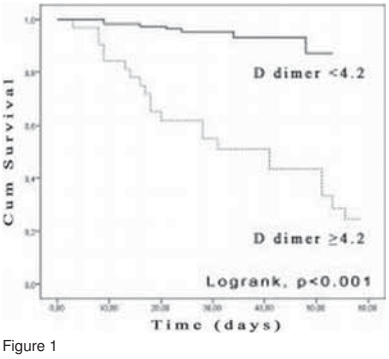

Figure 1

Conclusion: Our findings suggest that on-admission D-dimer level may be a simple, available and valuable biomarker that allows us to identify high-risk IE patients for in-hospital mortality. D-dimer ≥4.2 mg/L, CRP ≥13.6 mg/L were independently associated with IE related in-hospital death.

P4318 | BEDSIDE
Early surgery effect on 1-year survival in left-side infective endocarditis

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Background: Infective endocarditis (IE) is a severe disease. The in-hospital mortality varies from 10 to 20%. The optimal timing for surgical intervention to prevent mortality and complications remains controversial; only one randomized trial exits and several observational studies published do not allow definitive conclusions.
Purpose: To evaluate the potential effect on survival of early surgery (ES) in left side IE controlling for short-term survival and treatment selection biases.
Methods: Patients were enrolled in the Italian Registry of Infective Endocarditis (RIEI) between August 2006 to December 2010. The present analysis includes patients with left side IE only. According to the treatment, patients were classified in two groups: ES, if patients have undergone surgery within 2 weeks from the diagnosis of IE, and medical therapy or late surgery. We evaluated the effect of treatment on survival, after adjusting for biases using a Cox proportional hazards model that included inverse probability of treatment weighting, and ES as a time-dependent covariate.
Results: All 517 patients with left-side IE (389 in native valve + 128 in prosthetic valve) out of 677 cases registered in RIEI were included in the analysis. Overall, 184 patients (35.6%) have undergone ES and 138, among 333 initially treated with medical therapy, have undergone surgery after 2 weeks from diagnosis. During the first year of follow up we observed 87 deaths with a 1-year survival of 82,59% (95% CI 79.0-85.7). Risk of death seems lower, even if not statistically significantly, in patients that have undergone ES (Table 1).
Conclusions: Results from RIEI suggest that ES may be beneficial in left side IE, especially in native valve IE. Even with use of statistical techniques to control biases, we cannot definitely conclude that ES is beneficial in all patients with left–side IE. These resutls confirm the need of randomized clinical trial to define the effect of ES in patients with left side IE.

P4319 | BEDSIDE
Should results from the "EASE" study be widespread to all left-sided infective endocarditis?

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Aim: To describe clinical, microbiologic, and prognosis characteristics of episodes of left-sided infective endocarditis (IE) in a series of patients that met EASE (Early surgery versus conventional treatment for infective endocarditis) study criteria, and to analyze differences with the EASE study.
Methods: We analyzed 895 consecutive episodes of IE recruited prospectively at three tertiary referral centers between 1996 and 2011, 107 of whom met EASE study criteria (left-sided non-prosthetic IE, age 15-80 years, severe valve disease with vegetation length >10 mm, and without indication for urgent surgery nor prohibitive surgical risk). Subsequently, we have compared this population (Group I, n=107) with the conventional treatment branch from the EASE study (Group II, n=39). Finally, we divided Group I in two different subgroups: streptococcal infection and non-streptococcal infection.
Results: Age and gender distribution were similar in both groups. Regarding comorbidity, no differences were found in the prevalence of diabetes and immunosuppression, whereas our patients (Group I) had higher creatinine levels at admission (1.5±1.4 vs 0.9±0.7; p=0.001).
Infection location was similar in both groups (native mitral valve: 59%). Vegetation size was larger in Group I (18±8 vs 14±4; p<0.001).
Significant differences were found regarding microbiological profile, as infection due to streptococci was much more frequent in Group II (42.9% vs 64%; p=0.020). The presence of systemic embolisms at admission was higher in Group II (26.2% vs 44%; p=0.043). Central nervous system embolisms at admission were similar in both groups, while kidney (1.9 vs 18%; p<0.001) and spleen (8.4 vs 23%; p=0.017) embolisms were more commonly found in Group II. Interestingly, the incidence of new-onset systemic embolisms during hospitalization was similar in both populations. Mortality was higher in Group I (16.8% vs 3%; p=0.023). When comparing streptococcal vs non-streptococcal infection in Group I, a trend towards higher mortality was found in the latter subgroup (9.8% vs 21.2%; p=0.124).
Conclusions: Patients from our series had more comorbidity and a more virulent microbiological profile than the EASE population. As a result, mortality was higher in our patients. Patients with streptococcal IE had a better prognosis.
We consider that EASE result could be widespread provided that Streptococci were not the causative microorganism.

P4320 | BEDSIDE
Clinical impact of new onset atrial fibrillation in infective endocarditis

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Purpose: Atrial fibrillation (AF) is a highly prevalent arrhythmia with a clear-cut impact on patient's morbidity and mortality. Our purpose was to analyze the incidence and relevance of new onset AF in patients with infective endocarditis (IE).
Methods: We analyzed 816 consecutive episodes of left-sided IE prospectively recruited in three referral hospitals between 1996 and 2013. They were classified in three groups according to the heart rhythm at the time of IE diagnosis: Group I (n=79), episodes of IE who had new onset AF; Group II (n=495) those who remained in sinus rhythm, and Group III (n=242) patients with chronic AF.

Abstract P4318 – Table 1

	Crude effect of surgery			Effect of surgery corrected by short-term survival selection bias			Effect of surgery corrected by short-term survival and treatment selection bias		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Left side IE (N=517)	0.69	[0.43, 1.10]	0.120	0.62	[0.19, 2.05]	0.436	0.90	[0.31, 2.58]	0.840
Left native valve (N=389)	0.57	[0.31, 1.03]	0.064	0.68	[0.16, 2.92]	0.602	1.01	[0.26, 4.00]	0.984
Left protesic valve (N=128)	1.06	[0.50, 2.26]	0.874	0.51	[0.07, 3.90]	0.513	0.59	[0.11, 3.09]	0.536

Initially the main differences in in-hospital evolution and clinical outcome between patients with new onset AF and sinus rhythm were analyzed. Afterwards a comparison among the three groups was performed.
Results: Patients from Group I were older (66.6 vs. 60.4 years, p=<0.001). Gender distribution was similar in both groups. No differences were observed in previous cardiac disease between the two groups. Regarding to comorbidities, chronic renal failure (17.7% vs. 9%, p=0.017) was more frequent in Group I. Coagulase-negative staphylococci and S.aureus were the most frequently isolated microorganisms in both groups without differences between them. Heart failure (53.2% vs. 35.3%, p=0.003) at admission was more frequent in Group I, although moderate to severe valvular insufficiency was similar between the groups (p=0.475). There were no differences in vegetation size and periannular complications between the two groups.
During hospitalization, persistent signs of infection, septic shock (p=0.235), acute renal insufficiency (26.6% vs. 17.4% vs. 20.7%, p=0.131) and systemic embolisms (12.7% vs. 11.8% vs. 10.7%, p=0.820) were similar between the three groups. The need of surgery was similar between the three groups (51.9% vs. 59.4% vs. 58.1%, p=0.454), while mortality was higher in patients from Group I (44.7% vs. 22.8% vs. 33.8%, p=0.01). Those patients with new onset AF who developed heart failure showed an even higher mortality (p=0.042), suggesting a synergistic relation between them. In the multivariate analysis, new onset AF was an independent risk factor for heart failure (OR 2.92, CI (95%) 1.53-5.59, p<0.001) and mortality (OR 1.67, CI (95%) 1.01-3.09, p=0.04).
Conclusions: Patients with IE who present with de novo AF at the time of IE diagnosis are older than those who do not. The occurrence of new onset AF was an independent risk factor for heart failure and mortality and thus, of worse prognosis.

PULMONARY HYPERTENSION FROM BENCH TO BEDSIDE

P4322 | BEDSIDE
Persistent pulmonary hypertension after mitral valve replacement: analysis of the importance of pre-implantation pulmonary pressures

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Purpose: Persistent pulmonary hypertension (P-PH) after mitral valve replacement (MVR) leads to an increased risk of morbidity and mortality. We sought to determine the influence of systolic pulmonary artery pressure (sPAP) before surgery on the appearance of P-PH.
Methods: Patients undergoing MVR between January 2005 and December 2007 were analyzed. We excluded those with an available follow up shorter than 3 months. PH was diagnosed if sPAP estimated by doppler-echocardiography was >40 mmHg.
Results: A total of 111 patients with an average age of 61.3 years were studied. 67.6% were women and the most frequent etiologies were rheumatic and degenerative valvular disease (46.8% each). Intermedium sized-prostheses were implanted in most cases. No differences were found before the implant between age, gender, etiology of mitral disease and rates of atrial fibrillation among patients who underwent surgery with or without PH; however patients affected by PH before the implant had smaller body surface area. The type (mechanical of biological) and size of prostheses used in the implant were not different, but patients affected by PH before the surgery had higher rates of significant tricuspid regurgitation (TR) and underwent tricuspid annuloplasty more frequently.
After MVR, P-PH was present in 42,3% of patients after 12.6 months of mean follow up. P-PH was more frequently observed in elderly and female patients, in those with severe degrees of PH before surgery, and significant tricuspid regurgitation (≥3). On multivariable analysis, more severe degrees of PH before surgery (OR: 1.761; p=0.03) and significant TR (OR: 1.739; p=0.01) were independent predictors of P-PH after MVR. Surgical factors related to P-PH were prosthesis size and tricuspid annuloplasty. Both, tricuspid annuloplasty (OR: 0.345; p=0.025) and the implant of a smaller prosthesis (OR: 0.656; p=0.004) were independent predictors of P-PH after MVR.
Conclusion: MVR was associated with high prevalence of P-PH after mid term follow up. Both PH and significant TR before surgery were independent predictors of P-PH. Our data points out that MVR should be planned before the development of PH and greater TR. Smaller prosthetic size is also a risk factor for P-PH and bigger prostheses are desirable when possible.

P4323 | BEDSIDE
Effective regurgitant orifice area is an independent predictor of pulmonary hypertension in patients with aortic valve stenosis

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Purpose: Pulmonary hypertension (PHT) is frequently associated with aortic stenosis (AS) and can lead to a poor prognosis and more severe symptoms. The pathophysiological role of mitral regurgitation (MR) as a determinant of PTH is well established in other clinical models, as in heart failure with reduced ejection fraction (EF). However, some uncertainty persists in aortic stenosis patients. In this study a quantitative assessment of aortic valve area (AVA) and MR is prospectively performed to reveal their relation with PHT.
Methods: Consecutive patients with aortic flow velocity >2.5 m/s form the study population. End-diastolic (EDV) and end-systolic left ventricular volumes and left atrial (LA) volume are measured. Longitudinal shortening velocity, early and late lengthening velocities are assessed. Effective regurgitant orifice area (ERO) and regurgitant volume (RV) are obtained with PISA method. Systolic pulmonary artery pressure (S-PAP) is calculated adding the right atrial pressure to the tricuspid regurgitation pressure gradient.
Results: 113 consecutive patients are included; mean age is 79±8 years, EF 55±15%, NYHA 2.2±0.9, indexed AVA 0.56±0.18 cm^2/m^2, ERO 0.09±0.08 cm^2. 84 (74%) patients present MR, and among these 48 (42%) show ERO<0.10 cm^2. S-PAP result to be significantly different in the group of patients with ERO≥0.10 cm^2 compared to the groups with ERO 0-0.10 cm^2 and with ERO=0 cm^2 (mean S-PAP values in the 3 groups are 50±12 mmHg, 42±9 mmHg and 37±7 mmHg respectively; p<0.0001). At univariate analysis S-PAP correlates with VTD (R=0.37; p<0.0001), EF (R= -0.23; p=0.01), E (R=0.43; p<0.0001), E/E' (R=0.37; p<0.0001), LA volume (R=0.39; p<0.0001) and in particular with ERO (R=0.47; p<0.0001). There is no association between S-PAP and indexed AVA or mean gradient. In a multivariate regression model ERO (p=0.005) and VTD (p=0.03) remain associated with S-PAP, while E/E' and EF lose significance. When LA volume is added to the model, ERO remains the only variable significantly associated with S-PAP (p=0.02).
Conclusions: ERO results an independent predictor of PHT in patients with even mild MR and a wide range of aortic stenosis severity. This relation is not influenced by other variables commonly associated with LA pressure overload, such as E/E' or LA volume. This might reveal additional pathophysiological links of PHT in this context.

P4324 | BENCH
Characterization of intrinsic diastolic properties of the right ventricle. Importance of geometry-driven elastic restoring forces on rapid filling

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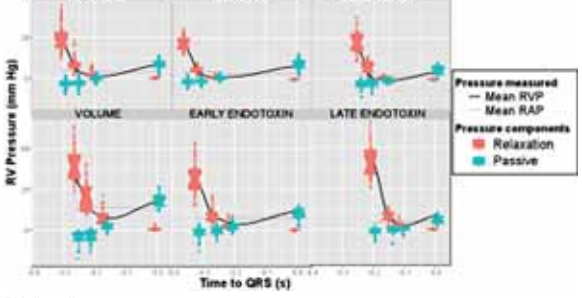
Fully characterization of right ventricular (RV) diastolic function is still a challenge. In early diastole, RV generates negative pressure but the mechanisms underlying RV suction remain unclear. Classical methods of pressure-volume (PV) data analysis fail to decouple relaxation from elastic recoil in early filling. We aimed to assess the contribution of elastic recoil to RV filling and determine its relationship with RV geometry.
Methods: 13 pigs were instrumented with a conductance-pressure catheter in RV. 3D echo images and PV data during transient cava occlusion were obtained after inotropic modulation, volume overload and endotoxin induced RV failure. Indices of RV diastolic function were obtained decoupling relaxation from passive diastolic pressure using previously validated algorithm. 3D RV inner surface meshes were analyzed computing septum curvature indices.
Results: Passive restoring forces generated suction in all phases contributing to rapid filling (Figure). Inotropic modulation didn't alter passive diastolic properties. Beta-blockade partially blunted passive suction (Pp -0.8±1.4 vs. -2.2±1.7 mmHg, P<.05) modifying operative volumes. Despite severe RV overload, maintenance of suction late after endotoxin infusion was possible by shifting the passive PV relationship to the right, so that equilibrium volume (V0) increased from 31±9 ml to 46±16 ml (P<.001). Changes in V0 correlated with the degree of septal curvature. In turn the latter was related to the transmural pressure gradient (P<.001).



RV diastolic pressure components.

Conclusions: Diastolic suction is generated by elastic restoring forces and is a major determinant of RV filling even during acute overload. Septal bulging towards

the LV preserves RV diastolic suction. For the first time, these aspects of diastolic function can be analyzed in vivo.

P4325 | BENCH

Long-term oral B3-agonist treatment reduces pulmonary vascular resistance and improves right ventricular function in a swine model of chronic postcapillary pulmonary hypertension

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Purpose: There are few therapies available for pulmonary hypertension (PH), particularly no specific therapy has demonstrated a consistent effect in postcapillary PH. Our purpose was to assess the effect of long-term oral treatment with a B3-adrenoceptor (B3-AR) agonist on pulmonary vascular resistance (PVR) and right ventricular (RV) function in chronic postcapillary PH.
Methods: Eight pigs with chronic postcapillary PH generated by surgical banding of the inferior pulmonary vein were randomized to oral treatment with a B3-agonist (Mirabegron 50 mg/12h for 14 days) or placebo. Right heart catheterization (RHC) and cardiac magnetic resonance (CRM) were performed at baseline and at the end of the treatment period. Pulmonary vascular resistance (PVR) was measured in Wood units by RHC. Changes in RHC and CMR parameters were compared between groups using Student T or Wilcoxon test.
Results: Baseline characteristics were well balanced between groups (table). After 14 days of treatment, subjects randomized to B3-agonist showed a significant reduction in PVR and an improvement in RV-arterial coupling and RV ejection fraction. No significant changes were observed in heart rate and systemic blood pressure.

Baseline characteristics and changes in the treatment group and placebo group

	Baseline characteristics			Change		
	Control (N=4)	B3-agonist (N=4)	P	Control (N=4)	B3-agonist (N=4)	P
Weight	41.9±8.4	37.9±12.3	0.61	7.4±2.4	11.6±1.9	0.033
HR (bpm)	79.5±13.8	83.5±8.4	0.64	–4.0±23.2	13.8±8.5	0.229
Mean systemic BP (mmHg)	100.0±8.5	93.8±5.9	0.27	1.2±16.0	0.5±8.7	0.937
Mean PAP (mmHg)	37.5±3.3	35.8±3.1	0.47	8.0±16.5	1.2±1.5	0.447
Indexed PVR (WU/m^2)	5.8±0.9	6.2±1.2	0.58	2.2±2.2	–1.2±0.6	0.027
Cardiac index (L/min/m^2)	5.4±1.1	4.5±0.2	0.24	–0.8±1.2	1.1±0.4	0.030
RV end-systolic volume (ml/m^2)	41.6±8.5	40.6±17.8	0.93	8.1±8.7	–3.5±2.5	0.042
RV ejection fraction (%)	58.5±6.5	53.6±4.1	0.25	–3.8±6.8	5.7±1.7	0.036
RV-arterial coupling (Ea/Emax)	0.69±0.17	0.59±0.16	0.42	0.08±0.16	–0.16±0.07	0.029

Conclusion: Long-term oral therapy with a B3-AR agonist significantly reduced PVR and improved RV performance in a translational experimental large-animal model of chronic PH. The absence of significant changes in heart rate and systemic blood pressure confers a good safety profile.

P4326 | BENCH

Airway delivery of AAV1.SERCA2a ameliorates vascular resistance and right ventricular performance in a preclinical model of postcapillary pulmonary hypertension

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Background: Recent evidence indicates that defective calcium homeostasis in vascular smooth muscle cells is a key contributing factor to excessive cell proliferation and disease progression in pulmonary hypertension (PH). Decreased sarcoplasmic reticulum ATPase pump (SERCA2a) lung expression has been described in human pulmonary arterial hypertension and experimental monocrotaline-induced PH in rodents, where its normalization through adeno-associated virus serotype 1 (AAV1) mediated gene transfer had regressive effects in vascular remodeling and improvement in pulmonary hemodynamics. In postcapillary PH, the role of SERCA2a downregulation and its potential as a therapeutic target remains unknown.
Aims: 1) To analyze the relationship between distal vascular remodeling and lung SERCA2a protein expression chenges in a large animal model of postcapillary PH, and 2) assess the beneficial effects of AAV1-SERCA2a gene transfer using a novel airway aerosolized delivery technique.
Methods: A post-capillary model of PH was created in swine by surgical restrictive banding of 2 pulmonary veins. After 8 weeks, animals were randomized to airway delivery of 10^{13} viral genomes using an intratracheal aerosolizer (n=5) or saline (n=5), and reevaluated 8 weeks later. A sham-operated group (n=4) served as control. Invasive pulmonary hemodynamics and right ventricular function (RVEF) and remodeling by MRI were assessed before randomization and at the final follow up 8 weeks later.
Results: Compared to the sham group, postcapillary PH animals showed significant arterial wall remodeling as assessed by increased medial thickness in small distal pulmonary arteries (<300 μm) along with increased indexed vascular resistance (PVR), and SERCA2a protein levels were decreased by 48% (p=0.036). SERCA 2a gene tranfer halted the progressive increase in PVR (mean[SD] change 6.3[6.1] vs -0.1[2.6] wood units/m^2 in saline vs SERCA-treated, respectively, p=0.047) assessed by invasive right heart catheterization. Furthermore MRI revealed preservation of RVEF after SERCA 2a gene transfer (mean[SD] change -13 [8] vs +0.1[9] % units, in saline vs SERCA-treated, respectively, p=0.048).
Conclusions: In a clinically relevant large animal model of postcapillary PH, SERCA2a protein downregulation was associated with distal arterial wall thickening and high PVR. AAV-mediated SERCA2a overexpression using a novel aerosolized delivery resulted in beneficial hemodynamic effects and improved cardiac function.

P4327 | BENCH

The novel endothelin receptor antagonist, Macitentan, improves right ventricular energetics and function in the Sugen5416/hypoxia rat model of severe pulmonary artery hypertension

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Purpose: Pulmonary artery hypertension (PAH) is characterized by vascular changes causing increased pulmonary resistance and eventual right heart failure (RHF). Altered myocardial substrate utilization may be associated with RHF, however these changes have not yet been well characterized. The aim of this study was to evaluate in vivo the right ventricular (RV) function, and RV glucose and fatty acid metabolism in an animal model of PAH using non-invasive positron emission tomography (PET). The effect of the novel endothelin receptor antagonist (ERA) treatment, Macitentan, was also investigated on the development of PAH and RV energetics.
Methods: Male Sprague-Dawley rats (n=11) weighing 150-200 g received a single injection (20mg/kg) of Sugen5416, a vascular endothelial growth factor receptor2 inhibitor, followed by three weeks of chronic hypoxia (10% O2). The rats were then randomized to treatment or no treatment with Macitentan (25 mg/kg daily) beginning five weeks post Sugen injection. Five and eight weeks post Sugen injection, substrate utilization was serially assessed with 2-[18F]fluoro-2-deoxyglucose (FDG) and 4-[18F]fluoro-6-thia-heptadecanoate (FTHA) PET scans for glucose and fatty acid metabolism respectively, and reported as a standardized uptake value (SUV). This data was correlated with in vivo functional measurements with echocardiography and multi gated acquisition scans.
Results: The Sugen-hypoxia (SuHx) model resulted in a progressive increase in RV FDG uptake over 8 weeks (SUV baseline: 1.80, PAH week 5: 3.81, PAH week 8: 3.69, $p<0.05$ between baseline and PAH week 8). RV FTHA uptake significantly increased from baseline to week 5 with the SuHx model (SUV baseline: 1.50, PAH week 5: 2.97, $p<0.05$). Macitentan significantly decreased RV/LV FDG uptake (SUV PAH week 8 untreated: 1.09 vs. PAH week 8 treated: 0.66, $p<0.05$). This was associated with improved RV ejection fraction (PAH week 8 untreated: 53.15% vs PAH week 8 treated: 73.22%, $p<0.01$) and with an improvement in pulmonary artery pressures measured by pulmonary artery acceleration time (PAH week 8 untreated: 17.32 ms vs. PAH week 8 treated: 24.38 ms, $p<0.001$)
Conclusion: PAH is associated with metabolic changes in the RV, characterized by increased fatty acid and glucose utilization with a proportionally greater increase in glucose uptake, likely representing increased glycolysis. Macitentan attenuated RV/LV FDG uptake and significantly improved RV function and hemodynamics. Clinical studies evaluating the link between metabolic and functional alterations in the RV and the effects of therapy are warranted.

P4328 | BENCH

Intratracheal administration of prostacyclin analog-incorporated nanoparticles ameliorates the development of monocrotaline-induced pulmonary artery hypertension in rats

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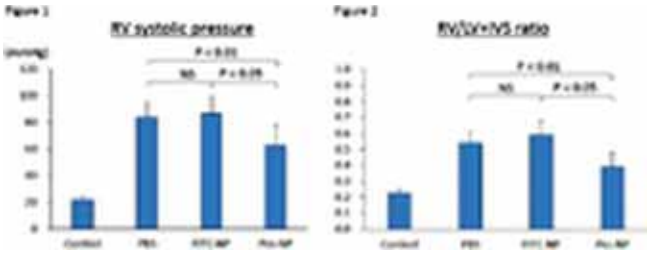
Background: Nanoparticles (NPs) have been used as a novel delivery system for transport of drug to target organs. NPs are taken up by target organ because of their small size. Drug release from NPs is controlled according to the NP composition. Thus, drug-incorporated NPs for local delivery might optimize the efficacy and minimize the side effects of drugs. Intravenous prostacyclin improves long-term survival in patients with pulmonary arterial hypertension (PAH). However, intravenous prostacyclin causes flashing, headache and catheter-related infections. We investigated the effects of intratracheal administration of prostacyclin analog-incorporated NP (Pro-NP) in a rat model of PAH.
Methods: Rats were received a single intratracheal administration of PBS, FITC-NP or Pro-NP 14 days after monocrotaline injection. Hemodynamics, right ventricular (RV) hypertrophy and pulmonary artery muscularization were assessed 28 days after monocrotaline injection. We examined survival rates after single administration of PBS or Pro-NP.
Results: After single administration, Pro-NP significantly decreased RV pressure (Pro-NP: 63±15 mmHg, FITC-NP: 87±13 mmHg, PBS: 84±11 mmHg) (Figure

1), RV hypertrophy (RV/LV+S ratio; Pro-NP: 0.39±0.11, FITC-NP: 0.59±0.09, PBS: 0.54±0.07) (Figure 2) and pulmonary artery muscularization (percentage of fully-muscularized small pulmonary artery; Pro-NP: 37±6%, FITC-NP: 70±3%, PBS: 63±7%). Pro-NP significantly improved survival rate (Pro-NP: 65.0% and PBS: 27.8%, P<0.05).



Figures 1 & 2

Conclusion: Intratracheal administration of Pro-NP ameliorates the development of the monocrotaline-induced PAH in rats. Inhaled Pro-NP might develop as a novel approach for treatment of PAH.

P4329 | BEDSIDE
A new era of therapeutic strategies for chronic thromboembolic pulmonary hypertension by two different interventional therapies

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Background: Pulmonary endarterectomy (PEA) is established for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH). Recently, percutaneous transluminal pulmonary angioplasty (PTPA) has been added for peripheral-type CTEPH, whose lesions exist in segmental, subsegmental, and more distal pulmonary arteries. We examined the latest survival and clinical outcomes of patients with CTEPH.
Methods and results: One hundred and thirty-six consecutive patients with CTEPH were enrolled. Twenty-nine were treated only with drug (Drug-group), and the other 107 underwent interventional therapies (Interventions-group) (39 underwent PEA [PEA-group] and 68 underwent PTPA [PTPA-group]). Total 213 PTPA sessions (failures, 0%; mortality rate, 0.5%) was performed in the PTPA-group (complications: reperfusion pulmonary edema, 7.0%; hemosputum or hemoptysis, 5.6%; vessel dissection, 2.3%; wiring perforation, 0.9%). Although baseline hemodynamic parameters were significantly more severe in the Interventions-group, the outcome after the diagnosis was much better in the Interventions-group than in the Drug-group (98% vs. 64% 5-year survival, p<0.0001), suggesting effectiveness of the interventional therapies. Hemodynamic improvement in the PEA-group was a 46% decrease in mean pulmonary arterial pressure (PAP) and a 49% decrease in total pulmonary resistance (TPR) (follow-up period; 74.7±32.3 months), while those in the PTPA-group were a 40% decrease in mean PAP and a 49% decrease in TPR (follow-up period; 17.4±9.3 months). The 2-year survival rate in the Drug-group was 82.0%, and the 2-year survival rate, 2-year occurrence of right heart failure, and 2-year re-vascularization rate in the PEA-group were 97.4%, 2.6%, and 2.8%, and those in the PTPA-group were 98.5%, 2.9%, and 2.9%, respectively.
Conclusion: The interventional therapies were more beneficial than medical therapy for survival of patients with CTEPH. The availability of both of these operative and catheter-based interventional therapies leads us to expect the dawn of a new era of therapeutic strategies for CTEPH.

P4330 | BENCH
Differential effects of prostacyclin analogues on right ventricular function in the isolated rat heart

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Purpose: Prostacyclin analogues are widely used in the treatment of pulmonary hypertension, but their direct effects on right ventricular (RV) function have only been sparsely investigated. The aim of this study was to compare the direct effects of different prostacyclin analogues on RV function.
Methods: Rat hearts (n=30) were isolated and perfused with Krebs Henseleit buffer in a pressure controlled Langendorff setup. The hearts were randomized to perfusion with increasing concentrations of the prostacyclin analogues epoprostenol, iloprost, treprostinil or the selexipag metabolite, MRE-269. The dose dependent effects on RV hemodynamics were monitored using a fluid filled balloon in the RV connected to a pressure transducer. Coronary flow was monitored using an inline flow probe to confirm a vasodilatory effect of the drugs. The presence of relevant prostanoid receptor subtypes in the RV was investigated by quantitative PCR (qPCR).
Results: QPCR confirmed the presence of the prostanoid receptors IP, EP1, EP2, EP3, EP4, DP, TP and FP in the RV myocardium and all four drugs increased coronary flow rate in a dose-dependent manner.
Treprostinil perfusion caused an increase in RV developed pressure (RVDP) (15%±8 p=0.016 and 18%±7 p=0.017) when administered in clinically relevant concentrations (0.5ng/mL and 1.5ng/mL). Supra-clinical concentrations blunted this response.
Iloprost did not improve RVDP in clinically relevant concentrations. Only in supra-clinical concentrations (600pg/mL and 2000pg/mL) did iloprost improve RVDP (19%±4 p=0.015 and 24%±7 p=0.045, respectively).
Epoprostenol and MRE-269 both showed a trend towards increasing RVDP when administered in supra-clinical concentrations.
Conclusion: The prostacyclin analogues treprostinil, iloprost and epoprostenol and the selexipag metabolite, MRE-269 all increased coronary flow rate in the isolated perfused rat heart. Only treprostinil and iloprost significantly improved RV function and solely treprostinil was effective when administered in clinically relevant doses. Supra-clinical doses had to be infused for iloprost to increase RV function.

P4331 | BENCH
Tenascin-C deficiency and the development of pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease entailing a deteriorating pulmonary vasculopathy with obstruction of small pulmonary arteries, smooth muscle cell hypertrophy and intimal fibrosis. It has been proposed that Tenascin-C (TnC), a key mediator of smooth muscle cell growth and survival is critically involved in the pathogenesis of PH. Aim of our study was to investigate the effect of TnC inhibition by direct gene manipulation on the development of PH.
Methods: We utilized mice with a homozygous TnC knock-out (TnC KO) and A/J wild types (WT). Both TnC KO and WT littermates were held in an environmental chamber with FiO2 of 10% or under normoxia for 4 weeks. We investigated the effect of TnC deletion and chronic normobaric hypoxia on parameters of pulmonary vascular resistance such as right ventricular systolic pressure (RSVP) and right ventricular hypertrophy (Fulton Index/ right to left ventricular- ratio). To assess the degree of smooth muscle cell hyperplasia, alpha-smooth muscle actin antibody staining was performed.
Results: TnC KO mice showed significantly increased right ventricular pressures after 4 weeks under normoxic conditions, compared with wild type controls. Both TnC KO and WT mice showed increased right ventricular pressures under nor-

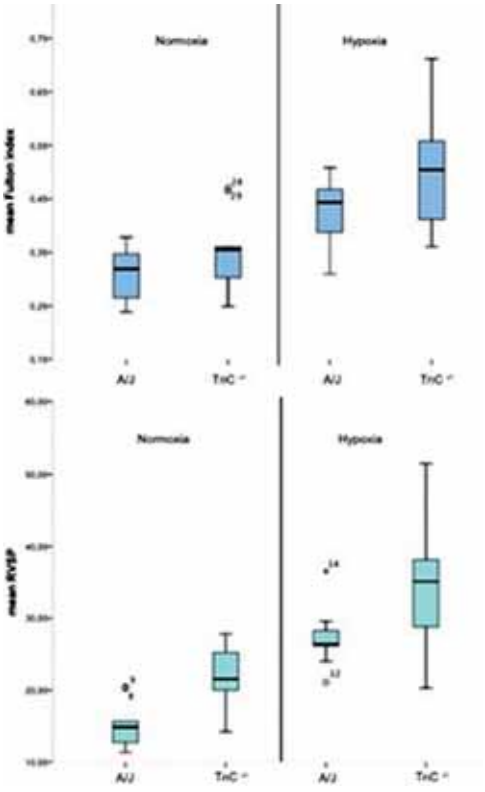

Figure 1

mobaric hypoxia. TnC KO mice revealed significantly higher right ventricular pressures (Fig. 1) and Fulton indices than controls.
Conclusion: TnC a extracellular matrix glycoprotein prominent during tissue remodelling and wound healing may play a pivotal role in the early pathogenesis of pulmonary hypertension.

RISK STRATIFICATION FOR IMPLANTABLE CARDIOVERTER DEFIBRILLATOR PATIENTS

P4333 | BEDSIDE
Very low rate of appropriate shock therapy in primary prevention patients who receive an implantable cardioverter defibrillator in a real world setting

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Background: During the past two decade implantable cardioverter defibrillator (ICDs) became the mainstay of sudden cardiac death (SCD) prevention, resulting in a pronounced increase in the device implantation for primary prevention of SCD. However, currently there are limited data on contemporary rates of appropriate life-saving shock therapy in real life primary prevention population.
Methods: The Israeli ICD Registry comprises all implants and other ICD operative procedures, nationwide, that are entered on line into a computerized secure database. The present study comprises 1605 consecutive cases were who were enrolled in the Israeli ICD Registry and prospectively followed up for information regarding survival, hospitalizations and ICD therapies since 2010.
Results: A total of 55 (5%) patients with ICD for primary prevention received an appropriate therapy during follow-up, 9 (0.8%) of which were appropriate ICD shock. The 2-year cumulative probability of arrhythmic events among patients implanted for primary and secondary prevention is presented in Table 1, demonstrating a very low rate of appropriate ICD shocks (1%) among patients implanted for primary prevention During follow-up, a total 48 (4%) died, mostly due to non-cardiac causes.

Major endpoints

Endpoint	Primary prevention (n=1185)	Secondary prevention (n=420)	P-value
Any appropriate therapy for VT/VF	4%	13%	<0.001
Appropriate shocks	1%	2%	0.036
Appropriate ATPs	4%	10%	<0.001
Any inappropriate therapy	4%	4%	0.91
Inappropriate shocks	2%	1%	0.85
Inappropriate ATPs	2%	3%	0.99
Death	4%	8%	<0.001
Cardiac death	2%	5%	0.82

Conclusion: Rates of appropriate shock are lower than previously reported. Most of the patients implanted for primary for primary prevention die due to non cardiac reasons, suggesting a need for contemporary risk stratification approaches prior to device implantation in this population.

P4334 | BEDSIDE
Differences in monomorphic VT occurring in ICD patients according to the indication (primary vs. secondary prevention): an analysis based on the stored electrograms

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Among ICD patients, more than 80% of appropriate therapies are due to monomorphic VT (MVT). In ICD primary prevention (PP) patients a programming of ICD therapies for tachyarrhythmias of ≥200 bpm or with a prolonged delay is associated with reductions in inappropriate therapy and all-cause mortality. It is unknown whether MVTs have different characteristics and/or responses to antitachycardia pacing (ATP) with respect to the indication: PP versus secondary prevention (SP).
Methods: We analyzed prospectively 551 MVTs (cycle length [LC]: 329±35; PP: 37%) occurring spontaneously in 67 ICD patients (LVEF: 35±8). ICD programming was standardized. We analyzed the following aspects: CL, percentage of variability of the 12 RR intervals prior to ATP (V-RR) – which was calculated by dividing the mean difference between each R-R interval with the next one by the CL ×100, and type of termination (type 1 [T1, immediate]: VT ceased immediately upon ATP completion; type2 [T2, delayed]: VT persisted for one or more beats after ATP).
Results: ATP was successful in 86% of VT (92% in PP vs. 84% in SP; p=0.007). VT terminated at ATP had a higher degree of V-RR (2.6±1.7 vs. 1.3±1.2; p<0.001), the third tertile of V-RR being associated with a better ATP effectiveness (98 vs. 82%; p<0.001). As shown in the table, MVTs occurring in SP patients present a lower V-RR (this could be a marker of MVT stability), they finish immediately after ATP less frequently, and they are slower but respond worse to ATP.

Table 1

Variable	PP versus SP	p
Fast MVT	49 vs. 37%	0.01
V-RR, %	2.6±1.4 vs. 2.3±1.8	0.04
Third tertile of V-RR	43 vs. 29%	0.003
T2	27 vs. 12%	<0.001

Conclusions: MVTs have different characteristics depending on the indication. In SP, MVTs seem to be slower, more stable and less frequently unsustained; therefore, they could not be benefited from a MADIT-RIT programming.

P4335 | BEDSIDE
Mortality risk score for implantable defibrillator patients with myocardial infarction

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Objective: The implantable cardioverter-defibrillator (ICD) is very effective in the prevention of sudden cardiac death, but its benefit is impaired by competing risks. This prompts the search for improved patient selection to identify those patients at high risk for mortality who may not derive benefit from ICD implantation. The purpose of this study is to develop a risk model to predict mortality in primary prevention patients with myocardial infarction.
Methods: This study included all patients with myocardial infarction who received an ICD for primary prevention. Covariates associated with mortality were entered in a multivariate Cox proportional hazards model to identify independent predictors for mortality. From these predictors, a continuous score was derived and divided into tertiles (low-risk, mid-risk, and high-risk). In addition, a simple score was based on the number of predictors, i.e. risk factors. The performance of the risk scores was determined by c-statistics.
Results: The study cohort consists of 567 patients (83% male gender, mean age 63±10 years) with a median follow-up of 3.4 (IQR, 1.6 - 5.4) years. A total of 127 patients (22%) died, with a cumulative incidence of 33% at 6-years follow-up. Multivariate analysis identified age, male gender, LVEF, use of diuretic, diabetes mellitus and impaired renal function as independent predictors of mortality. There was a significant relation between tertiles of the continuous risk score and mortality. At 6-years, cumulative mortality was 13% (low-risk), 26% (mid-risk) and 61% (high-risk), respectively (P<0.0001). Performance is 0.75, 95% CI (0.70 – 0.80). Using the simple risk score, cumulative mortality was 7% (0 – 1 risk factor), 30% (2 risk factors) and 63% (>2 risk factors) at 6-years, respectively. Performance is 0.70, 95% CI (0.66 – 0.74). ICD shocks were observed in 73 patients (13%); the cumulative incidence of shocks was not different between the risk-groups (17% low-risk vs. 15% high-risk).
Conclusion: In a population of primary prevention ICD patients with myocardial infarction, the application of a simple risk score identified patients at high-risk for mortality while having low-risk for appropriate ICD shocks. The decision to implant an ICD in patients with comorbidities should be balanced against the considerable risk of mortality due to these comorbidities.

P4336 | BEDSIDE
Risk stratification for inadequate defibrillation safety margins and appropriate ICD therapy: The age paradox

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Background: A strategy of routine ICD testing has become subject of debate, but allows for identification of patients who might benefit from system modifications. Non-invasive risk stratification using age has been postulated: an inverse relation has been reported with an inadequate safety margin, whereas the risk of appropriate therapy seems to increase with higher age. However, considerable variation exists between reports. Therefore, we performed a more detailed analysis, with distinction between ischemic and nonischemic heart disease (IHD; non-IHD).
Methods: Cohort study (n=732) in an universitary medical centre (2005-2013). Defibrillation testing was performed with sequential shocks (15-25-35 joule). An unsuccessful 2nd shock represents an inadequate safety margin (<10 joule). Percentages of inadequate safety margins and appropriate therapy were related to age.
Results: An inadequate safety margin was found in 4% in the entire cohort, with

interesting differences across age tertiles (Figure). These differences were entirely driven by the subset of patients with non-IHD: in multivariable analysis age was inversely related with the presence of an inadequate safety margin [aOR 0.95 (95% CI 0.92-0.99) p=0.009]. In contrast, the 2-year cumulative incidence of appropriate therapy was significantly higher in the upper age tertiles, entirely driven by the subset with IHD (Figure).
Conclusions: The present study confirms the inverse association between age and an inadequate safety margin, as well as the positive association between age and appropriate therapy. Notably, the observed correlations distinctly differ according to the underlying cardiac etiology. In case of confirmation by larger cohorts, age could serve as an important stratifier for patients who might benefit from ICD testing.

P4337 | BEDSIDE
Development of a risk score model to characterize patients that died during the first year after ICD implantation. Data from the Israeli ICD Registry

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Objectives: The goal of this study is a development of models that identify patients at risk of death during the first year after ICD implantation
Background: ICD implantation has become a principal therapy for secondary and primary prevention of sudden cardiac death. Although ICD implantation is an effective therapy in specific groups of patients. In some patients ICD Implantation is less effective or not effective at all.
Methods: Patient population derived from the Israeli ICD Registry - a prospective national registry of all patients who are referred for implantation or replacement of an ICD or CRT-D in Israel. Two groups of patients were compared: those who died during one year after ICD implantation and those who were still alive one year after ICD implantation. A primary end-point was a development of models for one year mortality after ICD implantation.
Results: A total of 1314 patients have completed at least one year follow up after first-time ICD or CRTD implantation at 22 centers. During one year after ICD implantation there were 63 (4.8%) fatal events. Age more than 75 years (hazard ratio [HR]:2.7; 95% confidence interval [CI]: 1.6 to 4.4), history of atrial fibrillation (HR: 1.9; 95% CI: 1.12 to 3.17), chronic lung disease (HR: 2.0; 95% CI: 1.1 to 3.76), anemia (defined as Hb level less than 13 Gr/Dl in men and less than 12 Gr /Dl in women) (HR: 2.3; 95% CI: 1.3 to 3.93) and decreased eGFR level (<30 min/ml/1.73m^2) (HR: 3.4; 95% CI: 1.74 to 6.6) were found to be independent risk factors for one-year mortality after ICD implantation. We propose a simple score for prediction of one year mortality after ICD implantation ("triple A, double C") including: Age more than 75 years (3 points), Anemia (2 points), history of Atrial fibrillation (1 point), significant Chronic renal failure (GFR<30 min/ml/1.73m^2 (3 points) and Chronic lung disease (1 point). This model needs to be validated in other cohorts.
Conclusions: In the present study advanced age (more than 75 years), history of atrial fibrillation, chronic lung disease, anemia and decreased eGFR level (<30 min/ml/1.73m^2) were found as independent risk factors for one-year mortality after ICD implantation. The resulting risk score consists of clinical parameters may identify patients at high risk of death during one year after ICD implantation.

P4338 | BEDSIDE
Iodine-123-metaiodobenzylguanidine imaging predicts arrhythmic events in patients with ischemic cardiomyopathy evaluated for primary prevention implantable cardioverter-defibrillator

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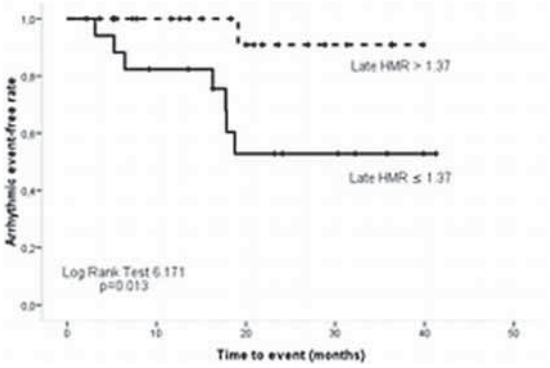
Purpose: We examine whether the assessment of cardiac sympathetic activity (CSA) by 123-Iodine Metaiodobenzylguanidine (123I-MIBG) can improve arrhythmic risk stratification in patients with ischemic heart failure (IHF) candidates for primary prevention implantable cardioverter-defibrillator (ICD).
Methods: 44 IHF patients referred for ICD therapy were enrolled. During evaluation of ICD implantation, patients underwent 123I-MIBG. Early and late 123I-MIBG imaging was performed to assess cardiac innervation (heart-to-mediastinum ratio –HMR- and cardiac washout rate). During follow up, appropriate ICD therapy and sudden cardiac death (composite endpoint) were documented. A multivariate Cox proportional hazards model was used to analyze the influence of 123I-MIBG in predicting the endpoint.
Results: 24 patients had ICD implantation. Patients with and without ICD implantation were comparable. During a mean follow-up of 18 [6,35-27,65] months the endpoint was documented in 8 (18%) patients (2 sudden death, 3 ICD therapy and 3 antitachycardia pacing), No patient was lost. Patients with arrhythmic event showed poor cardiac innervation (lower HMR, 1.26 vs 1.37, p=0.035 and higher washout rate 54.5 vs 32.9, p=0.003). According to area under curve (AUC) 1.37 of late HMR was the best predictor cut-off of endpoint (AUC 0.752; IC 95% 1.19-73-09; p=0.40). Patients with late HMR ≤1.37 reached significantly more frequently the endpoint (37.5 vs 7.7%; p=0.017) than patients with a late HMR >1.37. Late ≤1.37 (HR 8.98; IC 95% 1.10-73.09; p=0.040) was the only independent predictor for the endpoint.



Kaplan-Meier survival curve

Conclusions: IHF patients referred for primary prevention ICD therapy have a serious deterioration of CSA quantified by 123I- MIBG. Nevertheless, cardiac sympathetic innervation predicts future arrhythmic events.

P4339 | BEDSIDE
Combination of fibrosis by cardiac magnetic resonance and late heart-to-mediastinum ratio by cardiac 123I-MIBG imaging identifies very low risk candidates for primary prevention implantable cardioverter defibrillator

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Purpose: Identification of noninvasive prognostic markers of arrhythmic risk in patients with advanced heart failure is a growing need. We tested whether a myocardial scarring by cardiac magnetic resonance imaging (MRI) combined with cardiac sympathetic denervation by 123-iodine metaiodogenzylguanidine (123I-MIBG) imaging would improve risk stratification in patients evaluated for implantable cardioverter defibrillator (ICD).
Methods: 73 heart failure patients referred for ICD therapy were enrolled. During evaluation of ICD implantation, patients underwent 123I-MIBG and MRI. Early and late 123I-MIBG imaging was performed to assess cardiac innervation (heart-to-mediastinum ratio –HMR- and cardiac washout rate) and MRI to assess late gadolinium enhancement (LGE). Endpoint of the study was the composite of appropriate ICD therapy, ventricular tachycardia and cardiac death. A multivariate Cox proportional hazards model was used to analyze the influence of late HMR and LGE in predicting the endpoint.
Results: During a mean follow-up of 18.6 months the endpoint was documented in 11 patients (15%). The endpoint was significantly more frequently reached in patients with LGE ≥8.5 and late H/M ratio ≤1.32 (p=0,042). Cox regression analysis showed late HMR ≤1.32 (sensitivity 83%; specificity 64%), LGE ≥8.5 (sensitivity 73%; specificity 65%) and atrial fibrillation were independent predictors for

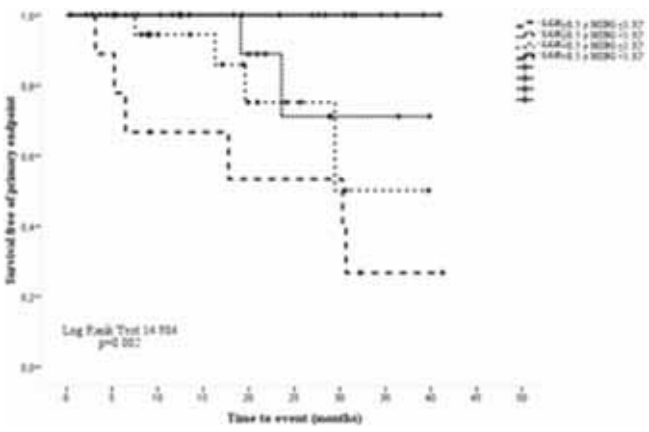
Figure 1. Kaplan-Meier event-free curve.

the endpoint (HR 5.48, HR 6.12 and HR 4.42, respectively). No patient with LGE <8.5 and late H/M ratio >1.32 suffered a cardiac event.
Conclusion: The combination of fibrosis by MRI with late HMR improves risk stratification in primary prevention ICD candidates identifying very low risk patients.

P4340 | BEDSIDE
Usefulness of cardiac magnetic resonance to predict left ventricular reverse remodeling and life threatening ventricular tachyarrhythmias in patients with idiopathic dilated cardiomyopathy

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Purpose: In idiopathic dilated cardiomyopathy (DCM), left ventricular reverse remodeling (LVRR) can lead to reduce ventricular arrhythmias (VAs). Current ESC guideline recommends implantable cardioverter-defibrillator (ICD) insertion for primary prevention with DCM patients who have a LV ejection fraction (LVEF) ≦35%, and are NYHA class II or III. However, the majority of patients with ICD implantation for primary prevention never receive appropriate delivery for life threatening VAs. The aim of this study was to evaluate the influence of late gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR) on LVRR and the association between LGE and life threatening VAs in DCM patients.
Methods: We studied 100 DCM patients with LVEF≦35% and NYHA class II or III (58±14 years, 65 males, LVEF 29±5%). All patients underwent CMR, measurement of biomarkers and echocardiography with conventional assessment. After the optimal medical therapy for 12 months, echocardiography was repeated for assessment of LVRR which defined as an absolute increase in LVEF from ≥10% to a final value of >35% accompanied by a decrease in LV end-diastolic volume ≧10%. Clinical events were defined as sudden cardiac death or sustained VAs in the follow-up period for 2100±877 days.
Results: LVRR was observed in 60 patients (60%) and strongly associated with a favorable long-term outcome ($p<0.01$). Multivariate regression analysis showed that the negative LGE was an independent predictor of LVRR. Clinical events occurred in no patient of LGE(–) group compared with 12 patients (16%) of LGE(+) group ($p<0.01$).

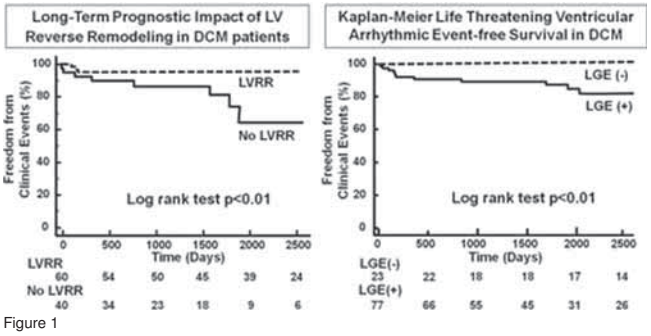

Figure 1

Conclusion: The negative LGE on CMR is strongly associated with LVRR and predicts preventing life threatening VAs. CMR may be a useful tool to select for primary ICD implantation in DCM.

P4341 | BEDSIDE
FADES, MADIT and SHFM-D risk model validation; Valid tools for risk stratification of ICD recipients in routine clinical practice?

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Introduction: Large trials have demonstrated the beneficial effect of ICD treatment. It remains a quest to predict which patients benefit from ICD implantation. For this purpose, different risk models have been developed. The aim of this study was to validate and compare the FADES, MADIT and SHFM-D models.
Methods: All patients suffering from ischemic heart disease and receiving a primary prevention ICD at our center since 1996 were evaluated. For each patient the three risk scores were calculated, missing values were imputed using a single imputation model. Individual model performance was evaluated by C-statistics. Model performances were compared by net reclassification improvement (NRI) and integrated differentiation improvement (IDI). The primary endpoint was event-free mortality.
Results: A total of 1305 patients were included (age 64±10yrs; 85%male). During a median follow-up of 4.5±3.9years, 233 (18%) patients died without the occurrence of ventricular arrhythmia and ICD intervention. All 3 risk models were predictive for event-free mortality (FADES: HR2.27; $p<0.001$; MADIT: HR1.81; $p<0.001$; SHFM-D: HR1.87; $p<0.001$). C-statistics were 0.69, 0.69 and 0.75, respectively for the FADES, MADIT and SHFM-D (figure). IDI improved 2 and 7% using SHFM-D ($p<0.001$), compared to MADIT or FADES respectively. NRI was similar in FADES and SHFM-D, however using SHFM-D resulted in 22% improvement as compared to MADIT ($p<0.001$).

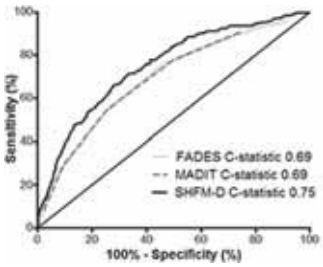

Figure 1. ROC analysis of risk models.

Conclusion: The FADES, MADIT and SHFM-D are reasonable models for prediction of event-free mortality in ischemic ICD recipients in routine clinical practice. However, the predictive and discriminatory value of SHFM-D model is clearly superior.

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Appropriate and inappropriate defibrillator shocks: predictors and impact on prognosis in a cohort of patients implanted for primary sudden cardiac death prevention

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Purpose: Despite the proven survival benefit of implantable cardioverter-defibrillators (ICDs) there is paucity of data regarding routine clinical practice. The aim of this study was to investigate the predictors of appropriate/inappropriate ICD shocks and their long-term prognostic impact in patients implanted for primary sudden cardiac death (SCD) prevention.
Methods: 776 consecutive patients (mean age 64, female 18.9%) undergoing ICD implantation between Jan 2005 and Dec 2010 were included. Baseline characteristics and semestral follow-up visits data were extrapolated from multicenter medical records. Multiple logistic regression models were used to identify significant predictors of ICD shocks. The effect of appropriate and inappropriate shocks on the primary outcome of all-cause death or cardiovascular hospitalization was examined by Cox proportional hazard models adjusting for significant confounders.
Results: Over a median follow-up of 29 months (IQR 17-47 months) 185 patients (23.8%) received an ICD shock (99, 72 and 14 receiving appropriate, inappropriate and both shocks respectively). The occurrence of atrial fibrillation during follow-up and an elevated resting heart rate were the two strongest predictors of inappropriate shocks (OR 3.13, 95% CI 1.34–7.30 and OR 1.21, 95% CI 1.02-1.40 [per 10 bpm increase], respectively) which were inversely associated with age (OR 0.81, 95% CI 0.69-0.94 [per 5 yrs increase]). At multivariable survival analysis, appropriate but not inappropriate shocks were significantly associated with the composite outcome of all-cause death or cardiovascular hospitalization (Table 1).

Table 1

Shocks subtypes	χ^2	Hazard ratio (95% CI)*	p-value
Any shocks = 185 (23.8%)	4.3	1.32 (1.02–1.72)	0.037
Only appropriate shocks = 99 (12.8%)	5.1	1.44 (1.05–1.98)	0.025
Only inappropriate shocks = 72 (9.3%)	0.76	1.20 (0.79–1.83)	0.387

note*Multivariable model adjusted for: age, gender, NYHA class, baseline heart rate, ischaemic heart disease, chronic kidney disease, baseline left ventricular ejection fraction and history of atrial fibrillation.

Conclusions: In "real-world" patients implanted with ICDs for primary SCD prevention the occurrence of shocks is a common event that negatively influences patients' prognosis and quality of life. Therapeutic strategies aiming at slowing the underlying cardiac disease progression together with optimization of devices programming should always be attempted in order to improve ICDs net clinical benefit.

P4343 | BEDSIDE
Refined patient selection for primary prevention implantable cardioverter defibrillator therapy using cardiac magnetic resonance imaging based left ventricular ejection fraction assessment

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Purpose: Primary prevention implantable cardioverter defibrillator (ICD) therapy

requires a left ventricular ejection fraction (LVEF) ≤35% according current guidelines. These guidelines are based on trials mainly using echocardiography for LVEF assessment. However, cardiac magnetic resonance imaging (CMR) is considered the gold standard for LVEF assessment with higher accuracy and reproducibility compared with conventional 2D-echocardiography. CMR based LVEF assessment may result in a refined patient selection but data on the follow-up of ICD patients selected according to CMR-LVEF assessment is lacking. The aim of this study was to evaluate benefit from ICD implantation using CMR-LVEF assessment.
Methods: 265 patients referred for primary prevention ICD implantation with CMR-LVEF≤35% were retrospectively included (71% male, mean age 66±10 years, 56% ischemic cardiomyopathy) between 2005-2012. Patients were selected who underwent CMR-LVEF assessment within 6 months prior to implantation. CMR-LVEF was measured after outlining of the endocardial contours in short axis cine images. The occurrence of appropriate device therapy (ADT) and all-cause mortality was evaluated during 3 years follow-up for the total population and in subgroups with LVEF <20%, LVEF 20-30%, and LVEF >30%.
Results: During three years follow-up, 16% of the total population received ADT and 8% died. Patients with LVEF <20% (n=74) had 10% ADT. However, mortality rate was higher compared with other subgroups (16%, p=0.01). In patients with LVEF>30% (n=52), the event-rate was low (8% ADT and 4% mortality). Patients with LVEF 20-30% (n=139) experienced significantly more ADT (22%, p=0.02) compared with other subgroups (mortality rate 4%).
Conclusions: Patients with CMR-LVEF>30% had a low ADT- and mortality rate. Patients with LVEF of 20-30% were at highest risk for ADT whereas patients with LVEF <20% were more likely to die. These results suggest that CMR based LVEF assessment allows refined patient selection with highest benefit of ICD implantation in patients with CMR-LVEF 20-30%.

OUTCOMES IN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR PATIENTS

P4345 | BEDSIDE
Tricuspid regurgitation after ICD implantation in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC)

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Introduction: Exacerbation of tricuspid regurgitation (TR) in patients (pts) with arrhythmogenic right ventricular cardiomyopathy (ARVC), who received implantable cardioverter-defibrillator (ICD), is supposed to negatively affect their prognosis. The risk of TR progression and its clinical consequences are still unclear.
Purpose: The aim of the study was to assess the progression of TR and its clinical outcome in a group of pts with ARVC after ICD implantation.
Methods: In a database of 53 pts with ARVC, who received ICD as a prevention of sudden cardiac death, we found 33 pts (mean age 46y, 27 male, 9 secondary prevention = 27%) with echocardiographic data suitable for analysis. Based on the results of echocardiography, patients were assigned to group A (worsening of TR) or group B (no worsening of TR). Clinical outcome for both groups was assessed with two-sided Barnard's test.
Results: In 64% of pts TR worsened after ICD implantation (group A: 21 pts, mean age 47,3y, 17 male, 29% secondary prevention), while in 36% of pts no progression of TR was seen (group B: 12 pts, mean age 44,8y, 10 male, 25% secondary prevention). Mean observation period was 105,5 months (group A) and 101 months (group B). Adequate interventions of ICD were detected in 15 pts (71,4%) from group A and in 6 pts (50%) from group B. In group A 3 pts (15%) died because of heart failure. In group B 1 patient (9%) died because of heart failure and 1 patient died in a traffic accident. No significant difference was found between both groups regarding adequate interventions of ICD (p=0,25) and deaths related to heart failure (p=0,68).
Conclusions: Progression of tricuspid regurgitation after ICD implantation was detected in 64% of patients with ARVC, but it was not associated with worsening of their clinical outcome. ARVC is a relatively rare disease, so further studies are needed in order to collect more data.

P4346 | BEDSIDE
The need for pacing in patients who qualify for an ICD: clinical implications

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Background: Implantation of subcutaneous implantable cardioverter defibrillator (ICD) is spreading and has been shown to be safe and efficient to terminate life-threatening ventricular tachyarrhythmias, however it does not provide brady-pacing.
Currently, data on the need for brady-pacing and cardiac resynchronization (CRT) in patients with ICD indication are limited.
Methods: The MADIT-II study enrolled post-MI patients with reduced ejection fraction (EF≤30%), randomized to either an implantable cardioverter defibrillator (ICD), or conventional medical therapy. Survival analyses and multivariate Cox-models were performed to assess the incidence and predictors of pacemaker (PM)/ CRT implantation in the conventional arm of MADIT-II, after excluding 32 patients (6.5%) with a previously implanted PM.
Results: During the median follow-up of 20 months, 24 of 458 patients (5.2%) were implanted with a PM or a CRT (Figure). Five of these patients (21%) received a CRT device. Symptomatic sinus bradycardia was the primary indication for PM implantation (n=9, 37%), followed by AV-block (n=5, 21%), tachy-brady syndrome (n=4, 17%), and carotid sinus hypersensitivity (n=1, 4%). CABG before enrollment (HR=6.88, 95% CI: 1.58-29.84, p=0.01), and baseline PR interval >200 ms (HR=3.07, 95% CI: 1.24-7.57, p=0.02) significantly predicted subsequent PM/CRT implantation. Patients with PM/CRT implantation had a significantly higher risk for subsequent heart failure (HR=2.67, 95% CI=1.38-5.14, p=0.003), but there was no increased risk of all-cause mortality (HR=1.06, 95% CI=0.46-2.46, p=0.89).

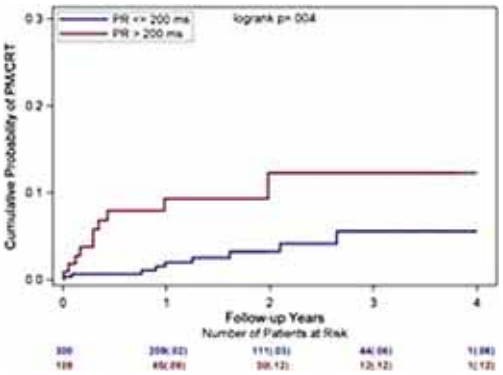

Figure 1

Conclusion: The need for ventricular pacing or CRT implantation in patients with MADIT-II ICD criteria was low, especially in those with a normal baseline PR-interval, and such patients should do well with a subcutaneous ICD.

P4347 | BEDSIDE
Monitoring of intracardiac ventricular electrogram amplitude using by implantable cardioverter defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy

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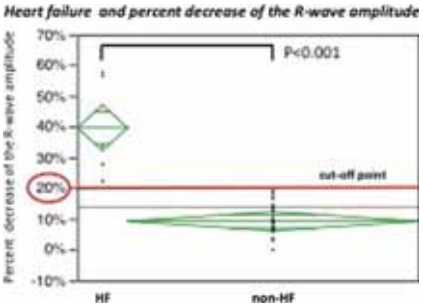
Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by progressive fibroadiposal replacement, leading to ventricular tachyarrhythmia and heart failure. The implantable cardioverter defibrillator (ICD) is frequently indicated for these patients and R-wave amplitude can be monitored by ICD.
Methods: Among our cohort of 350 ICD patients, we identified consecutive 37 ARVC patients (mean 48 years old, 73% men). We analyzed their intracardiac electrograms at device implantation and every 3-4 months, and evaluated the relationship with cardiac events.
Results: At device implantation, the mean R-wave amplitude was 8.3mV and low R-waves (<5.0mV) were observed in 11 patients (30%). During a mean follow-up of 79±53 months, appropriate ICD therapies were occurred in 15 (41%) patients including 87% of ventricular tachycardia (VT) and 13% of ventricular fibrillation (VF). Mean R-wave amplitude was higher in VF patients than in VT patients (16.2 vs. 8.2mV, p=0.03). However, there were no significant relationships between R-wave amplitude and occurrence of ventricular arrhythmias.
Heart failure (HF) hospitalizations were occurred in 6 (16%) patients and all of those R-wave amplitudes at admission were less than 5.0mV. The percent decrease of the R-wave amplitude was significantly higher in HF patients compared with non-HF patients (39.7 vs. 9.2%, p<0.001). Moreover, a cut-off value of 20% could clearly distinguished HF patients from others (Figure).



Conclusion: Decreasing R-wave amplitude and low amplitude itself were strong

predicting factors for HF in patients with ARVC. Continuous monitoring of R-wave amplitude using by ICD may be useful.

P4348 | BEDSIDE
Outcomes of the entirely subcutaneous implantable cardioverter defibrillator in patients with inherited cardiac diseases

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Purpose: A new entirely subcutaneous ICD (S-ICD) has been introduced, that does not require lead placement in or on the heart, which therefore has theoretical advantages particularly in young patients with inherited cardiac diseases. We report the largest experience to date in these patients with the S-ICD to evaluate efficacy and safety.
Methods: Patients with inherited cardiac diseases were selected if they had a class I or IIa indication for primary or secondary prevention of sudden cardiac death. Patients from our center with a S-ICD implanted between December 2008 and May 2013 were included in this study.
Results: A total of 44 patients with inherited cardiac diseases (59% male, mean age 37±12 years, 80% primary prevention) received the S-ICD. After 25 months of follow-up, 2 patients experienced 18 successful appropriate shocks: one patient with Brugada syndrome received 17 appropriate shocks, and 1 patient with hypertrophic cardiomyopathy received 1 appropriate shock. No sudden deaths occurred. Six patients (14%) received a total of 9 inappropriate shocks. Eight inappropriate shock episodes (8/9, 89%) were due to T-wave oversensing, which were mostly (6/8, 75%) solved by optimalization of the programming during exercise. In one patient with inappropriate shocks on TWOS during aberrant conduction, the device had to be explanted because reprogramming was not successful in avoiding further inappropriate shocks. Four patients (9%) experienced complications: 3 infections of which 1 was explanted, and 1 defibrillation testing problem in which the device had to be repositioned.
Conclusion: The S-ICD is an important new option for young patients with inherited cardiac diseases and is effective in terminating ventricular arrhythmias. There is, however, a considerable percentage of ICD related adverse events, especially inappropriate shocks due to sensing issues during exercise in this young population, which can be solved in most patients by optimized programming during exercise.

P4349 | BEDSIDE
Is patient retention during ICD follow-up influenced by age and/or method of follow-up? In-person vs Home Monitoring compared in the TRUST trial

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Introduction: A goal of patient follow up post-ICD implant is patient retention and engagement with clinic services. However, poor clinic accessibility may promote attrition, especially for the elderly. Remote Home Monitoring (HM) may resolve this challenge. We tested this in the TRUST trial.
Methods: ICD patients were randomized 2:1 to HM or to conventional monitoring (CM). Follow-up checks were scheduled at 3, 6, 9, 12 and 15 months post-implant in both groups. CM patients were evaluated with IPE only. HM patients were assessed remotely. HM and CM were compared for patient attrition during the trial (withdrawal and lost to follow up). The influence of age was assessed by comparing proportions of exited subjects ≥80 or <40 years.
Results: HM (n=908) and CM (n=431) patients had similar demographics (age 63 years (IQR 55-73), 72% male, LVEF 29%, primary prevention 73%, DDD 57%) and mean follow-up durations 407±103 (range 21-617) and 399±111 (range 32-582) days respectively (P=0.17). However, patient attrition during the trial was 42% greater in CM (87/431 vs HM 129/908, p=0.007).
Ages (median, IQR, range) were: HM 64, 55-73, 23-95 vs CM 65, 56-73, 20-89 years. Overall (HM+CM), retention among patients <40 years was 37/52 (71%) vs 115/131 (87.8%) for ≥80 years (p=0.015).
When contrasting HM vs CM, exit among subjects ≥80 years was: 7/95 (7.4%) vs 9/36 (25.0%), p=0.013; and for <40 years 8/38 (21.1%) vs 7/14 (50%), p=0.08.
Exit in IQR range (55-73 years) was 70/469 (14.9%) in HM vs CM 43/234 (18.9%), p=0.28
Conclusion: Both extremes of age and method of follow up affect patient retention post-ICD implant. Patient attrition is alleviated by remote management. Younger patients disengage from follow up more often. The elderly adhere more but favor remote care.

P4350 | SPOTLIGHT
Improvement of left ventricular function after acute myocardial infarction – early identification of candidates for implantable defibrillators

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Introduction: Implantable Cardioverter Defibrillator (ICD) therapy improves survival in patients with reduced left ventricular ejection fraction (LVEF) after acute myocardial infarction (AMI). Although the risk of sudden cardiac death (SCD) is highest in the first month after AMI, there is no survival benefit of early ICD implantation and the optimal time frame has yet to be established. The aim of this study was to investigate what proportion of post-AMI patients improved their LV function to such extent that the indication for ICD was no longer present.
Methods: Patients admitted for an AMI with reduced LVEF (≤40%) at discharge were eligible for inclusion. The main exclusion criterion was short life expectancy (<1 year). Patients underwent echocardiographic examinations (ECHO) at five days, one month and three months after the AMI.
Results: We prospectively included 100 patients admitted for an AMI. The majority of the patients (92%) were treated with revascularization and the mean LVEF at inclusion was 31%. At three months of follow-up 58% (n=50) of the patients had improved their LV function to such an extent that the indication for primary preventive ICD treatment was no longer met. In contrast 42% (n=38) of the patients either maintained or deteriorated in their LV function. The main improvement in LVEF had already occurred after one month and there was no significant difference in LVEF between one and three months. During the first weeks of follow up 9% (n=8) of the patients suffered from a life-threatening arrhythmia requiring resuscitation. The patients that acquired ventricular arrhythmias did not differ significantly from the other patients neither in baseline characteristics nor in LVEF at inclusion. Patients who did not improve their LVEF were more likely to have previously known congestive heart failure and low LVEF at inclusion. Among the patients (n=19) with LVEF ≤25% at discharge (n=19), only two did not have indication for ICD after three months.
Conclusion: At three months after an AMI only 42% of the patients with an initially reduced LVEF still had an indication for ICD implantation. In the majority of patients, the improvement could already be detected one month after AMI, implying that further delay of ICD implantation may not be

P4351 | BEDSIDE
Value of existing mortality risk scores in patient selection for prophylactic implantable cardioverter defibrillator implantation

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Introduction: Implantable cardioverter defibrillators (ICD) are recommended as primary prevention in patients with low ejection fraction (EF). However during follow up a large percentage of ICD recipients will not benefit from their device. The purpose of this study was to evaluate if existing all-cause mortality risk scores can help in risk stratification.
Methods: Four existing all-cause mortality risk scores were evaluated in 577 patients (mean age 64 years, 85% male) with ischemic cardiomyopathy and prophylactic ICD. All risk scores were based on combinations of simple clinical variables (like age, renal function, NYHA class, rhythm, QRS duration, EF, smoking, and COPD). To describe the performance of the scores, Kaplan-Meier survival and Cox regression analyses were performed. Primary endpoint was all-cause mortality. Secondary endpoints were appropriate shock therapy and benefit (defined as difference between the combined endpoint of appropriate therapy/mortality and mortality).
Results: Survival analysis showed a cumulative all-cause mortality of 28% at 5-year follow up. Appropriate shock therapy occurred in 21.7% of the patients. All tested risk models were able to identify a high or very high risk group with a 5-year all-cause mortality rate between 44 and 69%, compared to 20-25% in the intermediate risk group and 10-15% in the low risk group ($p<0.01$). Appropriate shock therapy was statistically significant more prevalent in the intermediate (22-30%) and high risk (24-32%) patients, compared to the low (13-23%) and very high risk patients (14%). Benefit of ICD implantation was highest in low and intermediate risk patients (10-21%), however in the (very) high risk patients there was still a benefit of 7-13%.
Conclusion: Using mortality risk scores, it is possible to estimate a mortality risk and identify low, intermediate and (very) high risk patients. However, a substantial percentage of high risk patients experience appropriate therapy and gain survival benefit from ICD implantation regardless of the high rate of 5-year mortality.
Therefore the decision whether to implant or not to implant in these high risk patients remains difficult and the decision whether to implant an ICD or not should be made on an individual basis after careful counseling.

P4352 | BEDSIDE
Usefulness of implantable cardioverter defibrillators in patients supported with ventricular assist devices

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Purpose: Implantable cardioverter-defibrillators (ICDs) reduce mortality in heart failure (HF). In patients requiring a ventricular assist device (VAD), the benefit from ICD therapy is not well established. The aim of this study was to define the impact of ICD on outcomes in VAD-supported patients.
Methods: We reviewed data for consecutive adult HF patients receiving VAD as a bridge to transplantation from 2003 to 2013. The primary outcome was survival to transplantation.

Results: A total of 97 VADs were implanted [34 left ventricular (LVAD), 63 biventricular (BIVAD), mean age 40±12 years, 90% male, left ventricular ejection fraction 18±9%, 74% dilated cardiomyopathy]. Mean length of support was 740 days (range 30–1460); 53 patients survived to transplantation. Sixty patients had an ICD (22 LVAD, 38 BIVAD). More LVAD patients had an appropriate ICD shock before implantation than after (16 vs 7; P=0.02). There was a trend toward higher shock frequency before LVAD implant than after (3.3±5.2 vs 1.1±3.8 shocks/y; P=0.06). Mean time to first shock after VAD implant was 129±109 days. LVAD-supported patients with an ICD were significantly more likely to survive to transplantation [1-y actuarial survival to transplantation: LVAD: 91% with ICD vs 57% without ICD; BIVAD: 54% vs 47%. ICD shocks on VAD support when appropriate and frequent predicted adverse outcomes and hospitalizations such as aortic regurgitation or right heart failure when on LVAD support.
Conclusions: Shock frequency decreases after VAD implantation, likely owing to ventricular unloading, but appropriate ICD shocks still occur in VAD patients. An ICD is associated with improved survival in LVAD-supported HF patients.

P4353 | BEDSIDE
Survival after primary prevention implantable cardioverter-defibrillator implantation in the elderly

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Introduction: The benefit of implantable cardioverter-defibrillators (ICD) remains controversial in elderly patients and may be attenuated by a higher risk of non-arrhythmic death. We examined the impact of age on device-delivered therapies and outcomes after prophylactic ICD implantation.
Methods: All patients, with coronary artery disease or dilated cardiomyopathy, implanted with an ICD in the setting of primary prevention in 12 centers in France between Jan. 2002 and Jan. 2012 were included in this retrospective observational multicentric study. Device-delivered therapies and complications were determined at routine clinic visits during a mean follow-up of 3.1±2 years
Results: The 5576 ICD recipients included in this registry were divided according to age: 18 to 59 (n=2153), 60 to 74 (n=2706) and ≥75 (n=704) years. There was a higher prevalence of both coronary artery disease (54%, 64%, and 66% respectively, p<0.0001) and atrial fibrillation (15%, 27%, and 35% respectively, p<0.0001) with increasing age. Median ejection fraction was significantly higher among older patients (25%, 26% and 28% respectively, p<0.001). Older patients presented with a higher number of non cardiovascular comorbidities (p=0.002). Mortality increased with age, as follows: 3.1% per year (18-59 years), 5.7% per year (60-74 years) and 7.5% per year (≥75 years) (p<0.001). Older age was independently associated with a higher risk of death (adjusted odds ratio 1.67, 95% CI 1.34-2.08 for age 60-74, and 1.83, 95%CI 1.36-2.46 for age >75 compared to age 18-59). However, proportions of cardiac deaths (55.6%, 57.8% and 57.5%, P=0.86), including sudden death (9.8%, 6.4% and 10.6%, p=0.13), were similar in the 3 age groups. Rates of appropriate therapies after primary prevention ICDs were similar among age groups: 6.9% (18-59 years), 7.3% (60-74 years), and 7.1% (≥75 years) per 100 person-years (P=0.88).
Conclusions: Whereas elderly patients exhibited higher global mortality after primary prevention ICD implantation, rates of sudden deaths and of appropriate device therapies were similar among age groups. Decisions regarding ICD implantation in elderly patients should not be based on age alone but should consider more widely factors that affect life expectancy.

P4354 | BEDSIDE
Clinical course and prognostic relevance of ATP-terminated ventricular tachyarrhythmias in ICD-patients

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Background: In patients with an implantable cardioverter defibrillator (ICD), ICD shocks due to ventricular tachycardia (VT) or ventricular fibrillation (VF) have been associated with a worse outcome. It is not known whether termination of VT/VF by antitachycardia pacing (ATP) has a similar worse impact on prognosis in clinical practice. Aim of the study was to evaluate the clinical course and prognostic relevance of ATP-terminated episodes in patients with ICD.
Methods and results: A total of 1398 consecutive patients of the prospective single-centre ICD-registry who underwent an ICD-implantation between 1992 and 2008 for primary or secondary prevention of sudden cardiac death were analyzed. During the median follow-up time of 6 years 749 (54%) patients experienced 17827 episodes of VT or VF which were terminated by ATP in 74% and by shock in 26% of patients. In approximately half (n=321/749) of those patients with VT/VF, the first episode was terminated by ATP. In a multivariate analysis adjusted for different baseline confounding parameters the occurrence of first ATP therapy was associated with a worse prognosis (HR 2.60, 95% CI 2.02-3.35). When excluding all patients with appropriate ICD shocks first ATP therapy remained associated with a worse prognosis (HR 1.92, 95% CI 1.38-2.67).
Conclusions: In ICD-patients about ¾ of ventricular arrhythmias are terminated by ATP. The occurrence of ATP-terminated episode is associated with an increased mortality rate.

P4355 | BEDSIDE
Use of ICD and life years gained in patients with a secondary prevention ICD indication

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Background: Secondary prevention is a class Ia indication for ICD implantation, independent of underlying cardiomyopathy. Data on costs per life year saved and QALY saved are scarce and either derived from mathematical models (Markov model, Monte Carlo simulation) or based on data from the 1990s.
Methods: Out of a registry encompassing 1'120 patients, all patients with a secondary prevention and ischemic or dilated cardiomyopathy (n=405) were identified. Rough hardware costs were estimated with 20'000 €/ICD-system. Life years saved were calculated as the difference between last follow-up or death and month of the first appropriate ICD therapy with 2 settings (A: all ICD therapies; B: >240 bpm only as a surrogate for sudden death without ICD). To calculate QALY, a factor of 0.85 was used as in previous studies.
Results: 405 patients were included, 325 with ischemic and 80 with dilated cardiomyopathy. Mean age was 65±11 years, mean follow-up was 80±54 months, 11% were female. 228 patients (56%) experienced setting A and 80 (20%) setting B. 172 (39%) patients died during follow-up and 648 ICDs were implanted. The cumulative incidences of ICD use and mortality at 5 and 10 years are shown in table 1.

Table 1. Cumulative incidences of ICD use and mortality at 5 and 10 years

	Ischemic	Non-ischemic
5 year ICD use	59%	52%
10 year ICD use	66%	64%
5 year mortality	25%	22%
10 year mortality	52%	41%

Total estimated hardware costs were 13 Mio €. 15'865 months were "saved" in setting A, 6'295 in setting B, accounting for estimated costs per QALY of 8'300 and 21'000 €, depending on the setting.
Conclusion: Patients with a secondary prevention indication for ICD therapy show a high use of their ICD with a 10-year therapy rate of about 65%. Costs per QALY saved range between 8'300 and 21'000 € and will drop further with additional follow-up.

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Long-term follow-up of patients with an implantable cardioverter defibrillator (ICD) due to Brugada syndrome: should we implant an ICD for elderly patients?

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Purpose: An implantable cardioverter defibrillator (ICD) is considered the main therapy for the prevention of sudden cardiac death in patients with Brugada syndrome (BrS). However, the relatively high incidence of complications remains a major problem, and the benefit of implanting ICD is still unknown, especially in elderly patients with BrS. The purpose of this study was to evaluate risks and benefits of ICD in elderly patients based on very long follow-up of BrS.
Methods and results: A total of 123 BrS patients with an ICD (37 for aborted sudden cardiac arrest, 54 for syncope, and 32 asymptomatic) were included in this study (118 males, mean age at time of diagnosis; 46.4±12.4 years). During mean follow-up period of 92±67 months, 30 patients (24.4%) experienced appropriate shocks. Age at the first attack of ventricular fibrillation (VF) was less than 70 years (mean 44.6±11.8 years) in all patients. At final follow-up, 29 of 123 patients were over 65 years old (mean 54.2±13.6 years), and only 1 of 29 had experienced appropriate shocks after 70 years of age. Thirty-nine patients (31.7%) had 61 ICD complications including 30 inappropriate shocks due to supraventricular tachycardia (SVT) (17 shocks), sinus tachycardia (4 shocks), T-wave oversensing (3 shocks), lead failure (3 shocks), and electromagnetic interference (3 shocks). SVT occurred in 28 patients (22.8%), and 11 of these patients experienced inappropriate shocks. The mean age at onset of SVTs and age at inappropriate shocks due to SVT were relatively high (51.4±13.0 and 57.3±11.1 years respectively). Lead failures occurred in later stages after implantation (mean 6.9±2.8 years) in 10 of 123 patients (8.1%), in whom the risk gradually increased up to 14.1% at 10-year and 37.8% at 15-year follow-up.
Conclusions: Long-term follow-up in BrS patients with ICD showed a very low incidence of VF in those older than 70 years. Considering the increasing risk of inappropriate shocks due to relatively late onset of SVT and lead failures, BrS patients older than 70 years may not benefit from ICD implantation or replacement.

CLINICAL ASPECTS OF IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY

P4358 | BEDSIDE

Postpacing interval during right ventricular overdrive pacing to discriminate supraventricular from ventricular tachycardias

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Introduction: Failure to differentiate supraventricular from ventricular arrhythmias is the most frequent cause of inappropriate implantable cardioverter-defibrillator therapies. We hypothesized that the postpacing interval (PPI) after overdrive right ventricular pacing may differentiate monomorphic ventricular tachycardias (VT) from sinus tacycardias and atrial tachycardias. This hypothesis is based on the entrainment maneuver. Reentrant tachycardia circuit for VTs would have shorter distance to RV apex than supraventricular tachycardias (SVT) have, and the conduction time between a ventricular pacing site and the tachycardia origin is expected to be shorter in VTs than in SVTs.
Methods: 220 tachycardia epizodes from 38 patients with single chamber ICDs that RV overdrive pacing could not terminate or change the tachycardia cycle length (TCL) were retrospectively reviewed. Epizodes classified as VTs (group 1, n=115) and supraventricular tachyarrhythmias (group 2, n=105) by three experienced reviewers. TCLs, postpacing intervals (PPI) and TCL-PPI were compared between groups.
Results: The cycle length of VTs were shorter than SVTs (320.69±30.32 vs 366.57±40.09 ms, p=0.001). Postpacing interval and TCL-PPI of group 1 were shorter than group 2 (504.78±128.33 vs 689.23±121.85, p=0.001, 184.08±322.66±106.67,p=0.001; respectively). ROC curve analysis demontrated a 195 ms cut-off value has a 90% sensitivity, and 51% specificity to predict inappropriate ICD therapies due to supraventricular tachyarrhythmias (AUC: 0.838).
Conclusions: Analyzing of postpacing interval during overdrive pacing from RV apex can discriminate supraventricular from ventricular tachycardias. This criterion is potentially useful in implantable devices that use a single ventricular lead.

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Shock reduction with multiple bursts of antitachycardia pacing in fast ventricular tachycardias

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Background: An empirical sequence of burst antitachycardia pacing (ATP) is effective in terminating fast ventricular tachycardias (FVT) in patients with implantable cardioverter-defibrillators (ICDs). However, it has not been demonstrated whether, in the case of failure of a first burst ATP, successive burst attempts increase the efficacy of the intervention, and if it is associated with a reduction in the need of high-energy shocks.
Purpose: The aim of our study was to determine if a strategy of multiple burst ATP sequences for termination of FVT resulted in a reduction of shocks compared to a strategy of a single bursts ATP before shock therapy.
Methods: We analysed data from the UMBRELLA trial, a multicenter prospective observational study sponsored by Medtronic including ICD patients followed by the CareLink remote Monitoring System. We compared the safety and efficacy of a strategy of programming a single burst ATP (Group 1) with a strategy of successive ATP sequences (Group 2) for termination of FVT episodes (cycle lengths between 250 and 320 ms) before shock therapy.
Results: Over a mean follow-up of 31 months, a total of 650 FVT episodes were detected in 154 patients (mean cycle length of 299±18 ms). Efficacy of the 1st burst ATP in Group 1 was 73% with a median duration of episodes of 8 seconds. Shocks were required in 27% of episodes. Efficacy of the 1st burst ATP in Group 2 was 77% with a median duration of episodes of 8 seconds. Efficacy of the 2nd burst ATP increased to 87% (median duration of 18 seconds), and to 91% with the 3rd or successive burst ATP (median duration of 31 seconds). Shocks were required in 9% of episodes in group 2. Multivariate analysis showed that non-ischemic cardiomyopathy (OR 2.4, 95%CI 1.3–4.4, $p<0.01$), sinus rhythm at implant (OR 3.3, 95%CI 1.8–5.9, $p<0.001$) and programming multiple burst ATP (OR 3.2, 95%CI 1.8–5.6, $p<0.001$) were independent predictors of ATP efficacy. Programming multiple ATP busts for FVT was associated with a 67% reduction in the need of high-energy shocks.
Conclusion: A strategy of multiple burst ATP sequences is associated with a 67% reduction in the need of shocks required for termination of FVT episodes.

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Time-dependence of first appropriate therapy in primary prevention implantable cardioverter defibrillator patients: is device replacement necessary in patients without prior ICD interventions

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Purpose: Implantable cardioverter defibrillator (ICD) is considered a lifelong therapy for the prevention of sudden cardiac death. However, it is still unresolved if patients who never experienced an appropriate ICD intervention during first generator longevity really need to undergo device replacement. In a single-center prospective observational cohort study we examined the time-dependence of first appropriate ICD therapy for ventricular arrhythmias in patients who underwent ICD implantation for primary prevention.
Methods: Primary prevention ICD patients were enrolled at the time of their first implantation and were evaluated thereafter for the first occurrence of appropriate ICD therapy for ventricular arrhythmias.
Results: Of 623 ICD recipients, 126 (20,2%) had appropriate ICD therapy. Incidence of first appropriate ICD therapy was 8.2% in the first year post-implant, increased to 13.7% in year 2, while in year 5 it was 28.3% (Fig. 1). Notably 39 patients received their first appropriate therapy after device replacement. No predictive factors for lower need of ICD therapy could be identified in patients without prior appropriate ICD intervention.

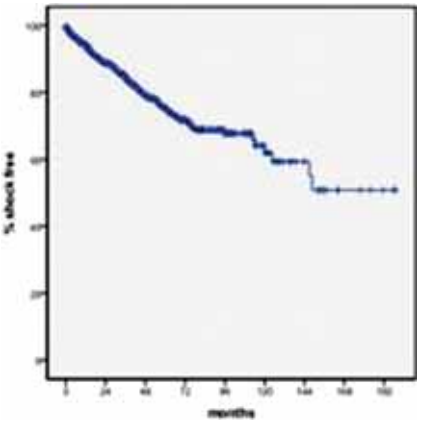

Figure 1. Incidence of first appropriate ICD therapy.

Conclusions: In a primary prevention population the risk of first appropriate ICD therapy persists over long lifetime and necessitates continuing device therapy irrespective of shock-free intervals.

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Differences in clinical predictors of shock outcome during routine ICD testing: Ischemic versus nonischemic heart disease

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Background: Controversy about the necessity of routine ICD testing has fuelled renewed interest into identification of non-invasive risk factors for test shock failures. Despite differences in myocardial substrate and associated patient characteristics, previous risk stratifications did not address the distinction between ischemic and nonischemic heart disease (IHD; non-IHD).
Methods: Cohort study of ICD implantations in an universitary medical centre (2005-2012). Testing was performed with sequential shocks (15-25-35 joule). An unsuccessful second shock represents an inadequate safety margin (<10 joule).
Results: Overall (n=684), first and second test shocks failed in 17% and 4%, respectively.
For IHD (n=424), patients with a previous sustained VT treated with amiodarone were at increased risk of shock failure [aOR 6.2 (95% CI 2.7-14.4)]. In these patients, shock failure rates (1st, 2nd) were 48% and 7%, respectively. For non-IHD (n=260), younger age (<60 years, n=131) and LV dilatation showed independent associations [aOR 3.2 (95% CI 1.4-7.6); aOR 4.5 (95% CI 1.9-10.6)]. First shock failure rates were 25% and 34%, respectively. In both subgroups an inadequate safety margin was observed in 11%.
Conclusion: Dependent on the underlying etiology, risk factors for test shock failure differ, and despite a rather low 4% overall risk of an inadequate safety margin, a substantial subset of patients can be identified with a 1-out-of-9 risk. Systematic evaluation of available test data may contribute to a patient-tailored testing strategy, by identification of individuals who might benefit from system modifications.

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T-wave morphology markers from the 12-lead surface ECG for prediction of appropriate implantable cardioverter-defibrillator discharges and all-cause mortality

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Purpose: Predictors of implantable cardioverter-defibrillator (ICD) shocks and survival can improve patient selection. Electrocardiographic (ECG) markers are simple to obtain and have been demonstrated to predict mortality.
Methods: We retrospectively analyzed the predictive value of T-wave morphology descriptors (TWM-d) in 1,076 consecutive pts undergoing ICD or CRT-D implantation between 1998 and 2010, where digital ECG was available for analysis using automatic established algorithms. All-cause mortality and first appropriate ICD shock were defined as endpoints. Univariate Cox regression when dichotomizing at population median was calculated. Parameters with P<0.10 were included in multivariate regression.
Results: Mean age was 64±12 yrs, left ventricular ejection fraction (LVEF) 30±12%, 81% male, and 55% primary prevention. Over 5.0±2.7 yrs, 258 pts (24%) received a first appropriate ICD shock (cycle length 285±62 ms, 42% VF zone, 39% VT zone, 19% unknown). All-cause mortality was 27% (290/1076) and predicted by several TWM-d (Table). In contrast, none of the TWM-d predicted appropriate shock.

Results of Cox regression analysis

	All cause mortality			
	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Age >67 yrs	3.1 (2.4–4.0)	<0.01	2.5 (1.9–3.3)	<0.01
Male gender	1.3 (0.9–1.8)	0.10		
NYHA functional class >II	1.8 (1.4–2.2)	<0.01	1.4 (1.0–1.8)	0.03
LVEF <30%	1.4 (1.1–1.8)	<0.01	1.0 (0.8–1.4)	0.71
Primary prophylactic ICD	1.5 (1.2–1.9)	<0.01	1.1 (0.9–1.5)	0.38
Peripheral vascular disease	2.9 (2.2–3.9)	<0.01	2.1 (1.5–2.8)	<0.01
Absolute T wave residuum	1.5 (1.2–1.9)	<0.01	0.9 (0.7–1.1)	0.25
T-wave morphology dispersion	1.6 (1.3–2.0)	<0.01	1.3 (1.0–1.7)	0.03
Total cosine R-to-T	0.7 (0.6–0.9)	<0.01	0.9 (0.7–1.2)	0.44
T-wave loop dispersion	0.6 (0.5–0.8)	<0.01	0.8 (0.6–1.0)	0.10

HR, hazard ratio; CI, confidence interval.

Conclusions: The predictive value of TWM-d for mortality is confirmed in ICD patients. In the same patients, these variables cannot predict shocks, demonstrating that ICD arrhythmias do not correlate with ICD patient mortality.
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Renal sympatehtic denervation: new treatment option for the treatment of electrical storm in patients with ICD

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Introduction: Electrical storm is a catastrophic event that affects patients (P) with severe cardiomyopathy and is not a rare complication in P with ICD. The causes are multifactorial. Adrenergic hyperactivity plays an important role in the initiation and maintenance of ventricular arrhythmias (VA). Renal sympathetic denervation (RSD) has been demonstrated to decrease the adrenergic influence on cardiovascular system and it has been used for the treatment of P with refractory hypertension. There are anecdotal reports showing benefits of this procedure for the treatment of P with electrical storm. Objective: To evaluate the effects of RSD in P with ICD hospitalized with electrical storm.
Methods: We included in this series 9P (mean age 64.7±6.26 years; 5P with Chagas disease, 2P with dilated idiopathic cardiomyopathy and 2P with ischemic cardiomyopathy, mean EF 32±1%) admitted with at least three episodes of VT/VF (ranging from 8 to 106 episodes) requiring shocks or repeated ATP therapies within 24h. All P were considered refractory to antiarrhythmic therapy, including maximum tolerated dose of amiodarone, lidocaine, magnesium sulfate and beta-blocker and were not candidates for ablation of the arrhythmogenic focus (3P had intracavitary thrombus; 4P polymorphic VT, and 2P had prior failed ablation). After clinical stabilization all P underwent RSD. Radiofrequency energy was applied to both renal arteries, starting from the distal portion towards the proximal portion with a distance of at least 0.5 cm between each lesion by means of irrigated tip catheter. Mean procedure time was 30 min.
Results: All P tolerated the procedure well without complications. The mean number of lesions was 5.5±3.4/artery/P. After the procedure there was supression of VT/VF episodes in all P. Two P had incessant accelerated idioventricular rhythm within the first 24h after RSD and were successfully treated by 5J internal shock with no VA recurrence. One P had VT one week later which was successfully treated by ATP. No more episodes of sustained VA were seen during the follow-up (mean of 5.3±3 mo, ranging from 1 week to 10 mo).
Conclusions: a) RSD is an effective and safe technique for the treatment of electrical storm b) RSD may be indicated in P when other forms of non-pharmacological treatments are contraindicated or ineffective; c) larger sample size and longer follow-up are needed to confirm our results.

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Can serologic markers of fibrosis predict future shocks in ICD recipients with dilated cardiomyopathy?

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Purpose: We investigated prospectively whether serum markers of collagen turnover could be used as predictors for the occurrence of malignant ventricular arrhythmias in patients with non-ischemic dilated cardiomyopathy (NIDC) implanted with an implantable cardioverter defibrillator (ICD) for primary prevention. Extracellular matrix (ECM) alterations in NIDC may provide electrical heterogeneity, thus potentially contributing to the occurrence of ventricular arrhythmia and subsequent SCD.
Methods: Serum C-terminal propeptide of collagen type-I (CICP), C-terminal telopeptide of collagen type-I (CITP), matrix metalloproteinase (MMP)-1, and tissue inhibitor of matrix metalloproteinases (TIMP)-1 were measured as markers of collagen synthesis and degradation in 70 patients with mildly to moderate symptomatic heart failure due to NIDC with LVEF <35%, who received an ICD for primary prevention of SCD. Patients were evaluated for any appropriate ICD delivered therapy, whether shock or antitachycardia pacing, during a 1-year follow-up period.
Results: Appropriate device therapies were delivered in 14 of the 70 patients during the follow-up period, with antitachycardia pacing in 2, antitachycardia pacing with shocks in 4, and shocks in 8. Preimplantation MMP-1 levels were significantly higher in patients who had appropriate ICD-delivered therapy than in those who did not have any therapy (27.7±1.6 ng/ml vs. 24.1±2.5 ng/ml, respectively, p<0.001). The same was true for baseline serum concentrations of TIMP-1 and CITP (89±14 ng/ml vs. 58±18 ng/ml, p=0.008 and 0.46±0.19 ng/ml vs. 0.19±0.07 ng/ml, p<0.001, respectively).
Conclusions: Undoubtedly, ECM alterations play a crucial role in the constitution of an arrhythmogenic substrate in NIDC and, given the availability of therapies to prevent fatal ventricular tachyarrhythmias, the quest for factors that have a very good correlation with appropriate ICD discharges in these patients is logical. Our results confirm the role of serum markers of collagen turnover as predictors of arrhythmic events in ICD recipients and could provide an auxiliary tool in this context.

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Automated AV nodal vagal stimulation to reduce inappropriate shocks

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Purpose: Patients with an ICD having high ventricular rates (VR) during atrial fibrillation (AF) are at increased risk of receiving inappropriate shocks. Endocardial AV node vagal stimulation (AVNS) has recently emerged as a new approach to reduce VR during AF. Hypothetically, AVNS software allows differentiation of rapidly conducted supraventricular tachycardia from VT. The primary purpose of this multi-center study was to evaluate whether AVNS can be implemented into an ICD and decrease the VR during rapidly conducted AF to prevent inappropriate ICD shocks.
Methods: High-frequency AV-nodal stimulation (AVNS) was delivered via a conventional right atrial pacing lead positioned in the interatrial septum. For a conventional CRT-D-System a software algorithm, which allowed initiation of short high frequency bursts (50 Hz, 160 ms) synchronized to the R-wave, was designed. The AVNS software was triggered on AF combined with manual activation or 7 subsequent short VV intervals. Patients with a history of paroxysmal or persistent AF scheduled for a CRT-D implantation/upgrade were eligible. If proper atrial lead position was confirmed, the algorithm was tested and optimized during spontaneous (implant, 1-, 3- and 6-month visits) or induced AF episodes (implant). In addition, the efficacy of the automated algorithm was evaluated in spontaneous AF episodes during follow-up between 1 and 6 months after implant.
Results: 44 patients were enrolled in 4 centers. In 32 of 43 patients, atrial lead placement attempts were successful (74%), after a median implant time of 37 minutes (q1 - q3 = 17 – 84 minutes). The average increase in VV interval during implant was 40% (range 7%-130%). Optimal lead placement was directed towards the coronary sinus ostium in the following septal areas: posterior inferior (30%), posterior superior (21%), inferior (26%), other (21%) or unknown (2%). Pacing characteristics were stable in between visits. Between 1 and 6 months after implant, automatic AVNS activations occurred in 4 patients with rapid AF and

in 3 cases AVNS slowed the VR out of the VT/VF zone. No adverse events were associated with the AVNS software. Atrial lead dislodgement rates (6%) were comparable to those observed in common septal atrial lead positions.
Conclusions: Chronic intermittent selective AV nodal vagal stimulation via an atrial lead using automated software effectively slowed the rate of rapidly conducted AF out of VT/VF zone. AVNS seems to be a safe technique that can be implemented into a common ICD system to prevent inappropriate shocks.

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The relationship between age and inappropriate implantable cardioverter defibrillator therapy in MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy)

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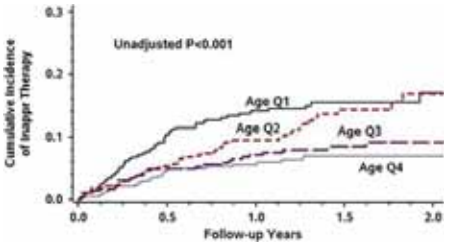
Purpose: There are limited data regarding the relationship between age and inappropriate therapy among patients with an implantable cardioverter-defibrillator (ICD) and resynchronization therapy. We aimed to investigate this relationship and the effect of innovative ICD programming on inappropriate therapy by age groups in MADIT RIT.
Methods: In the MADIT-RIT study 1500 patients were randomized to three ICD programming arms: A) conventional with VT therapy ≥170; B) high-rate cut-off with VT therapy ≥200, and C) prolonged 60 sec delay for VT therapy ≥170.
The relationship between age, the risk of a first inappropriate ICD therapy, and ICD programming was assessed among patients enrolled in the MADIT-RIT.
Results: Cumulative incidence function graphs showed an inverse relationship between increasing quartiles of age (Q1: ≤55, Q2: 56-64, Q3: 65-71, and Q4: ≥72 years) and the risk for inappropriate therapy. (Figure)
Multivariate analysis showed that each increasing decade of life was independently associated with 34% ($p<0.001$), 27% ($p<0.001$), and 26% ($p<0.001$) reduced risk for inappropriate shock, inappropriate antitachycardia pacing, and any inappropriate therapy, respectively. These trends were evident in the 3 randomized programming arms. Furthermore, innovative ICD programming, in arms B and C as compared with arm A, was associated with a significant reduction in the risk of inappropriate therapies across all age quartiles ($p<0.001$ for all).



Conclusions: Among patients with a primary prevention indication for an ICD, there is an inverse relationship between age and inappropriate ICD therapy. Innovative ICD programming of high-rate cut-off or prolonged delay for VT therapy is associated with significant reductions in inappropriate therapy among all age groups.

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Ventricular antitachycardia pacing efficacy and safety in heart failure patients wearing a cardiac resynchronization device with defibrillation back-up

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Purpose: Patients at high risk of ventricular tachycardia/fibrillation (VT/VF) and sudden cardiac death may benefit from the implant of an implantable cardioverter-defibrillator (ICD). Several randomized studies have shown that antitachycardia pacing (ATP) is safe, effective in terminating fast ventricular tachycardias (VT). Only limited data exist on the occurrence of ventricular rhythm acceleration after ATP. Aim of our observational research was to evaluate the efficacy and safety profile of ATP in a large cohort of patients wearing a cardiac resynchronization device with defibrillation back-up (CRT-D).
Methods: 1404 CRT-D patients (80% male, mean age 67±10 years) were prospectively followed up in 74 Italian cardiology centers. Expert electrophysiologists reviewed VT/VF electrograms stored in the device memory and classified the episodes as appropriate or inappropriate detections and evaluated ATP therapy outcomes. We selected the group of real VT/VF which started on sinus rhythm and the group of inappropriate VT/VF detections due to AT/AF misclassification. Primary endpoints were ATP efficacy, the number of real VT episodes which, after ATP treatment, resulted in episode acceleration, syncope or supraventricular tachyarrhythmias (AT/AF) and the number of false VT episodes which after ATP were followed by real VT/VF.
Results: Over a median follow-up of 31 months, 448 patients suffered 2892 real VT/VF episodes; 512 VT/VF were not treated, because they self-terminated or were in an only-monitoring detection zone, while 2380 VT/VF were treated. First therapy was a shock in 226 (9%) episodes and an ATP in 2154 (91%) episodes, whose median (25th–75th percentile) VT cycle length was 330 ms (300-360 ms). Each patient ATP efficacy was characterized by a median (25th-75th percentile) of 86% (50%-100%). ATP restored sinus rhythm in 1562/2154 (73%) episodes at first attempt and in 1789/2154 (83%) as a whole. VT/VF accelerations occurred in 42/2154 (1.9%) episodes in 25 patients, 4/2154 (0.2%) VT/VF episodes were followed by new AT/AF episodes in 4 patients and 4/2154 (0.2%) VT/VF episodes resulted in syncope in 4 patients. Among 962 AT/AF-related inappropriate VT/VF detections in 168 patients, 353 (37%) episodes were treated by ATP in 96 patients and true VTs followed in 4 (1.1%) episodes in 2 patients; 3 episodes terminated spontaneously, 1 was terminated by a subsequent ATP.
Conclusions: In a large cohort of CRT-D patients, ATP is highly effective in terminating VT episodes with a good safety profile, since ATP-induced AT/AF or VT as well as VT accelerations were rare.

MECHANISTIC ASPECTS OF DEVICE THERAPY

P4369 | BEDSIDE
Prognostic significance of subsequent shock delivery in patients with initial non-shockable rhythms after out-of-hospital cardiac arrest

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Purpose: The prognostic significance of conversion from non-shockable to shockable rhythms in patients with initial non-shockable rhythms who experience out-of-hospital cardiac arrest (OHCA) remains unclear. We hypothesized that the neurological outcomes in those patients would improve with a subsequent shock delivery, and that the time from initiation of cardiopulmonary resuscitation by emergency medical services personnel to the first defibrillation (shock delivery time) would influence those outcomes.
Methods: We analyzed the data of 569,937 OHCA adults with initial non-shockable rhythms; the data were prospectively collected in a nationwide Utstein-style Japanese database between 2005 and 2010. Patients were divided into two cohorts: subsequently shocked (n=21,944, 3.9%) and subsequently not-shocked (n=547,993, 96.1%) cohorts. The endpoints were prehospital return of spontaneous circulation (ROSC), one-month survival, and one-month favorable neurological outcomes (cerebral performance category scale, category 1 or 2) after out-of-hospital cardiac arrest.
Results: In the subsequently shocked cohort, the ratios of prehospital ROSC, 1-month survival, and 1-month favorable neurological outcomes were significantly higher than those in the subsequently not-shocked cohort (7.64% vs. 4.08%, 4.81% vs. 2.59%, and 1.79% vs. 0.60%, respectively; all $P<0.001$). Multivariate logistic regression analyses for 11 prehospital variables revealed that when the shock delivery time was <20 min, subsequent shock delivery was significantly associated with increased odds of prehospital ROSC (adjusted odds ratio [aOR], 4.06, 1.73; 95% confidence interval [CI], 3.47–4.75, 1.59–1.88; for shock delivery times <9 min and 10–19 min, respectively), 1-month survival (aOR, 4.70, 2.16; 95% CI, 3.99–5.53, 1.98–2.37; for shock delivery times <9 min and 10–19 min, respectively), and 1-month favorable neurological outcomes (aOR, 6.55, 2.97; 95% CI, 5.21–8.22, 2.58–3.43; for shock delivery times <9 min and 10–19 min, respectively). However, when the shock delivery time was ≥20 min, subsequent shock delivery was not associated with increased ORs of 1-month neurological outcomes (aOR, 0.97, 0.82; 95% CI, 0.73–1.27, 0.53–1.25; for shock delivery times 20–29 min and ≥30 min, respectively).
Conclusions: In OHCA patients with an initial non-shockable rhythm, subsequent shock delivery following conversion to shockable rhythms during EMS resuscitation efforts was associated with increased odds of prehospital ROSC, 1-month survival, and 1-month favorable neurological outcomes when shock was delivered within 20 min.

P4370 | BEDSIDE
The diagnostic accuracy of commercially available automated external defibrillators

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Background: Although the outspread of AEDs has improved the survival of cardiac arrest, misdiagnosis of the automated external defibrillator (AED) have been recently reported. We investigated the diagnostic accuracy of the AEDs using surface electrocardiograms (ECGs) of ventricular fibrillation (VF), ventricular tachycardia (VT), supraventricular tachycardia (SVT).
Methods and results: ECGs (VF 31, VT 48, SVT 97) were stored during EP studies and transmitted to AEDs through cables of the pad electrodes. The follow-

ing four AEDs were investigated in regards to whether they advised defibrillation: LifePak CR Plus (CR), HeartStart FR3 (FR3), CardioLife AED-2150 (AED-2150) and -9231 (AED-9231). For VF, AED-2150 and -9231 advised shock to all cases, and CR and FR3 advised shock to all but one case of VF. For VT, the ratios of shock advised were 56%, 20%, 56% and 63% for CR, FR3, AED-2150 and AED-9231, respectively. For high rate VT, FR3 had the tendency to advise shock for irregular VTs. However, FR3 did not respond to regular VTs with HR 250 bpm and above. By contrast, CR advised defibrillation for VTs with HR lower than 150 bpm. For narrow and wide complex SVT, the ratios of shock advised were 0% and 0%, 3% and 18%, 24% and 0%, 43% and 48%, respectively for CR, FR3, AED-2150 and AED-9231. FR3 advised no shock to SVT, whereas AED-9231 tended to treat high rate events despite them having narrow QRS complexes, for SVT faster than 180 bpm. The shock pattern for FR3 was different in character from AED-9231 (kappa coefficient (κ) = 0.479, $p<0.001$). CR and AED-2150 had characteristics somewhere between the above 2 AEDs (κ = 0.818, $p<0.001$).

	CR Plus	FR3	2150	9231
Vf n=31	97%	97%	100%	100%
VT n=48	56%	20%	56%	63%
SVT narrow QRS n=76	0%	0%	3%	18%
SVT wide QRS n=21	24%	0%	43%	48%

Conclusion: All AEDs diagnosed VF almost correctly. For the diagnosis of VT and SVT, the evident discrepancy was present among investigated AEDs.

P4371 | BEDSIDE
Implantable cardioverter defibrillator therapy in a young population: differences between conventional and subcutaneous devices

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Background: Implantable cardioverter-defibrillators (ICDs) are the most effective therapy for primary and secondary prevention of sudden cardiac death (SCD). Currently, two device options are available: transvenous and subcutaneous (S-ICD). The later has the advantage of avoiding transvenous leads and is becoming widely used in children, young adults and patients for whom venous access may be difficult to achieve. Nevertheless, it is unclear whether the positive aspects of the S-ICD outweigh its disadvantages.
Aim: Our aim is to study a population of patients (pts) under 35 years of age, who had a conventional or S-ICD implanted and evaluate the safety and efficacy of the devices.
Methods and results: At our instituion, about 250 ICDs are implanted each year. All pts under 35 years old who implanted ICDs (either conventional or subcutaneous) from November/2009 to December/2013 were included in this analysis (n=44, 70% men, mean age 25±8 years, youngest patient with 10).
Main indications were hyperthrophic cardiomyopathy (36%), idiopathic or post-myocarditis cardiomyopathy (16%), left ventricular noncompaction (14%) and Brugada syndrome (11%). 80% of the devices were implanted for primary prevention. 13 pts (29,5%) had appropriate shocks (VF n=7, VT n=5).
S-ICDs were implanted in 12 pts [39% of all S-ICDs (31) implanted in this period of time], the remaining had conventional ICDs implanted.
Median time of follow-up was 29 [20-42] months. There was no significant difference in the incidence of complications such as infection (n=1, 8.3% in the S-ICD group vs. n=2, 6.3%, p=n.s.) or inappropriate shock therapy (n=3, 25.0% in the S-ICD group vs. n=7, 21.9%, p=n.s.). There were no undetected fatal arrythmias. There were no complications related to transvenous lead insertion (pneumothorax or hematothorax and cardiac perforation) and there were no lead dislodgement or fracture in either group. No patient referred discomfort related to the device and no patient was pacemaker-dependent.
Conclusion: In our S-ICD candidate population (no pacemaker-dependent patients), no differences were observed on efficacy or safety of subcuteneous versus transvenous devices.

P4372 | BEDSIDE
Prognostic impact of anti-tachycardia pacing on mortality in patients with implantable cardioverter-defibrillators

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Background: Implantable cardioverter-defibrillator (ICD) shocks are associated with an increased risk of mortality in patients with depressed left ventricular systolic function. However, whether ICD shocks are simple marker of mortality or the shocks themselves contribute to increase mortality is unknown.
If appropriate shocks are marker of poor outcomes, it is postulated that appropriate anti-tachycardia pacing (ATP) is also associated with an increased risk of mortality.
Objective: To clarify the prognostic implication of ATP in ICD recipients with structural heart disease.
Methods: Of 332 ICD recipients, 233 patients (79% men, mean age 64±11 years, 46% ischemic heart disease, mean left ventricular ejection fraction [LVEF] 39±14%, 39% primary prevention) who did not receive appropriate shocks during a follow up period were studied with respect to ICD therapies and death. ICD therapies those followed the onset of ventricular tachyarrhythmia were considered to be appropriate and other therapies were considered to be inappropriate.
Results: During a median follow up period of 1726 days, 89 (38%) patients received at least one appropriate ATP. A history of ischemic heart disease (hazard ratio 0.507, p=0.004), monomorphic ventricular tachycardia (hazard ratio 1.919, p=0.004), LVEF (hazard ratio 0.972, p=0.003), amiodarone (hazard ratio 0.543, p=0.012), and beta blockers (hazard ratio 1.855, p=0.037) were independent predictors of ATP.
A total of 59 patients among the 233 patients died. In a Cox proportional-hazards model adjusted for the baseline prognostic factors, age (hazard ratio 1.049, p=0.003), LVEF (hazard ratio 0.962, p=0.002), serum creatinine (hazard ratio 1.324, $p<0.001$), diabetes (hazard ratio 2.275, p=0.005), atrial fibrillation (hazard ratio 2.050, p=0.016), beta blocker (hazard ratio 0.510, p=0.030), angiotensin-converting enzyme inhibitor or angiotensin II–receptor blocker (hazard ratio 0.541, p=0.035) and ATP (hazard ratio 2.030, p=0.018) were associated with all-cause mortality.
Conclusions: Among ICD recipients with structural heart disease, ATP is a marker of poor outcomes.

P4373 | BEDSIDE
Right ventricular pacing may decrease coronary artery blood flow

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Implantation of atrio-ventricular dual chamber (DDD/R) pacemakers is performed in the majority of patients with sick sinus syndrome. Right ventricular pacing alters electrical conduction leading to dyssynchrony of myocardial contraction and thus may lead to left ventricular dysfunction and heart failure. Aim: Evaluation of the effects of DDD pacing on coronary artery blood flow.
Methods: Twenty six patients with sick sinus syndrome, dual-chamber atrio-ventricular pacemaker and preserved atrio-ventricular conduction were evaluated. All had complete baseline transthoracic Doppler echocardiographic studies. Right atrial pacing was compared to DDD pacing at different pacing rates from 70bpm to 110bpm. AT each stage and pacing mode, sampling of blood velocity of the left anterior descending coronary artery (LAD) was performed. In addition, ventricular outflow and inflow velocities as well as well as tissue Doppler imaging were performed.
Results: During pacing rates 70-90bpm, peak diastolic LAD velocities and time velocity integrals were significantly lower during DDD pacing compared to right atrial pacing, however at pacing rates 100-110bpm these parameters were similar. Coronary artery flow index evaluated as the product of heart rate and LAD diastolic time velocity integral were lower during pacing rates 70-90bpm during DDD pacing compared to right atrial pacing. Myocardial oxygen supply/demand ratio index evaluated as the ratio of LAD diastolic velocity integral/ systolic blood pressure ratio was lower during DDD pacing.
Conclusions: Atrioventricular dual chamber pacing is associated with reduction in LAD diastolic blood velocity and integral, lower coronary flow and lower myocardial blood flow/ oxygen demand ratio.

P4374 | BEDSIDE
Impact of COPD and bronchodilatatory treatment on the incidence of ventricular arrhythmias and all-cause mortality in ICD-patients

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Introduction: Beta agonists are known to be associated with a worse prognosis of patients with heart failure if given systemically and chronically. It is not known if bronchodilatatory drugs like inhaled beta agonists have a similar unfavourable effect. Aim of the study was to evaluate the impact of chronic obstructive pulmonary disease (COPD) and bronchodilatatory treatment on the outcome of patients with ICD.
Methods: A total of 1380 consecutive patients of the prospective single-center ICD-registry who underwent an ICD-implantation between 1992 and 2008 for primary or secondary prevention of sudden cardiac death were analyzed. The median follow-up time was 6 years.
Results: Two hundred forty-two (18%) patients suffered from COPD (among those 30 patients with asthma bronchiale). In a multivariate analysis inhaled beta agonists were associated with an increased incidence of ventricular arrhythmias whereas inhaled anticholinergics and theophylline were not. ICD-patients with COPD had a doubled mortality rate compared to patients without COPD after 1 (9% s. 5%) and 5 years (34% vs. 19%). Inhaled beta agonists were associated with a lower mortality rate whereas no association was found between inhaled anticholinergics or theophylline and mortality rate.
Conclusions: One fifth of ICD patients have a COPD. Patients with COPD have a doubled mortality rate. Inhaled beta agonists are associated with an increased incidence of ventricular arrhythmias whereas inhaled anticholinergics and theo-

Table 1. Clinical characteristics of ICD patients with and without COPD

	Patients with COPD (n=242)	Patients without COPD (n=1138)	p-value
Age (years)	66 (61–72)	65 (56–70)	< 0.0001
Female	16%	19%	n.s.
Ischemic heart disese	54%	53%	n.s.
Ejection fraction < 30%	56%	53%	n.s.
Beta blocker	53%	79%	< 0.0001
Inhaled beta agonist	58%	0.2%	< 0.0001
Inhaled anticholinergics	54%	0.2%	< 0.0001
Theophylline	18%	0.1%	< 0.0001

phylline are not. Inhaled beta agonists are associated with a lower mortality rate whereas treatment with anticholinergics or theophylline is not associated with a change in mortality rate.

P4375 | BEDSIDE
Fragmentation of paced QRS complex: a new marker of antitachycardia pacing effectiveness among ICD patients without cardiac resynchronization therapy

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Background: The likelihood of antitachycardia pacing (ATP) terminating reentrant ventricular tachycardias (VT) increases with shorter conduction times from the pacing site to the origin of VT. We speculated that the paced QRS complex (P-QRS) from the right ventricular apex could be a marker of ATP efficiency because the presence of notches reflects delays in the activation of the left ventricle and may therefore be associated with longer times of stimulus conduction.
Objective: To determine prospectively the relationship between the duration of a notch ≥0.1 mV in the P-QRS (DN) and the effectiveness of ATP.
Methods: We followed 286 ICD patients with left ventricular dysfunction (LVEF: 31±9; ischemic cardiomyopathy: 66%; pacing site: right ventricular apex; no cardiac-resynchronization therapy) for 41±27 months from implant. ICD programming was standardized. P-QRS (100 bpm) was obtained at device implant (50 mm/s). Fragmentation of the P-QRS was defined by the presence of any notch with a voltage of ≥0.1 mV in two contiguous leads. DN was measured in the lead with the longest notch.
Results: A total of 955 VTs with a CL of 335±32 ms occurred consecutively in 108 patients. ATP was successful in 84% of VTs. DN correlated significantly with the probability of ineffective ATP (C=0.67; p<0.001), the cutoff point with the best sensitivity and specificity being 50 ms (65% and 72%, respectively). The adjusted mean ATP effectiveness per patient was 76% [95% CI: 72-85], Generalized Estimating Equations Method (GEEM). Patients with a DN ≥50 ms had a lower ATP efficiency: 67% [56-77] vs. 92% [87-97] and a higher proportion of VTs terminated with shocks (SH): 31% [21-42] vs. 8% [2-14]; p<0.001 for both (GEEM). Although the occurrence of VT was similar (41 vs. 40%), the incidence of VT-related SH was higher in patients with a DN≥50 (25 vs. 14%; p=0.01, log-rank test) in the overall study population (n=286). By multivariate analysis (Cox-regression analysis), a DN ≥50 ms was found to be an independent predictor of patients undergoing at least one shock due to VT during the follow-up (OR=2.3; 95% CI: 1.2-4.2; p=0.006).
Conclusions: When ATP is applied to the right ventricular apex, a fragmented P-QRS (defined by a DN ≥50 ms) is associated with a lower ATP effectiveness and a higher risk of SH due to VT.

P4376 | BENCH
Biventricular stimulation unmasks local repolarization prolongation in dogs with proarrhythmic remodeling due to chronic dyssynchronous left ventricular activation

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Introduction: We recently showed that chronic dyssynchronous ventricular activation (DVA) with a left bundle branch (like) activation pattern, without chronic bradycardia, did not result in repolarization prolongation (QT and left ventricular (LV) monophasic action potential duration); dofetilide (IKr block) was required to demonstrate that repolarization reserve was significantly reduced. Based on an analysis of regional differences of LV activation recovery intervals in dogs with chronic bradycardic right ventricular pacing (electroanatomical mapping), we hypothesized that repolarization would be prolonged in the earliest activated LV regions and therefore masked by the later activated regions when evaluating QT/JT interval and that this could be unmasked by a temporary biventricular paced activation (BiVA).
Methods: DVA was created by left bundle branch block (ablation) or right ventricular pacing after creation of AV-block and maintained for 4 weeks by VDD pacing using 2 leads. BiVA was performed with an additional lead implanted epicardially in the latest activated region (basolateral) of the LV free wall. In 8 dogs, the effect on QRS and JT interval was evaluated both acutely (0 weeks) and after 4 weeks of DVA, during VVI pacing at 60/min.
Results: QRS was not affected by remodeling and BiVA shortened QRS both at t=0 and t=4 weeks (from 120±10 to 100±8ms and 119±12 to 95±12ms, respectively, both P<0.001; n=8). At t=0, JT intervals were not prolonged during BiVA (255±20ms) compared to DVA (251±19 ms), whereas after 4 weeks remodeling, JT intervals were significantly prolonged by BiVA (298±23 ms; DVA 259±28 ms; p<0.001).
Conclusion: Chronic DVA activation does not result in JT prolongation. In contrary, temporary BiVA increases JT, but only after remodeling, whereas the QRS shortening is independent of remodeling. This is in agreement with the hypothesis that chronic DVA results in LV repolarization prolongation, limited to the early-activated regions.

P4377 | BEDSIDE
Pacemaker detection of new-onset subclinical atrial tachyarrhythmia

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Purpose: Cardiac-device detected subclinical atrial fibrillation (AF) is associated with increased risk of stroke1. However, there is paucity of data on subclinical AF among Asians. We aim to study the prevalence and epidemiology of new onset subclinical atrial tachyarrhythmias (ATR) among pacemaker recipients in our locality.
Method: Between 2008 and 2013, 572 pacemaker recipients followed-up in our nurse-led pacemaker clinic were screened. Patients with no history of AF, who had new onset subclinical ATR documented by pacemakers were recruited. Pacemaker detected ATR is defined as any atrial arrhythmia with atrial rate >200 beats per minute lasting ≥1 minute. Patients were followed-up for any mortality, new-onset AF, stroke, or congestive heart failure (CHF) requiring hospitalization.
Results: Thirty-two patients (5.6%) (18 males, 14 females) had pacemaker-detected subclinical ATR (AF in 30 and atrial tachycardia in 2 patients respectively). The mean age was 78±13 years-old. Pacemakers were indicated for sinus node dysfunction, atrioventricular block and both conditions in 13 (41%), 17 (53%) and 2 (6%) patients respectively.
The mean follow-up duration was 6±5.7 years after pacemaker implantation. The mean CHADS2VASc score was 4±1.6. The mean interval between pacemakers implant and onset of subclinical ATR was 3.4 years. Only 9 patients (28%) reported palpitation before pacemaker detection of ATR.
At the end of follow-up period, three patients (9.4%) developed new-onset stroke. Six patients (19%) were admitted for CHF. Three patients (9.4%) died due to non-cardiac causes.
Anticoagulants or anti-platelets were initiated after detection of subclinical ATR in 6 (19%) and 11 (34%) patients respectively. The remaining patients were already on anti-platelets for other vascular indications. The low rate of anticoagulation was related to patient refusal or excessive bleeding risk.
Conclusion: Our study represents an elderly Asian population of pacemaker recipients with high CHADS2VASc score and low rate of anticoagulation. Asymptomatic subclinical AF is common among these patients and is associated with new onset stroke and CHF. Early device-detection of subclinical AF and prompt initiation of anticoagulation plays a paramount role in stroke prevention.

P4378 | BEDSIDE
Prehospital epinephrine administration accelerates conversion from initial pulseless electrical activity to shockable rhythm in patients with out-of-hospital cardiac arrest

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Introduction: In the recent guidelines for cardiopulmonary resuscitation (CPR), defibrillation for initial shockable rhythm has received strong emphasis. However, it remains controversial as to whether defibrillation of a shockable rhythm that followed a pulseless electrical activity (PEA) would be associated with an improved outcome in patients with out-of-hospital cardiac arrest (OHCA). Moreover, the effectiveness of prehospital epinephrine administration (EPI) for rhythm conversion from initial PEA to shockable rhythm is unknown. We hypothesized that EPI would accelerate conversion from initial PEA to shockable rhythm in patients with OHCA, and that it would improve 1-month survival.
Methods: We analyzed the data of 138,044 OHCA adults (age ≥18 years) with initial PEA. The data were prospectively collected in a nationwide Utstein-style Japanese database between 2005 and 2010. Patients were divided into 2 cohorts: EPI (n=12,877, 9.3%) and Non-EPI (n=125,167, 90.7%). According to the current guidelines, all patients with subsequent shockable rhythm were defibrillated during resuscitation efforts by emergency medical services (EMS) personnel. The primary endpoint was prehospital conversion to shockable rhythm. The secondary endpoint was 1-month survival after OHCA.
Results: The proportion of conversion of initial PEA to shockable rhythm was significantly higher in the EPI cohort than in the Non-EPI cohort (10.0% vs. 5.4%, P<0.001). Multivariate logistic regression analysis for 8 prehospital variables revealed that EPI was significantly associated with an increased possibility of prehospital conversion to shockable rhythm (adjusted odds ratio, 2.08; 95% confidence interval, 1.94–2.22). There was no significant difference between the 2 cohorts in 1-month survival (5.9% vs. 6.4%, P=0.07). However, EPI was significantly

associated with an increased possibility of 1-month survival (adjusted odds ratio, 1.35; 95% confidence interval, 1.17–1.55) when EMS personnel administrated epinephrine within 10 min from the initiation of CPR.
Conclusions: In patients with initial PEA after OHCA, EPI significantly accelerated conversion of initial PEA to shockable rhythm during resuscitation efforts by EMS personnel, and that when epinephrine was administrated by EMS personnel within 10 min from the initiation of CPR, 1-month survival improved.

ELECTROCARDIOLOGY

P4380 | BEDSIDE
The poor increase of inferior P-wave amplitude after sympathetic stimulation predict sick sinus syndrome

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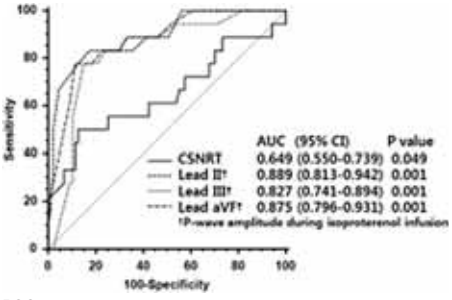
Purpose: We hypothesized that the poor increase of inferior P-wave amplitude during sympathetic stimulation might be a helpful diagnostic tool for sick sinus syndrome (SSS).
Methods: Three dimensional endocardial mapping of right atrium (RA), P-wave amplitude of inferior axis and corrected sinus node recovery time (CSNRT) were compared in consecutive 121 atrial fibrillation patients with (n=21) and without SSS (n=100).
Results: The distances from the superior vena cava (SVC) to the early activation site (EAS) of RA were negatively correlated with P-wave amplitude of lead II (r=-0.37, p<0.001), III (r=-0.41, p<0.001) and aVF (r=-0.43, p<0.001). The significant cranial shift of EAS (the distance from SVC to EAS: 10.9 vs. 5.5 mm, p=0.010), and the increase of P-wave amplitude of lead II, III and aVF during isoproterenol infusion (all p<0.001) were observed in patients without SSS. However, the cranial shift of EAS (16.5 vs. 14.2 mm, p=0.375) and the increase of P-wave amplitude were not observed in those with SSS. While the conventional CSNRT >550 ms showed the sensitivity of 50% and specificity of 86.2% to diagnose SSS, the poor increase of P-wave in lead II and aVF (<0.1mV) during isoproterenol infusion showed the improved specificity of 97% and sensitivity of 71.4%, respectively.



ROC curve.

Conclusions: The significant cranial shift of EAS and the increase of P-wave amplitude of inferior leads during isoproterenol infusion were impaired in AF patients with SSS. The poor increase of inferior leads showed improved performance to diagnose SSS than conventional CSNRT.

P4381 | BEDSIDE
Antazoline for termination of atrial fibrillation during the procedure of isolation of pulmonary veins

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Introduction: Pulmonary vein isolation is an established method of definite treatment of atrial fibrillation (AF). Periprocedural onset of AF usually terminates spontaneously within minutes, but not in all cases. A rapid electrical cardioversion (ECV) may be used to restore sinus rhythm. However, it requires general anaesthesia and does not prevent from immediate AF recurrence. The other choice is pharmacological cardioversion. Antazoline is an antihistaminic agent with antiarrhythmic quinidine-like properties. Due to the lack of large randomized trials the drug is not listed in any of the formal guidelines.
The aim of our retrospective study was to evaluate the efficacy of antazoline in termination of periprocedural onset of AF in patients undergoing pulmonary vein isolation.
Materials and methods: Consecutive 141 patients who received antazoline to terminate AF during isolation of pulmonary veins between January 2009 and April 2013 were analysed retrospectively. The antazoline was administered during the procedure in the electrophysiological laboratory after the circumferential ablation in the ostia of pulmonary veins and before confirmation of isolation. The total dose of antazoline required for sinus rhythm restoration was recorded. Early success was defined as restoration of sinus rhythm within 20 minutes after antazoline infusion. Late success was defined as a restoration of sinus rhythm within 12 hours. No ECV was used in this cohort of patients.
Results: The early efficacy of antazoline was 83.6% in paroxysmal and 31.1% in persistent AF patients. Late efficacy of antazoline was 91% in paroxysmal and 51,4% in persistent AF. Clinical variables that were independently predictive of early antazoline ineffectiveness were: female (odds ratio [OR] 5,2; 95% confidence interval [CI] 1,35-20,1; p=0.017), AF at the beginning of procedure (OR 31,2; 95%CI 2,94-333,8; p=0,0043) and higher dose of antazoline (OR 1,011 95%CI 1,005-1,016; p=0,0002 [per 1mg of antazoline]). The independent predictor of late ineffectiveness was addition of metoprolol to antazoline (OR 4,91; 95%CI 1.40-17.3; p=0,013). Due to antazoline related side effects infusion was discontinued in: 3 pts (2,1%) -due to nausea, 2 pts (1,4%) - right bundle branch block, 1 pt (0,7%) - unsustained ventricular tachycardia (130 beats per minute) and 1 pts (0,7%) - hypotension (<90/60 mmHg).
Conclusions: Antazoline seems to be an effective and safe agent in termination of AF in patients undergoing pulmonary vein isolation and there is a need of randomized and controlled trials to prove this concept.

P4382 | BEDSIDE
High frequency of j wave in hypercalcemia

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Introduction: Early repolarization or J wave has generally been considered benign for decades. However, there is increasing evidence that J wave is associated with an increased risk of ventricular fibrillation and sudden cardiac death. J wave may be affected by various biological conditions such as low body temperature, ischemia, and electrolytes disturbances. The aim of this study was to investigate the effects of hypercalcemia on J wave.
Methods: By a chart review of patients with measurements of serum total calcium levels and electrocardiogram recordings at our institution from 2005 to 2013, we identified 83 patients (54 woman [65%]; age, 63±14 years) with hypercalcemia defined as a serum calcium level >12mg/dL. The etiologies of hypercalcemia were cancer (n=33), primary hyperparathyroidism (n=24), renal dysfunction (n=21), and others (n=5). We compared electrocardiogram findings between patients with hypercalcemia and 249 age- and sex-matched healthy controls without hypercalcemia.
Results: Among electrocardiogram parameters, the PR interval and QRS duration were longer in patients with hypercalcemia than controls. The QT and corrected QT intervals were shorter in patients with hypercalcemia than controls. J wave was more common in patients with hypercalcemia (n=22, 27%) than controls (n=12, 5%) (odds ratio, 7.37; 95% confidence interval, 3.37-16.67; P<0.001). Furthermore, Brugada type ST-segment elevation in the right precordial leads was found in 6 patients with hypercalcemia (7%) but was not found in controls (0%) (P<0.001). Among patients with hypercalcemia, J wave was present in the inferior leads in 9 patients (11%), in the lateral leads in 5 patients (6%), and in both of the inferior and lateral leads in 2 patients (2%). After serum calcium levels declined to normal range, J wave disappeared in 6 of 7 patients in whom electrocardiograms were repeatedly recorded and Brugada type ST elevation was attenuated in another patient. The corrected QT interval was shorter in hypercalcemia patients with J wave than those without J wave (P<0.01), while PQ interval and QRS duration were similar between the two groups. No arrhythmia event occurred in patients with hypercalcemia.
Conclusion: We found that hypercalcemia was associated with J wave.

P4383 | BEDSIDE
High incidence of early repolarization pattern in patients with myocardial bridging with and without sudden cardiac death

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Background: Early repolarization (ER) pattern has been previously associated with arrhythmic mortality and with an increased risk of ventricular fibrillation. Myocardial bridging (MB) is a well-recognized phenomenon that has been considered as a benign condition. However a few cases reported that MB was associated with sudden cardiac death (SCD) or ventricular arryhthmia. We evaluated the prevalence and prognostic significance of ER in patients with myocardial bridging.
Methods: In consecutive patients without SCD (n=200, age, 60.44±9.42 years) and with SCD (n=45, age, 48.49±18.17 years) who had undergone coronary angiography. We assessed the prevalence of ER pattern and prognostic implication in relation with MB. Patients with structural heart disease, coronary artery occlusive disease and other channellopathies were excluded. ER was defined as a J-point elevation of 0.1 mV or more in at least 2 inferior or lateral leads, manifested as QRS notching or slurring. We also stratified ER pattern according to the degree of J-point elevation (≥0.1 mV or >0.2 mV) and analized pattern of ST-segment (Horisontal/descending or Rapid ascending/upsloping).
Results: In patients without SCD, the prevalence of ER pattern ≥0.1 mV was more common in MB patients (41/100; 41%) than controls (5/100; 5%) (P<0.001). In patients with SCD, MB was observed in 4 (9%) patients. The tendency of high prevalence of ER pattern was observed in MB patients (2/4, 50%) than those without MB (9/41, 22%) (P=0.247). The horizontal/descending ST variant was more common than rapid ascending/upslope ST variant (61% vs. 39%, p=0.659).

There was no difference in sex, age, body mass index, left ventricular hypertrophy between patients with and without MB. In multivariate analysis, MB (odd ratio: 11.296, 95% CI 4.101-31.12, p<0.001) was an independent risk factor for ER pattern. During the follow up period of 59.2±32.7 months, the incidence of SCD was not different between patients with ER and without ER (0% vs. 0%).
Conclusions: ER was very common in MB patients both with and without SCD. However, the correlation and prognosis of ER in MB patient needs further studies.

P4384 | BENCH
A new ECG pattern reflecting end stage phases of arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD)

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Introduction: Arrhythmogenic right ventricular dysplasia / cardiomyopathy (ARVD) is a progressive disease with an end stage form in which there is a severe loss of ventricular myocites, dilatation of the right ventricle (RV), biventricular involvement and heart failure. Some ECG findings may reflect this very pathological substrate.
Methods: We have analyzed the ECG findings of 50 patients with ARVD (mean age 58±14 years; 64% male). An ECG pattern of end stage disease was defined with the presence of all of the following criteria: low voltage in the limb (≤0.5 mV) and precordial leads (≤1 mV), a QRS width ≥120 ms, presence of epsilon waves in precordial leadas and negative or flat T waves in V1-V3 and beyond.
Results: Patients with the end stage ECG pattern (n=9) were significantly older, with larger dimensions of the longitudinal RV length (RVL) and RV diameter at the base (RVBD) and with a lower left ventricular ejection fraction (see table). All of them were in NYHA functional class III – IV in spite of adequate medical therapy. Only 2 of this patients had a preserved left ventricular ejection faction (LVEF ≤55%), and in 3 of them was below 35%. All of them were on sinus rhythm, but three patients had a history of paroxysmal atrial fibrillation. Distribution of negative T waves in the precordial leads was: V1-V3 (n=2), V1-V4 (n=6) and V1-V6 in one patient. Mean time of follow-up from age of onset of symptoms was significantly longer in end stage patients (22±5 vs. 16±7 years; p<0.05), thus reflecting a longer evolution of the disease.

End stage	n	Age	QRSw (ms)	Epsilon	Limb (mV)	Precordials (mV)	RVBD (mm)	RVL (mm)
Yes	9	67±12	139±9	100%	0.3±0.09	0.5±0.1	55±3	73±5
No	41	56±14	105±24	17%	0.7±0.2	1.4±0.4	42±6	60±11
p		<0.5	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Conclusions: Patients in the end stage phase of ARVD have a similar ECG pattern, with low amplitude of the QRS complex in limb and precordial leads and widening of the QRS complex, evident epsilon waves and extensive repolarization abnormalities in the precordial leads.

P4385 | BEDSIDE
Electrocardiographic abnormalities do not predict recurrent arrhythmias in patients with idiopathic ventricular fibrillation

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Background: Patients presenting with cardiac arrest due to ventricular fibrillation (VF) without evidence of structural heart disease or channelopathies are diagnostically and therapeutically challenging. Some data suggest a VF recurrence rate as high as 10% per year. Nevertheless, the long term prognosis in this cohort remains unclear. We aimed to evaluate predictive value of electrocardiographic (ECG) abnormalities at baseline for prediction of recurrent ventricular arrhythmias during follow-up in patients with idiopathic VF.
Methods: Consecutive patients with idiopathic VF (n=46, age at event 40±16 years, 65% male) were followed for a mean time of 9±7 years (range 1-26 years). All patients had structurally normal hearts, confirmed by echocardiography and/or cardiac MR. Ischemic heart disease and channelopathies were ruled out. All patients were implanted with an ICD and subsequent follow-up included device-based data as well as clinical outcome. ECG prior to ICD implantation was available in 45 patients and was used for analysis.
Results: At baseline, 56% had abnormal ECG findings. During follow-up, 3 patients developed reduced ejection fraction, but no patients received any definite diagnosis by the end of follow-up. 9 patients (20%) had appropriate ICD therapy at a median of 2 {0-13} years after implant. 7 patients had inappropriate ICD shocks. One patient had a ventricular storm. All patients survived. Neither clinical factors, imaging nor ECG findings could predict appropriate ICD therapy (table).
Conclusion: The vast majority of patients who survived idiopathic VF in our cohort, contrary to earlier reports, had no VF recurrence during long-term follow-up. ECG abnormalities are common but not specific and do not offer a predictive value for future appropriate ICD therapy.

ECG and ICD therapy

ECG characteristics at baseline	No ICD therapies, n=36	ICD discharge/ATP, n=9
Completely normal ECG	16 (44%)	4 (44%)
Early repolarization in inferior-lateral leads	0	0
Notched S upslope in V1	4 (11%)	1 (11%)
Left or right axis deviation	5 (14%)	1 (11%)
LBBB/RBBB	6 (17%)	1 (11%)
T-negative in other than V1 or III	7 (19%)	1 (11%)
RSR' pattern	5 (14%)	2 (22%)

No significant differences between patients with and without ICD therapies.

P4386 | BEDSIDE
Prevalence and prognostic value of early repolarization (j wave) in patients with hypertrophic cardiomyopathy

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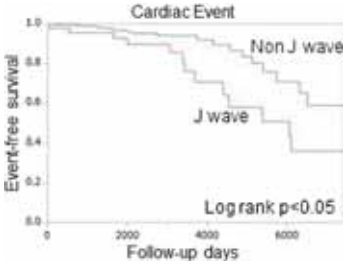
Background: The J wave syndrome is associated with cardiac events which sometimes occur in hypertrophic cardiomyopathy (HCM). However, few data exist regarding the prevalence and prognostic value of a J wave in HCM.
Methods and results: We studied 233 consecutive patients with HCM (144 men, mean age 62±17 years). Mean duration of follow up was 94.9±61.5 months. The J wave was defined as a J-point elevation of ≥0.1 mV from baseline, with notching or slurring in at least two consecutive inferior and/or lateral leads. The total prevalence of a J wave was observed in 44 patients (18.8%). Cardiac event, such as documented ventricular tachyarrhythmia or sudden cardiac death were occurred in 32 patients (13.7%). When patients were divided into two groups (Group 1; 32 with cardiac events and Group 2; 201 without cardiac events), the prevalence of J wave was significantly higher in Group 1 than in Group 2 (43.8% vs 14.9%, P<0.01). An amplitude of J wave was lower in Group 1 than that in Group 2 (0.19±0.07mV vs 0.25±0.07mV, P=0.013). Patients in Group 1 were significantly more likely to have a history of ventricular tachyarrhythmia including non-sustained ventricular tachycardia (P<0.01), or syncope (P<0.01), and a family history of sudden death (P<0.01). There were no significant differences in QRS duration, QTc interval, left ventricular end-diastolic dimension, left ventricular ejection fraction, and left atrial diameter between two groups.



Kaplan-Meier curve.

Conclusions: These results demonstrate that the presence of a J wave may be associated with an increased risk for cardiac events in patients with HCM.

P4387 | BEDSIDE
Long-term outcomes in patients with arrhythmogenic right ventricular cardiomyopathy and first-degree atrioventricular block

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Purpose: Some studies have demonstrated that PR interval prolongation is associated with adverse cardiac events including heart failure (HF). However, the prevalence and prognostic effects of first-degree atrioventricular block (AVB) have not been evaluated in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). The purpose of this study was to investigate the clinical impact of first-degree AVB on the adverse cardiac outcomes in patients with ARVC.
Methods: The study population consisted of consecutive 94 patients with ARVC (72 men, mean age: 47±14 years). We evaluated the association between baseline characteristics including the 12-lead electrocardiogram (ECG) parameters such as PR intervals and clinical outcomes.
Results: The mean PR interval was 185±38ms and 24 (26%) had first-degree AVB (PR interval >200ms). There were no significant differences between the patients with and without first-degree AVB in terms of age, family history, epsilon-wave, late potentials on siginal averaged ECG, RVEF, LVEF. During a mean follow-up of 11.0±7.7 years, there were 19 events of HF hospitalizations. Kaplan-Meier analysis revealed that the ARVC patients with first-degree AVB were at increased risk for HF hospitalization compared with those who had normal atrioventricular conduction (46%, 11/24 vs. 11%, 8/70, respectively, p=0.017, Fig. 1). In multivariate analysis, first-degree AVB at baseline was the independent predictor of hospitalization of HF in patients with ARVC (HR5.0, 95%CI 1.8-14.9, p=0.002).

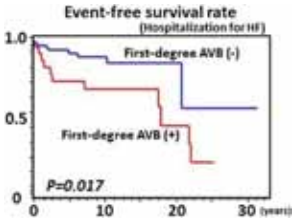

Figure 1. Freedom from HF hospitalization.

Conclusion: Prolongation of the PR interval was a strong independent determinant for increased risks of hospitalization of HF in patients with ARVC.

P4388 | BEDSIDE
The QRS morphology pattern in V5R is novel and simple parameter for differentiating the origin of idiopathic outflow tract ventricular arrhythmias

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Introduction: There have been many reports about the electrocardiography (ECG) characteristics of idiopathic outflow tract ventricular arrhythmias (OT-VAs). However, differentiating near regions using the 12-lead ECG still remains complicated. On the other hand, synthesized 18-lead ECG derived from 12-lead ECG can provide virtual waveforms of right-sided chest leads (V3R, V4R, V5R) and back leads (V7, V8, V9). The aim of this study was to evaluate the usefulness of 18-lead ECG for differentiating the origins of OT-VAs.
Methods: Fifty patients whose OT-VAs were cured by radiofrequency catheter ablation (RFCA) were divided into 4 groups depending on the successful RFCA sites: anterior and posterior of right ventricular OT (RVOT-ant-group: n=9, RVOT-post-group: n=16), right coronary cusp or junction of these two cusps (RCC-RLJ-group: n=9), and left coronary cusp (LCC-group: n=16). ECG characteristics were compared among these 4 groups.
Results: Five QRS morphology patterns in V5R were observed during VAs (R, Rs, rS, qR, and QS). The dominant QRS morphology pattern was significantly different among 4 groups (See the table). However, it was difficult to differentiate 4 sites by only one of previously reported parameters.

QRS in V5R and OT-VAs origins

	RVOT-post n=16	RVOT-ant n=9	RCC-RLJ n=9	LCC n=16	
rS	15 (94%)	1 (22%)	1 (11%)	0 (0%)	
Rs	1 (6%)	7 (78%)	1 (11%)	1 (6%)	
qR, QS	0 (0%)	0 (0%)	5 (56%)	0 (0%)	
R	0 (%)	0 (0%)	2 (22%)	15 (94%)	
	Sensitivity	Specificity	PPV	NPV	p
"rS" for predicting RVOR-post	94%	91%	83%	97%	<0.001
"Rs" for predicting RVOT-ant	78%	93%	70%	95%	<0.001
"q" for predicting RCC-RLJ	56%	100%	100%	93%	<0.001
"R" for predicting LCC	94%	97%	94%	97%	<0.001

The dominant QRS morphology pattern in V5R was significantly different among 4 groups. Therefore, QRS morphology pattern in V5R is useful for predicting the OT-VAs origins with high specificity.

Conclusion: The QRS morphology pattern in V5R is simple parameter and useful to differentiate the OT-VAs origins precisely.

P4389 | BEDSIDE
Interatrial conduction time and incident atrial fibrillation: a prospective cohort study

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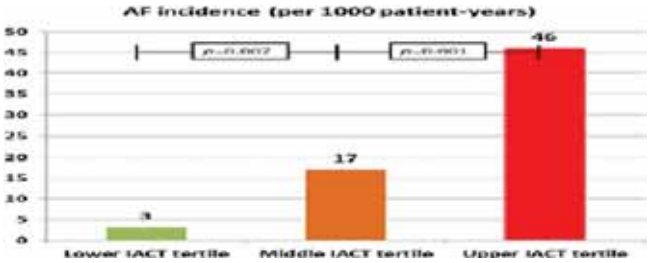
Background: Atrial electrical conduction properties have been implicated in atrial fibrillation (AF) pathogenesis. The aim of this study was to prospectively assess the potential association of interatrial conduction time (IACT) with incident AF.
Methods: The study included individuals referred for invasive electrophysiologic study (EPS), aged ≥50 years, without AF history or valvular disease. IACT was defined as the interval between the high right atrium electrogram and the distal coronary sinus atrial electrogram.
Results: 612 subjects were included (median follow-up 43 months, interquartile range 40-47). AF incidence was 21.7 cases per 1000 person-years. IACT was a significant predictor of AF with a c-statistic of 0.770 (95% confidence interval 0.702-0.838). In the time-dependent analysis, IACT was a significant stratifier of AF risk (log rank 28.0; p<0.001). The corresponding incidences of AF in each tertile of IACT were 3, 17 and 46 per 1000 person-years, respectively (all differences between tertiles were significant). IACT remained significant in the multivariable Cox regression analysis, after adjustment for age, sex, hypertension and left atrial diameter, with each millisecond of prolonged IACT corresponding to 7% (95% confidence interval 2-12%) higher adjusted risk of incident AF.



Conclusion: IACT is independently associated with incident AF. The invasive nature of the measurement is a limitation for its use as a clinical risk stratifier (although it could be used in patients referred for EPS), but these results are also indicative of a strong pathophysiological connection between atrial conduction times and substrate alterations ultimately leading to AF.

ATRIAL FIBRILLATION – CLINICAL

P4391 | BEDSIDE
Association between left ventricular geometry and diastolic function in patients with hypertension and the incidence of paroxysmal atrial fibrillation: speckle tracking echocardiographic study

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Purpose: Hypertension (HTN) is one of the major causes of atrial fibrillation (AF) accompanied with left atrial (LA) remodeling caused by pressure and/or volume (LAV) overload that is intimately associated with left ventricular (LV) diastolic function. Relationship between LV geometry or diastolic properties in HTN and the incidence of paroxysmal AF (PAF) has not been fully examined. We examined the relationship using the novel 3-dimensional speckle tacking echocardiography (STE).
Methods: Consecutive 85 patients with HTN (age69±7) and 60 controls (69±9) were enrolled. HTN were divided into 4 groups according to LV geometry (A: normal geometry, n=21. B: concentric remodeling, n=20. C: concentric hypertrophy, n=24. D, eccentric hypertrophy, n=20). Isovolumic relaxation time (IVRT) was measured by Doppler echo. We evaluated LV ejection fraction, E/e', pulmonary capillary wedge pressure (PCWP), Tau, LV diastolic stress, LV strain and LV myocardial stiffness by 3D-STE in sinus rhythm. ePCWP was estimated as 10.7–12.4 x log LA active emptying function/minimum LAV as we previously reported. Tau was calculated as IVRT/(ln 0.9 x systolic blood pressure – ln PCWP). LV diastolic stress was calculated as radius at end diastole x PCWP / end diastolic thickness (Th). LV strain was calculated as (end systolic Th – end diastolic Th)/end systolic Th. LV myocardial stiffness was estimated as LV stress/strain.
Results: The incidence of PAF for past 2 years and LV properties among 5 groups are shown in the table.

	Control	Normal geometry	Concentric remodeling	Concentric hypertrophy	Eccentric hypertrophy	P-value
Incidence of PAF, %	0	10	10	13	35	<0.001
LV mass, g/m^2	88±14	92±13	97±12*	133±26*#	132±15*#	<0.05
LV EF, %	67±6	66±6	67±5	68±9	67±9	NS
E/e'	10±2	11±3	11±2*	13±4*#	13±3*#	<0.05
ePCWP, mmHg	7±3	7±2	8±3	10±4*#	12±4*#§	<0.05
Tau, msec	31±10	39±17*	42±13*	50±15*	52±21*#	<0.05
LV diastolic stress	18±7	18±5	16±6	18±8	30±11*#§&	<0.05
LV strain	0.4±0.1	0.4±0.1	0.3±0.1*#	0.3±0.1*#	0.2±0.1*#	<0.05
LV stiffness	52±25	55±23	64±43	83±41*#	116±42*#§&	<0.05

*p<0.05 vs. control, # p<0.05 vs. normal geometry, § p<0.05 vs. concentric remodeling, & p<0.05 vs. concentric hypertrophy

Conclusion: The incidence of PAF was significantly increased in HTN with eccentric hypertrophy associated with increased LV diastolic stress without reduction of systolic function. The treatment to reduce the incidence of AF in HTN must be not for systolic function but for diastolic function.

P4392 | BEDSIDE
Predictors of left atrial thrombus resolution in patients with atrial fibrillation receiving oral anticoagulation therapy

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Background: Formation of left atrial (LA) thrombus is one of the most unfavorable scenarios among patients with atrial fibrillation (AF). Such patients typically receive oral anticoagulation therapy. However, studies providing information about predictors of LA thrombus resolution are lacking.
Methods: 64 patients (36% women; mean age at diagnosis 64±8,8 years) with

AF and LA thrombus diagnosed by TEE, who received subsequent oral anticoagulation therapy and underwent follow-up TEE were included in this study.
Results: After a mean follow-up period of 88±107 days thrombus' resolution was documented in 30 cases (47%). Heart failure and lower LVEF (left ventricular ejection fraction <45%) were associated with unsuccessful LA thrombus resolution (p=0.007, and p=0.035). Interestingly, the prognostic value of international ratio (INR) level and CHA2DS2-VASc did not reach statistical significance (p=0.11 and p=0.33, respectively).
Conclusion: In patients with AF and LA thrombus diagnosed by TEE, who are receive oral anticoagulation therapy, heart failure and low left ventricular ejection fraction are predictors of unsuccessful LA thrombus resolution.

P4393 | BEDSIDE
Statin use reduces incidence of adverse events in patients with atrial fibrillation in the ACTIVE-W, ACTIVE-A and AVERROES studies

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Purpose: Atrial fibrillation (AF), the most common cardiac arrhythmia, independently increases the risk of cardioembolic stroke. Anticoagulants are effective for stroke prevention in patients with AF but have important limitations such as a high bleeding risk. Previous studies have shown that statins reduce the incidence of cardiovascular events and recurrent venous thrombosis. We explored the effect of statin use on the incidence of adverse events in patients with AF, treated in the ACTIVE-W, ACTIVE-A and AVERROES studies.
Methods: For all patients in the ACTIVE-W & A and AVERROES studies, statin use on baseline was documented. Cox proportional hazard models were used to estimate the association between statin use and the risk of a subsequent adverse event, adjusted for the covariates age, sex, heart failure, diabetes, use of hypertensive drugs. A pooled analysis was performed for all patients, stratified by study treatment group. Analyzed adverse events were stroke or systemic embolism (SE), ischemic or unspecified stroke or SE, vascular death, and major bleeding.
Results: Of 20260 included patients with AF, 6445 had statin use on baseline documented and 13391 had not. Statin use was associated with a reduced incidence of stroke or SE (adjusted hazard ratio (aHR) 0.82; 95%CI 0.72-0.94; p=0.004), ischemic or unspecified stroke or SE (aHR 0.88; 95%CI 0.76-1.01; p=0.06) and vascular death (aHR 0.87; 95%CI 0.77-0.97; p=0.01; Table 1). No association between statin use and major bleeding was observed (aHR 1.02; 95% CI 0.86-1.2). Consistent estimates were found upon separate analyses for patients with antiplatelet or anticoagulant therapies.
Conclusions: Our data indicate that statin use was consistently associated with a reduced incidence of adverse events in patients with AF, independent of the antithrombotic therapy. These results provide rationale for future studies to determine the additional value of statins for stroke prevention in AF.

P4394 | BEDSIDE
Antithrombotic treatment pattern and baseline characteristics of dabigatran and vitamin K antagonist cohorts in North America - The GLORIA-AF registry program

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Purpose: GLORIA-AF (Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation) is a large, multinational, registry program run in 3 phases to investigate patient characteristics influencing the selection of antithrombotic treatment to prevent ischemic stroke in patients with newly diagnosed non-valvular atrial fibrillation (AF) at risk for stroke (CHA2DS2-VASc score ≥1). Phase II of the registry was instituted early after availability of dabigatran etexilate (DE).
Methods: Periodic interim analyses were scheduled in Phase II on a regional level. North America was analyzed first as US was among the first countries to approve DE for stroke prevention in AF. The treatment pattern of antithrombotic drugs was summarized and patients initiating DE or vitamin K antagonists (VKA) for stroke prevention in AF were characterized with a focus on stroke and bleeding risk.
Results: Of the 1672 analyzed patients, DE was initiated in 32.1% and VKA in 29.2%. Other NOACs were prescribed in 15.1%; ASA in 11.4% and 0.8% of the patients received other antithrombotic combinations. 11.4% of the patients did not receive any antithrombotic therapy to prevent ischemic stroke.
The 536 patients initiating DE (59.0% male; median age 71 years) and the 488 patients started on VKA (53.7% male; median age 74 years) were analyzed regarding CHA2DS2-VASc and HAS-BLED risk score variables and other patient characteristics.
A high stroke risk (CHA2DS2-VASc ≥2) was seen in 87.1% and 91.6% of patients on DE and VKA respectively. Bleeding risk was low in patients prescribed DE and VKA (mean HAS-BLED 1.3 vs 1.4).
Patients started on DE vs. VKA showed roughly similar rates of history of stroke (10.3% vs 10.0%), MI (10.6% vs 13.9%), and hypertension (77.8% vs 79.9%). Also history of bleeding (7.1% vs 8.6%), coronary artery disease (25.6% vs 28.5%), and hepatic disease (1.3% vs 2.3%) were broadly aligned between DE and VKA patients. Compared to those prescribed DE patients given VKA were older, had more abnormal kidney function (0.9% vs 4.7%), diabetes mellitus (23.3% vs 32.8%), and congestive heart failure (12.1% vs 19.1%).
Conclusions: The antithrombotic treatment pattern in North America shows that among newly diagnosed AF patients eligible for oral anticoagulation (CHA2DS2-VASc ≥1), only 76.4% received oral anticoagulation, whilst 23.6% received inadequate or no antithrombotic therapy among participating clinical practice sites. In the post-approval period preferential prescribing in relation to specific risk factors was not pronounced in newly diagnosed patients receiving DE or VKA.

P4395 | BEDSIDE
Safety of a dual antiplatelet regimen following percutaneous left atrial appendage closure in high risk patients - a single-centre experience

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Introduction: Left atrial appendage (LAA) occlusion has been shown to be a legitimate alternative therapy to oral anticoagulation (OAC) in reducing thromboembolic risk in patients with non-valvular atrial fibrillation (AF). Currently full OAC is recommended for up to 6 months after closure and is associated with increased haemorrhagic risks in many high risk patients.
Objective: To evaluate patient safety, feasibility, short and midterm outcomes following percutaneous left atrial appendage (LAA) closure in patients with high thromboembolic risk, in whom long-term OAC was contraindicated or impractical.
Methods: Retrospective single centre study of all patients with LAA occluder devices from October 2009 - November 2013. Short term OAC was applied in the early period, and from early 2012- dual antiplatelet therapy (DAPT) for 6-8 weeks followed by a single agent antiplatelet. Routine follow up transoesophageal echo (TOE) was performed at 6-10 weeks, and clinical assessments at 6 and 12 months following procedure.
Results: A total of 81 (96%) patients, with bleeding issues outruling long term OAC, had a device implanted successfully, of which 95% were performed as day cases under conscious sedation. 76% were male with a mean age of 76±16 years, and a mean CHADS2-VASc score of 5.1±2.4
Serious procedural complications included 1 cardiac tamponade requiring immediate pericardiocentesis (survived initially then died day 7 from urinary sepsis) and 1 TIA. Minor complications included 1 (1.2%) pseudoaneurysm of right femoral vein, 1 large groin haematoma, 2 intraprocedural thrombi resolved, and 2 (2.4%) arrhythmias requiring overnight monitoring.
Follow up TOEs mean 135 days showed well-seated devices in 96% with minor gaps (5-7mm) in 3.6%. Thrombi were found on the atrial aspect of devices in 5 patients (6%), all of whom had been taking Dabigatran (4 on 110mg BD and 1 on 150mg BD). Prolonged administration of 150mg BD Dabigatran resolved thrombi without sequelae.
No device related thrombi were observed among the 34 patients who received only DAPT until follow up TOE.
At max 3 year follow up (mean 15±10 months), 1 patient in the DAPT treated group had a TIA, i.e. 2.94% vs expected 5.3% annual stoke risk as predicted by mean CHADS2-VASc score for this group.
Conclusions: We find percutaneous LAA occlusion a feasible, safe and effective outpatient procedure for stroke prevention in patients with AF and high bleeding risks. Short term Dual antiplatelet therapy was a particularly safe and effective regimen vs OAC, and remains our standard therapy in this challenging field.

Abstract P4393 – Table 1. Effect statin use in AF

Outcome	Statins, no (N=13391)		Statins, yes (N=6445)		Crude HR (95% CI)	P value	Adjusted HR* (95%CI)	P* value
	N of events	%/yr	N of events	%/yr				
Stroke or SE	857	3.1	286	2.4	0.78 (0.68–0.89)	<0.001	0.82 (0.72–0.94)	0.004
Ischemic or unspecified stroke or SE	786	2.8	277	2.3	0.83 (0.72–0.95)	0.006	0.88 (0.76–1.01)	0.06
Vascular death	1209	4.2	407	3.4	0.82 (0.73–0.91)	<0.001	0.87 (0.77–0.97)	0.01

*Adjusted for study treatment group, age, sex, heart failure, diabetes, use of antihypertensive drugs.

P4396 | BEDSIDE
Atrial fibrillation in women of reproductive age compared to age-matched men

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Objectives: Data about young women with atrial fibrillation (AF) is lacking. The aim of current study was to compare the clinical features, management and outcomes of young women and men hospitalized with AF in a real-world population.
Methods: Retrospective analysis of all patients aged 15 to 49 years hospitalized with AF in our country from 1991 through 2010 was made. Patients were divided into two groups according to gender. Clinical characteristics and outcome were analyzed.
Results: During the 20-years period, 1251 patients aged 15 to 49 were hospitalized for AF; 350 (28%) were women and 901 (72%) were men with a mean age of 38years. Women were significantly more likely to have hypertension, diabetes mellitus, underlying valvular and rheumatic heart disease, while men were significantly more likely to be current smokers. The in-hospital mortality and stroke rates were comparable between the 2 groups. More women were discharged on warfarin anticoagulation than men (40.6% versus 28.7%), while more men received aspirin on discharge (40.8% versus 31.1%) [table].

	Women (n=350)	Men (n=901)	P Value
Age in year (mean ±SD)	38±8	38±7.8	0.37
Body mass index (kg/m^2) (mean ±SD)	27±8	29±11	0.46
Current smoker	7 (2)	231 (25.6)	0.001
Hypertension	59 (16.9)	104 (11.5)	0.01
Diabetes mellitus	40 (11.4)	66 (7.3)	0.02
Chronic renal impairment	7 (2)	7 (0.8)	0.07
Valvular heart disease	48 (13.7)	34 (3.8)	0.001
Rheumatic heart disease	22 (6.3)	29 (3.2)	0.01
Heart failure	25 (7.1)	46 (5.1)	0.16
Acute coronary syndrome	3 (0.9)	24 (2.7)	0.05
Total hospital stay (days) (mean ±SD)	4±4	3±3	0.004
In hospital mortality	6 (1.7)	10 (1.1)	0.39
Warfarin (on Discharge)	142 (40.6)	259 (28.7)	0.002
Aspirin (on Discharge)	109 (31.1)	368 (40.8)	0.002

Data are expressed in numbers (%) of patients unless otherwise indicated.

Conclusions: Our study demonstrates significant gender differences in the risk profiles, etiologies and treatment of young patients with AF in our area. Further studies from other parts of the world are warranted.

P4397 | BEDSIDE
Decennial analysis of interventional left atrial appendage closure

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Background: Data on long-term follow-up (LTFU) after interventional closure of the left atrial appendage (LAAC) in patients with non-valvular atrial fibrillation (AF) is scarce.
Objective: We sought to determine the outcome of patients after LAAC with the first generation device.
Methods: The Cardioangiologisches Centrum Bethanien (CCB) LAAC registry database was analysed. Between October 2001 and July 2007, forty-five AF patients (23 male, mean age 71±6 years; mean CHA2DS2-VaSc 4.3±1.7 (range 1-7); mean HASBLED score 3.3±1.2 (1-5) received LAAC. Post-implant dual-platelet inhibition with clopidogrel 75mg/d and aspirine (ASA) 300mg/d was prescribed for 6 months, followed by ASA300mg indefinitely. The primary endpoint was defined as any thrombembolic complication and/or any bleeding complication.
Results: The median FU was 7.4 years (1-12.4 years) resulting in 292 patient years. Fourteen patients died due to heart failure (n=4), non-cardiac reasons (n=7) or due to unknown etiology (n=3). No patient died from a bleeding or a stroke. Five ischemic strokes occurred a median of 794 days (range 304-3706 days) after LAAC. The observed annual stroke rate was 1.7% (RR 0.43; 95% CI 0.24-0.74; p=0.0028). In 6 patients bleedings occurred (2 acute procedural, 4 during follow-up). The observed annual bleeding rate was 2.1% (RR 0.56; 95% CI 0.48-0.66; p<0.0001).
Conclusion: During LTFU after LAAC in patients with non-valvular AF lower event rates than expected are observed for both thrombembolic and bleeding complications.

P4398 | BEDSIDE
Sociodemographic and cardiovascular status but not anticoagulant choice independently predict quality of life in patients with atrial fibrillation: results from the PREFER in AF registry

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Background: Atrial fibrillation (AF) confers significant morbidity through its symptoms, complications, and associated therapies. Only small studies have evaluated clinical determinants of quality of life (QoL) in AF. We evaluated these in a large cross-sectional study of unselected AF patients, and compared QoL measures between patients on vitamin K antagonists (VKAs) versus the novel oral anticoagulants (NOACs: dabigatran, rivaroxaban and apixaban).
Methods: The PREFER in AF registry (Prevention of Thromboembolic Events – European Registry in Atrial Fibrillation) enrolled 7243 consecutive AF patients aged above 18 years across centres in 7 European countries. Sociodemographic data, co-morbidities, AF characteristics, and therapies were evaluated for independent predictors of EQ5D index value, an overall measure of QoL derived from the EQ5D-5L health questionnaire, using univariate and multivariate logistic regression. Paired comparisons of EQ5D index value and visual analogue scale were made between patients taking VKAs versus NOACs who were matched for age, gender, maximum EHRA score, CHA2DS2-VASc score, and HAS-BLED score, using propensity scoring (227 per group).
Results: Reduced EQ5D index value (≤0.77) was independently associated with: age >65 years (OR: 1.57), female gender (OR: 1.75), unskilled occupation (OR: 1.97), heart failure (OR: 1.75), prior myocardial infarction (OR: 1.64), prior stroke (OR: 1.62), atrial tachyarrhythmia at assessment (OR: 1.26), and amiodarone therapy (OR: 1.28) (p<0.01 all cases). No differences in EQ5D index value and the visual analogue scale were found between matched VKA and NOAC users.
Conclusions: Sociodemographic and cardiovascular status, as well antiarrhythmic but not anticoagulant choice, appear to influence QoL in patients with AF.

P4399 | BEDSIDE
Quality of life and associated clinical factors in patients with non-valvular atrial fibrillation: analysis from Chinese Registry of Atrial Fibrillation

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Purpose: The data of quality of life in Chinese patients with non-valvular atrial fibrillation was sparse. The purpose of this study was to assess quality of life parameters in patients enrolled in the Chinese Registry of Atrial Fibrillation.
Methods: Chinese Registry of Atrial Fibrillation is a non-interventional, multicenter and cross-sectional study. From July to December 2012, patients with atrial fibrillation were enrolled in 111 hospitals in mainland China, most of who were non-valvular atrial fibrillation (NVAF) patients. Quality of life (QOL) was assessed by using the SF-36 (Medical Outcomes Study Short-Form Health Survey). Clinical parameters were collected including demographics, medical history, stroke risk (CHADS2 and CHA2DS2-VASc score), rate or rhythm-control strategies, antithrombotic treatment. Univariate analyses were used to identify the relation between patients' characters and quality of life by using rank test for categorical variables and linear correlation analysis for continuous variables.
Results: Overall, 3562 NVAF patients were analysed. The mean age was 68.86±11.63 years and 56.74% was male. The mean scores in eight dimensions of SF-36 were 65.55 (SD=26.33) for physical functioning (PF), 42.59 (SD=45.37) for role physical (RP); 77.36 (SD=22.44) for bodily pain (BP); 46.41 (SD=21.27) for general health (GH); 62.76 (SD=19.21) for vitality (VT); 64.57 (SD=22.07) for social function (SF); 59.11 (SD=45.56) for role emotional (RE); and 66.72 (SD=17.78) for mental health (MH). Women had significantly poorer QOL than men in patients with NVAF (p<0.001).There was a significantly negative correlation between age and scores of SF-36 in all the 8 dimensions (p<0.0001), which suggested older patients were expected with poorer QOL. Also, patients with higher CHADS2 score, history of cardiovascular events and thrombosis events were expected with poorer QOL (p<0.001). Patients who received rate-control treatment had poorer QOL compared with rhythm-control treatment or no treatment (p<0.001 except in BP dimension). For antithrombotic therapy, warfarin was associated with better QOL compared with antiplatelet therapy and no treatment (p<0.01).
Conclusions: The study first reported the QOL in a large cohort of Chinese patients with NVAF, which was generally poorer compared to healthy population. The results suggest that several clinical characters had significant impact on QOL in NVAF patients, including gender, age, risk of stroke, medical history, antiarrhythmia treatment strategies and anticoagulation treatment.

P4400 | BEDSIDE
Quantitative assessment of left atrial mechanics and substrate abnormality assessed by three-dimensional echocardiography and electroanatomical mapping system in patients with atrial fibrillation

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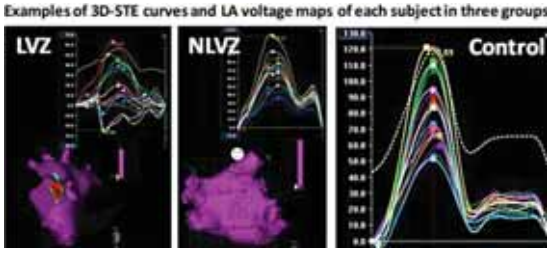
Purpose: A vulnerable electrophysiological substrate was known to be required for atrial fibrillation (AF) maintenance. Little is known about the impact of this remodeling on the mechanics of left atrium (LA). The aim of this study was to evaluate the relationship between LA remodeling and LA mechanics in patients with paroxysmal atrial fibrillation (PAF).
Methods: A total of 31 patients with PAF undergoing pulmonary vein antrum isolation (PVAI) and 31 age matched healthy subjects (Control group) were enrolled. LA global peak area strain (GPS) as index of LA reservoir function and standard deviation of the time to peak strain in each LA segment (%SD-TPS) as index of LA asynchrony were measured using 3D speckle-tracking echocardiography (3D-STE). In PAF patients, contact bipolar voltage maps of LA were constructed during sinus rhythm before PVAI. Low voltage zone (LVZ) was determined with local bipolar electrogram amplitude of <0.5 mV. The patients were divided into two groups with LVZ (LVZ group) and without LVZ (NLVZ group). We compared the clinical, echocardiographic, and electrophysiological parameters between three groups.
Results: LVZ was detected in 10 patients. Figure shows the voltage map of LA and LA area strain curves in the representative cases in three groups. GPS was significantly reduced (43.0±18.1, 59.0±20.0 and 64.9±19.0, respectively, p=0.01), and %SD-TPS was significantly higher (14.1±5.3, 8.8±6.3 and 7.2±3.7, respectively, p=0.002) in patients with LVZ than those without LVZ and normal controls. LA volume index was similar in three groups.



Conclusions: The LA mechanical dysfunction underlied in AF patients with early remodeling. We propose the hypothesis for AF pathogenesis that LA regional remodeling and heterogeneity may lead to LA mechanical deformation.

PACING, INFRA LOOP RECORDER, AND OTHER TECHNIQUES IN ARRHYTHMIAS

P4402 | BEDSIDE
Effect of heart rate on native and paced QRS duration during right ventricular apical versus septal pacing

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Purpose: Prolongation of QRS duration is associated with worse prognosis. Little is known regarding the behavior of the QRS duration in response to incremental heart rate. We investigated the effect of pacing-induced heart rate increase on the native and paced QRS duration in implanted device recipients with normal and reduced left ventricular ejection function (EF).
Methods: We studied 239 outpatients who were implanted with a dual-chamber pacemaker (48%) or ICD (52%) and had normal (n=92) or reduced (n=147) EF (61±4% and 34±9%, respectively, p<0.001). Lead position was right ventricular apical in 108 patients (45%) and septal in 131 (55%). Both normal and reduced EF patients maintained atrioventricular conduction at baseline; 71% of normal-EF and 46% of reduced-EF patients had baseline narrow QRS (<120 msec) whereas the remaining patients had bundle branch block (BBB). QRS duration was measured at baseline and during continuous DDD overdrive pacing at 100bpm with long or short AV delay to ensure permanent intrinsic ventricular activation (IA-QRS) or complete ventricular capture (VP-QRS). Four subgroups were identified: normal EF/narrow QRS (n=71); reduced EF/narrow QRS (n=67); normal EF/BBB (n=21); reduced EF/BBB (n=80).
Results: Reduced-EF patients, compared with normal-EF patients, had similar baseline heart rates (63±10bpm), but significantly longer QRS duration at baseline (140±34msec vs. 112±25msec, respectively, p<0.001) as well as at 100bpm with respect to both IA-QRS (141±34msec vs. 110±27msec, respectively, p<0.001) and VP-QRS (196±39msec vs. 161±16 msec, respectively, p<0.001). Compared with baseline, the IA-QRS decreased significantly in the normal EF/narrow QRS patients (97±13msec vs. 101±12msec, respectively, p<0.001) and did not differ significantly in the other patient groups (p=NS), whereas the VP-QRS increased significantly in all subgroups (p<0.001) except in patients with normal EF/BBB (p=0.47). The paced QRS duration increased significantly in all subgroups (p<0.01) during both apical and septal pacing. Based on ROC analysis, a change in IA-QRS of >0msec in narrow QRS patients, and in VP-QRS of >3msec in BBB patients, best identified patients with reduced EF (ROC areas 0.675 and 0.712).
Conclusions: Heart rate increase is associated with significant paced QRS prolongation particularly in patients with reduced EF regardless of QRS duration, and also in patients with both normal and reduced EF regardless of pacing site. The behavior of the QRS duration in response to heart rate increase appears useful in identifying patients with underlying structural heart disease.

P4403 | BEDSIDE
Miniaturized reveal LINQTM insertable cardiac monitoring performance in different body types

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Purpose: The Reveal LINQTM is a miniaturized insertable cardiac monitor (ICM) which is 87% smaller than the predicate Reveal XT and utilizes a new implant procedure. This study assessed the sensing capabilities of the new ICM in different body types.
Methods: The Reveal LINQTM Usability study is a prospective, multicenter clinical trial assessing the performance of the new Reveal LINQ System. We report Phase I of the study, which enrolled and inserted 30 subjects, and evaluated sensing performance in different body types. Data was collected at baseline and one month follow-up visits.
Results: The mean age was 55±15 years; 63% were female. BMI was 26.7±4.9 (range 18.2 – 37.6). R-wave amplitudes were 0.584±0.325 mV at implant and 0.596±0.336 mV at one month Elevated BMI was associated with decreased R-wave sensing at implant (Slope= -28.6, p-value= 0.018) and 1 month follow-up (Slope= -28.0, p-value= 0.026). The association remained between BMI and R-wave amplitude when accounting for gender. While R-wave values decreased with increasing BMI, sensing was over the recommended amplitude of 0.2mV at implant (n=29, 96.7%) and follow-up (n=28, 93.3%).
The ICM was implanted 9.1±6.2mm deep in the subcutaneous tissue; however, no major migration of the ICM was detected at 1 month follow-up (1.4±3.3mm). No procedure-related or system-related adverse events occurred during initial 1 month follow-up period.

Regression models of BMI for R-waves

Variable	Coefficient for implant	p-value	R^2	Coefficient for follow-up	p-value	R^2
Univariable			0.185			0.166
BMI	–28.6	0.018		–28.0	0.026	
Multivariable			0.20			0.20
BMI	–27.5	0.024		–26.4	0.036	
Gender	–90.1	0.44		–128.5	0.29	

Conclusion: The new implant procedure and subcutaneous location of the miniaturized Reveal LINQTM ICM result in acceptable sensing performance, experiencing no major migration, regardless of body-type.

P4404 | BEDSIDE
Combined pulmonary vein isolation and left atrial appendage occlusion with Watchman device – experience in an Australian centre

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Background: Left atrial Appendage (LAA) occlusion has recently been shown to be superior to anticoagulation with warfarin in long term reduction in stroke risk in non-valvular AF (NVAF). LAA occlusion is usually performed as an isolated procedure. We describe procedural outcomes a large series of patients undergoing combined AF ablation with pulmonary vein isolation (PVI) and LAA occlusion with the Watchman® device.
Results: Seventy-two patients 65.3 + 6.8 years (range 43-82 years, 71% male, CHADS2 score 1.5 + 0.95, CHADSVASC score 2.5 + 1.0) underwent successful combined PVI and LAA occlusion with a Watchman® LAA occluder device in our centre since Nov 2009. The majority of patients were therapeutically anticoagulated with warfarin or a novel oral anticoagulant on the day of the procedure, and ACT was run at 300-400 sec peri-procedurally with heparin. There have been no procedural complications. The total case time was 225.7 + 36.4 min including LAA occluder implantation time of 44.5 + 17.1 min. The total fluoroscopy time was 33.6 + 12.8 min and DAP 18.6 + 16.0 Gy cm^2. The atrial septal punctures for PVI were performed under intracardiac echo (ICE) guidance, while the LAA occluder was implanted with transoesophageal echo (TOE) guidance. The most posterior sheath across the septum is retained for LAA occluder implant and the other sheath is removed.
The average LAA occluder device size was 24 + 3 mm (21-33mm), number of deployments 1.25 + 0.62 per case, and number of devices per case 1.0 + 0.2. Acceptable device position is determined by TOE, with 93% cases showing no peri-device leak at device deployment and subsequent release.

Eight patients have undergone successful redo PVI for recurrent AF unhampered by the presence of the LAA occluder device.
Conclusion: Combined PVI and LAA device occlusion with a Watchman® device is safe and does not preclude repeat PVI for recurrent AF.

P4405 | BEDSIDE
The influence of late-gadolinium enhanced cardiac MRI defined scar on left atrial electrophysiological properties in patients with persistent atrial fibrillation

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Purpose: Structural fibrotic change in atrial fibrillation (AF) contributes to the AF substrate. Late-gadolinium enhanced (LGE) cardiac magnetic resonance imaging (CMRI) can detect pre-existing left atrial (LA) scar. The mechanism of genesis of fractionated atrial electrograms (AEGMs) is unclear. We sought to determine the influence of underlying atrial fibrosis on conduction velocity (CV), voltage and fractionated AEGMs.
Methods: Patients undergoing ablation for persistent (Ps) AF underwent LGE-CMRI. LA scar maps were created and imported into Ensite Velocity peri-procedurally. Patients who were in AF underwent DCCV to SR. Unipolar electroanatomical mapping (EAM) was performed at various pacing cycle lengths (CL) from two LA sites, and localised electroanatomical voltage maps were created using a 20 pole spiral catheter at various LA sites defined by LGE-CMRI scar density: healthy tissue, patchy, and dense scar. EAM data was exported into Matlab and CV calculated. CV, the % of fractionated AEGMs (AEGMs with NavX CFE mean score <80ms), and mean voltage were compared to scar density, at each LA site. Statistical analyses were performed using unpaired two-tailed Student's t-test.
Results: A total of 35 LA sites were analysed from 14 patients (age 65±11 yrs, LA 41±7mm). There was no statistical difference in the CV across the scar categories at 600ms CL (Healthy 1.17±0.09m/s, Patchy 1.07±0.08m/s, Dense scar 0.98±0.07m/s). CVs in Healthy and Patchy scar regions had similar mean CVs and pooled analysis against Dense scar regions demonstrated a significant difference in CV at 300ms CL (Healthy/Patchy scar 1.05±0.05 vs. Dense scar 0.86±0.06m/s, $P<0.05$). Tissue voltages were higher in healthy regions compared to scar (Healthy 2.43±1.03mV; Patchy scar 1.65±0.85mV; Dense scar 1.49±0.45mV, $p<0.01$). There was a higher % of fractionated AEGMs in healthy compared to patchy or dense scar regions (65.9±15.9% vs. 42±19.5%, $p<0.05$). LA sites with >50% fractionated AEGMs had significantly higher voltages compared to those with <50% fractionated AEGMS (2.07±0.82mV vs. 1.14±0.36mV, $p<0.001$).
Conclusions: LA scar influences CVs in patients with PsAF, however this manifests only at shorter CLs, and is likely to be exaggerated at the short CLs seen during AF. Sites of fractionated AEGMs appear to correlate to healthy tissue regions with higher voltages. The underlying mechanism of AEGM fractionation may have a functional, rather than a structural basis.

P4406 | BEDSIDE
Can rhythm control by catheter ablation improve exercise capacity in asymptomatic patients with long-standing persistent atrial fibrillation?

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Background: Radiofrequency catheter ablation (RFCA) for asymptomatic atrial fibrillation (AF) is not indicated due to limited data on it's clinical efficacy. This study evaluated the change in oxygen kinetics and cardiopulmonary performance parameters after RFCA for asymptomatic (CCS-SAF class 0) long-standing persistent AF patients.
Material and methods: A total of 44 patients with asymptomatic long-standing persistent AF (age 61±8, 84.1% male) divided into 2 age and gender matching groups who treated with RFCA for rhythm control (Group 1, N=20) and who did not (Group 2, N=24). All underwent treadmill cardiopulmonary exercise test (modified Bruce protocol, Quark CPETÒ, COSMED, Italy) before and after each treatment (7±3 months). Metabolic equivalent (MET) as exercise capacity, peak oxygen uptake (PeakVO2, ml/min/kg), the slope of the increase in VO2 to the increase in work rate (DVO2/DWR, ml/min/W), the slope of the increase in ventilation to the increase in CO2 output (VE-VCO2 slope), and O2-pulse at peak (ml/beat) were compared
Results: The PeakVO2 value before and after RFCA in group 1 were 22.8±5.0 and 23.2±5.4 respectively (4±27% increase, P=0.681), as similar to the change of group 2 (from 22.7±5.0 to 23.0±5.0, P=0.713). The METs increased from 8.7±1.9 to 9.4±2.5 (P=0.063) in group 1 in contrast to group 2 (from 8.7±2.3 to 8.4±2.5, P=0.301). The change of METs before and after treatment in each group showed significant difference (P=0.038). The O2-pulse at peak increased in both groups (group 1 from 11.5±4.2 to 13.6±3.8, P=0.042; group 2, 9.6±3.2 to 10.6±3.2, P=0.024). The O2-pulse at peak was significantly higher in group 1 (P=0.004). However, the value of DVO2/DWR and VE-VCO2 slope were not different between before and after RFCA, and between 2 groups. There was no significant difference in highest treadmill grade between 2 groups (5.0±0.9 vs. 4.9±1.1, P=0.556). During exercise, maximal exercise heart rate was significantly lower in group 1 after treatment (125±28 vs. 160±26 bpm, P=0.003).
Conclusion: The results from the present study indicate that improvement of maximal aerobic capacity and exercise tolerance are negligible in asymptomatic patients with long-standing persistent AF following successful catheter ablation.

P4407 | BEDSIDE
Improving management of atrial fibrillation across a health system using a clinical network

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Purpose: Atrial fibrillation is a common condition in emergency departments (ED) and despite published guidelines, variation in practice is common. Our team works with 40 ED across Victoria, Australia to improve care by uptake of evidence-based practice and reduction in variation in practice. In 2013, we offered a 9-month evidence based care improvement project on the management of atrial fibrillation.
Methods: This was a before and after knowledge translation/ quality improvement project. An expert panel made up of cardiologists and emergency physicians developed recommended treatment strategies based on best available evidence / guidelines which was disseminated to ED. ED participated by an expression of interest process. Local clinicians planned and implemented changes to local practice. The outcomes of interest were the proportion of patients managed according to a local treatment pathway and the proportion with duration of symptom, rate control vs. rhythm control strategy and CHADS2 score (or equivalent) documented. Analysis was by before and after comparison of proportions (Chi square/ Fisher's test).
Results: 9 ED participated in the project. 296 patients made up the before cohort and 263 were in the after cohort. The proportion managed according to a treatment pathway increased from 9% to 68% ($p<0.0001$), the proportion with symptom duration recorded increased from 66% to 83% ($p<0.0001$) and the proportion with CHADS2 score recorded increased from 17% to 46% ($p<0.0001$). Success factors included use of clinical champions and feedback about performance against targets. Barriers included high staff turnover (rotating medical staff) and time for staff education/feedback.
Conclusion: This project has led to clinically and statistically significant improvements in management of atrial fibrillation across a health system, although there is still room for improvement. Work continues to embed these gains and make further improvements. Additional ED are participating in 2014.

P4408 | BEDSIDE
Audit of safety and efficacy outcomes of patients undergoing left atrial box isolation for atrial fibrillation

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Purpose: Isolation of the pulmonary veins alone (PVI) is associated with a 50% to 70% clinical success rate in paroxysmal atrial fibrillation but is significantly lower for persistent atrial fibrillation. More comprehensive ablative strategies have evolved that may offer higher success rates. Posterior left atrial box isolation is one such technique for which there is only limited and conflicting data with regard to its safety and efficacy. Our purpose was to examine safety and efficacy outcomes of the above procedure.
Methods: We performed an audit of 100 patients undergoing LA box isolation over the last four years. Recurrence of arrhythmia was detected by evaluating symptoms and continuous 24 hour ECG monitoring at 2, 6 and 12 months post procedure.
Results: The average age of the group was 55.5±9.5 years. Average duration of atrial fibrillation was 5.4±5.2 years. Persistent atrial fibrillation was present in 72 patients. Left atrial enlargement was documented in 43. At least one anti arrhythmic drug had been trialled in 95%. Patients underwent circumferential PVI plus linear posterior LA lines to complete box isolation. Complete LA box isolation was achieved in all but one patient. At a mean follow up of 12.5±4.2 months 74 patients were free from atrial fibrillation. Of this group 50% were taking no anti arrhythmic medication. Eight of this group developed clinically significant atrial flutter. Twenty five patients had recurrence of atrial fibrillation, 84% of whom had previous persistent AF. Recurrence was of a persistent pattern in 52%. The average time to recurrence was 5.7±4.9 months. There was a higher prevalence of left atrial enlargement in those with recurrence versus those without. Fourteen patients underwent repeat procedures. There were no adverse events relating to the procedure.
Conclusion: This provisional data on clinical efficacy and safety from a single series would suggest that a strategy of left atrial box isolation is safe and effective worthy of further evaluation in a multicentre registry.

P4409 | BENCH

Gender/tachycardia interactions in atrial fibrillation: impact upon platelet aggregation and nitric oxide signalling

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Purpose: Female sex is a risk factor for stroke in atrial fibrillation (AF) yet the physiological bases for this are unknown. We sought to assess platelet dysfunction, with a particular emphasis on integrity of nitric oxide (NO) signalling, in a cohort of patients with AF.
Methods: Patients (n=87) presenting with AF were evaluated at hospital admission. ADP-induced aggregation and its inhibition by the NO donor sodium nitroprusside were evaluated using whole blood impedance aggregometry. Plasma concentrations of asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) were determined by HPLC, plasma concentrations of myeloperoxidase (MPO) and thrombospondin-1 (TSP-1) were determined by ELISA and platelet thioredoxin-interacting protein (Txnip) content was determined by immunohistochemistry.
Results: Patients were aged 72.0±1.2yrs, 48.3% female with 25.3% being new onset AF cases. Females displayed greater ADP response (9.7 [8.0, 11.5]Ω vs. 7.4 [5.3, 10.1]Ω, $p<0.05$) and smaller NO response (13.3±4.3% inhibition 27.1±4.6% inhibition, $p<0.05$) than males. Heart rate (HR) was similar across genders though elevated in new onset AF compared to chronic AF (132 [96, 156]bpm vs. 80 [65, 112]bpm, $p<0.001$). The effect of HR and gender on platelet function was evaluated by ANCOVA, indicating that for all levels of HR, females were hyperaggregable ($F[1, 83]=0.702$, $p=0.405$), with diminished NO responses ($F[1, 73]=0.049$, $p=0.825$), compared to males. Multivariate analyses showed that new onset AF ($\beta=0.250$, $p<0.05$) and platelet aggregability ($\beta=0.357$, $p<0.01$) were associated with impaired NO response. Female sex ($\beta=0.208$, $p<0.05$), as well as plasma TSP-1 ($\beta=0.317$, $p<0.01$), plasma SDMA ($\beta=-0.240$, $p<0.05$) and HR ($\beta=0.204$, $p<0.05$) were associated with platelet aggregability.
Conclusion: Among patients with AF, females display significant platelet hyperaggregability and associated diminution of the anti-aggregatory effects of NO: these factors may contribute to differential thromboembolic risk.

P4410 | BEDSIDE

Atrial fibrillation in the young: Nothing more deceptive than an obvious fact

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Atrial fibrillation in young patients has many differences when compared to older subjects with diagnosed AF. They have less co-morbidities, and a lower incidence of thrombo-embolic and bleeding events.
Objective: Our aim was to compare co-morbidities between young and older patients with AF with a cut-off point of 55 years.
Patients and methods: We utilized our AF Cohort, a data-base with 3096 patients, started in 1995 with follow-up until Dec 2013. The population was divided into two groups, group I: below age 56; n=399 (12%), group II: age above 56 years, n=2698 (87%)
We analyzed demographics, co-morbidities, mortality and type of AF ot the first consultation. Comparisons were performed between groups.
Results: The groups were quite different. Table 1 summarizes the data. Hypertension, obesity, type II diabetes, obstructive sleep apnea were significantly prevalent in group I. Thyrotoxicosis was also more prevalent in the young.

	Group I: Young (n=399)	Group II: Older (n=2698)
Age y, mean SD	45,3±10	73,2±8
Female gender %	22,3	46,1
CHA2DS2VASc >1%	28,6	85,0
HTN %	48,6	67,0
Diabetes II	23,8	13,4
Obesity %	21,1	10,9
CHF %	5,3	10,2
CHD %	6,8	17,1
Valvular HD %	8,5	18,5
Thyrotoxicosis %	5,0	2,8
Previous embolic event %	3,8	7,2
Paroxysmal AF %	53,8	28,9
Permanent AF %	3,5	19,9
Obstructive sleep apnea %	5,8	1,3
Dead %	6,8	21,2

Conclusions: Younger patients with AF appear to have more prevalent co-morbidities that predispose to AF. Obesity, hypertension, type II diabetes and obstructive sleep apnea were relatively common in this population.

VASCULAR CELL DYSFUNCTION I

P4412 | BENCH

Local immune activity in acute coronary syndrome: Ox-LDL abrogates lps-tolerance in mononuclear cells isolated from human coronary artery

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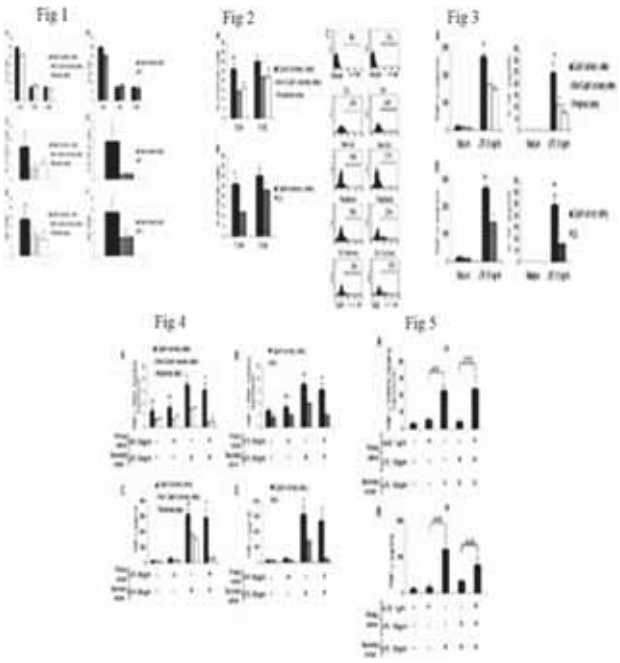
Purpose: OxLDL plays a major role in the initiation and progression of atherosclerotic lesions even though further factors are needed to promote fibrous cap rupture and thrombotic occlusion of the arterial lumen. Pathogens have been implicated in this process but it remains unclear how they can cooperate with oxLDL in amplifying the destructive inflammatory response.To phenotypically analyze culprit coronary inflammatory cells, evaluate their responsiveness to endotoxins and ascertain whether oxLDL alters the sensitivity of coronary mononuclear cells to bacterial components.
Methods: Mononuclear cells isolated from culprit and non-culprit coronary blood samples of patients with ST-segment elevation myocardial infarction (STEMI) and controls were analyzed for cell-specific surface markers and cytokines by flow-cytometry.
Results: CD14+ cells contained elevated levels of TLR4, expressed high CD80, and produced huge amounts of inflammatory cytokines in response to LPS. Using a well-established model of endotoxin tolerance, we next showed that mononuclear cells isolated from control coronary artery, but not from culprit coronary artery, were tolerant to LPS, but pre-treatment of such cells with oxLDL abrogated LPS tolerance. Flow-cytometry analysis also showed that IL-17A, IL-21 and IFN-γ were over-produced by CD4+ and CD56+ cells isolated from the culprit coronary artery.



Conclusions: All this data indicate that monocytes circulating in the culprit coronary artery of patients with STEMI are primed to synthesize high levels of inflammatory cytokines and suggest that oxLDL can amplify the inflammatory response of such cells to endotoxins.

P4413 | BENCH

Endogenous erythropoietin in the general population: reference values, biochemical and genetic associations

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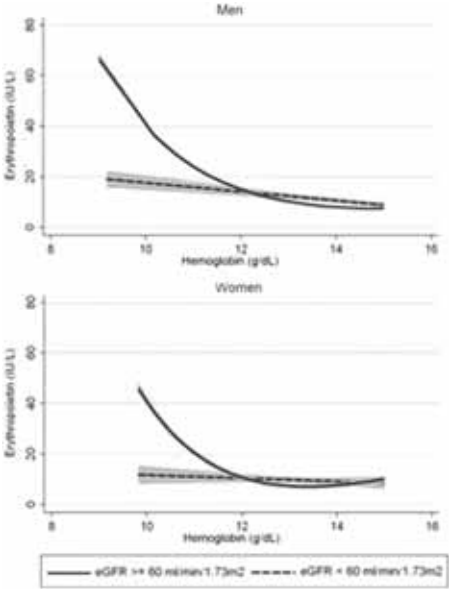
Purpose: The aim of this study was to determine EPO reference ranges and its associations with clinical, biochemical and genetic determinants in the general population.
Methods: We used data from 6,777 subjects enrolled in a prospective population study. Fasting venous blood samples were obtained in the morning from all participants from 2001-2003. Genome-wide association study was performed to identify genetic determinants of EPO levels.

Results: Mean age (± SD) was 53±12 years and 49.9% was female. Median (IQR) EPO concentrations were 7.6 (5.8 – 9.9) IU/L in men vs. 7.9 (6.0 – 10.6) IU/L in women (p<0.001). A strong correlation was found between EPO and multiple cardiovascular risk factors in both sexes, including BMI, waist circumference, glucose, blood pressure and cholesterol (all p<0.05). In men and women with a normal renal function there is a strong curved relation between hemoglobin levels and EPO, whereas in subjects with an impaired renal function (eGFR <60 mL/min/1.73m^2) EPO rose linear (p<0.001 for interaction). The non-coding SNP rs7776054 and the coding SNP rs66650371, located in HBS1L-MYB, are associated with EPO levels (both P<9x10-21).



Relation EPO/Hb stratified by eGFR.

Conclusions: We provide sex and age specific reference values for endogenous EPO. Erythropoietin levels are positively correlated with cardiovascular risk factors in both men and women. Even a mildly impaired renal function blunts EPO production. A locus in HBS1L-MYB is associated with EPO levels.

P4414 | BENCH
Age-related dysfunction of endothelial progenitor cells and improvement with thymosin beta-4 treatment

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Purpose: Endothelial progenitor cell (EPC)-based therapy has been demonstrated to be effective in experimental animal models but appear inconsistent in clinical trials. One reason may be that EPC therapy in clinical studies is often employed in older individuals in whom these cells are harvested. We investigate age-related EPC dysfunction and hypothesize that treatment of human EPCs with thymosin beta-4 (Tβ4), a novel peptide which has angiogenic properties, may improve EPC number and function.
Methods: We recruited 96 subjects between ages of 20 to 90 years. Peripheral blood mononuclear cells were isolated using Ficoll density gradient centrifugation and grown on fibronectin-coated plates. Enumeration of EPCs was performed using flow cytometry of CD34+ and KDR+ markers. Colony forming unit (CFU) assay was conducted to determine EPC function. EPCs were treated with Tβ4 (1000ng/mL) for 3 days.
Results: At baseline, EPC number (%CD34+/KDR+) and function (CFU) were significantly reduced in older individuals (70-90 years) (%CD34+/KDR+: 0.25±0.06%; CFU: 10.2±1.5) compared to the younger counterparts (20-40 years) (%CD34+/KDR+: 0.37±0.08%; CFU: 23.1±3.4) (P<0.01). There was a modest association between age and EPC number (r=-0.45, P=0.03). Tβ4 treatment significantly improved both EPC number and function in older patients by 22% (0.25±0.06% to 0.31±0.04%) and 17% (10.2±1.5 to 11.9±1.2) (P<0.05) respectively.
Conclusions: EPC number and function were significantly impaired in older subjects. Tβ4 treatment improved EPC number and function and may be used as adjunct in clinical EPC therapy trials.

P4415 | BENCH
Autologous connective tissue tunnels (in situ Biotubes) as new biological solution for hemodialysis access

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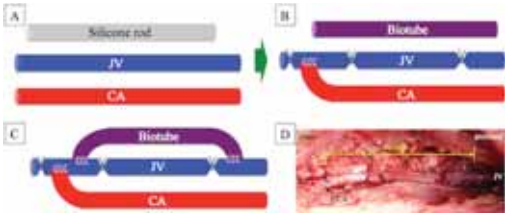
Purpose: In patients receiving hemodialysis, vascular access via an autologous arteriovenous (AV) shunt is preferred because of its lower rates of all-cause mortality and infection. However, a substantial number of shunt will fail because of stenosis or obstruction at anastomotic site or venous outflow. On the other hand, we developed autologous in vivo tissue-engineered vascular grafts (Biotubes) with long-term patency (over 5 years). In this study, Biotubes were firstly developed in situ as autologous connective tissue tunnels and successfully bypassed in a canine AV hemodialysis shunt model.
Methods and results: Silicone rods as molds (diameter; 5 mm, length; 10 cm) were embedded into subcutaneous spaces of beagle dogs along with external jugular vein (n=4). After 4 weeks connective tissue tunnels, which withstood aortic pressure, were developed as "in situ Biotubes" by removing the molds. Both ends of Biotubes were bypassed by side-to-side anastomoses to venous outflow of an AV shunt model (diameter; 5 mm), prepared by anastomosis between carotid artery and jugular vein. Clopidogrel and dalteparin were administered after surgery. Palpable thrill and typical turbulent flow pattern by pulsed-wave Doppler were observed by palpation and ultrasound at 2 weeks. Flow velocities and B-mode imaging showed little dilation and stenosis of Biotubes.



Conclusion: Autologous connective tissue tunnels developed in situ (in situ Biotubes) could bypass venous outflow of specially designed canine AV shunt model. The in situ Biotubes satisfied the higher requirement of hemodialysis shunt and have potentially for clinical application.

P4416 | BENCH
Effect of NO and H2S cross talk on the vascular tone in young normotensive and spontaneously hypertensive rats

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Purpose: The aim of study was to compare vasomodulating effect of nitric oxide (NO) and hydrogen sulfide (H2S) in young Wistar rats and spontanously hypretensive rats (SHR) to clarify the impact of a possible interaction of NO and H2S signaling pathway in the prehypertensive stage. While NO primary participates in vasorelaxation of cardiovascular system, H2S has a biphasic effect on the vascular tone, that is concentration-dependent.
Method: In the experiments 8 Wistar rats and 8 SHR were included. Systolic blood presure (sBP) was measured by the plethysmographic method and vasoactivity of isolated thoracic aorta (TA) was recorded by sensors of changes of isometric tension.
Results: Compared with the control group, SHR had not increased sBP, however a myocardial hypertrophy was observed in this group. Endothelium-derived vasoralxation of TA induced by acetylcholine (10^{-10}–10^{-5} mol/l) was not changed in SHR compared to controls. Acute nonspecific inhibition of NO sythesis after aplication of NG-nitro-L-arginin methylester (L-NAME, 10^{-5} mol/l) evoked, in contrast to Wistar rats, a significant increase in TA basal tone, comparable with maximum contractile response induced by noradrenaline (10^{-6} mol/l). A pretreatment with L-NAME (10^{-6} mol/l) inhibited the endothelium-dependent relaxation in both groups, but in SHR group significantly higher. Biphasic effect of H2S was confirmed in both experimental groups, however, the increased sensitivity was demonstrated in SHR: lower doses of H2S (80 and 100 μmol/l) induced vasorelaxation, whereas the same doses evoked vasocontraction in Wistar rats. Pretreatment with L-NAME (10^{-6} mol/l) signifikantly increased H2S-induced relaxation responses in both experimental groups, moreover, in SHR we obseved an increased sensitivity of relaxing response to lower doses (40 μmol/l). Application of modulatory dose of H2S (40 μmol) in Wistar rats did not affect acetylcholine-induced (3x8 mol/l) vasorelaxation, but significant inhibition was demonstrated in SHR. On the other hand, the pretreatment with H2S significantly increased the release of NO from exogenous donor, nitrosoglutation (GSNO: 0.25 and 0.5 mmol/l) in both groups, but significantly more in SHR compared to normotensive rats, which led to an enlarged TA vasodilatation.
Conclusions: The data demonstrated, that in SHR an interaction of NO and H2S signal pathways are starting already in prehypertensive stage and may contribute

to compensation of the increased vascular tone associated with the development of hypertension. Supported by Ministry of Health-2012/51-SAV-1.

P4417 | BENCH
Dietary carboxymethyllysine accelerates vascular aging in a RAGE-dependent manner

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Background: Arterial aging is accelerated by endogenous and exogenous factors. Advanced glycation end-products (AGEs) are endogenously produced and are present in foodstuffs. Nε-carboxymethyllysine (CML) is a potent endogenous endothelial activator via the activation of the receptor for AGEs (RAGE) but is also a major dietary AGE.
Objective: This work aimed at investigating the effects of dietary CML intake and RAGE involvement in aortic aging in the mouse model.
Methods: Wild-type or RAGE–/– C57BL/6j male mice were fed an unglycated bovine serum albumin (BSA)-enriched diet (controls) or received a CML–glycated BSA diet (50, 100 or 200 μgCML/g) for 3, 6 or 9 months. Aortic endothelium-dependent relaxation (EDR) was measured in isolated organ chambers. RAGE and vascular cell adhesion molecule-1 (VCAM-1) expression was quantified. Arterial stiffness was assessed by aortic pulse wave velocity (PWV) measurement via magnetic resonance imaging (MRI). Aortic wall surface and elastin disruption were analyzed.
Results: After 9 months of CML diet (200 μgCML/g) EDR was reduced in the wild-type mice ($p<0.001$). CML accumulation ($p<0.001$) and RAGE and VCAM-1 ($p<0.05$) overexpression were also increased in the aortic wall. However, RAGE–/– mice were protected against dietary CML-induced endothelial dysfunction. Compared to control diet, animals exposed to the CML diet showed a dose-dependent increase in aortic PWV ($p<0.05$). Elastin disruption was found to a greater extent in the CML-fed mice ($p<0.05$). RAGE–/– mice fed the CML-enriched diet were protected from aortic PWV increase.
Conclusions: Chronic CML ingestion induced endothelial dysfunction and accelerated arterial stiffness in a RAGE dependent manner.

P4418 | BEDSIDE
Adiposity and metabolic health in adolescence and arterial stiffness in young adulthood. The ALSPAC study

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Purpose: A number of studies have indicated that overweight and obese individuals do not all have increased cardiovascular (CV) risk and assessment of their metabolic health status might assist in better risk stratification. We therefore assessed whether metabolic health status can modify the vascular risk associated with adiposity in adolescence and young adulthood.
Methods: The study population consisted of 1775 subjects (52% females) who underwent vascular assessment at 17 years in the ALSPAC study. Metabolic health was assessed at 15 and 17 years. Subjects were classified as metabolic unhealthy if they had 3 or more of the following risk factors at each age (systolic blood pressure (SBP)>75th centile, high density lipoprotein (HDL)<25th centile, body mass index (BMI) >75th centile, triglycerides>75th centile and glucose>75th centile) at each age. Overweight and obesity were defined using age and sex specific BMI thresholds proposed by the International Obesity Task Force in post pubertal children. The subjects were classified in 4 groups. Those who were normal weight and metabolic healthy at both periods (NWMH), those who have been normal weight but metabolic unhealthy at any period (NWMU), those who were overweight/obese (O/O) at any period but metabolic healthy (OOMH) and those who have been O/O and metabolic unhealthy at any period (OOMU). Arterial stiffness was measured by carotid to femoral pulse wave velocity (PWV) and carotid distensibility at 17 years.
Results: The incidence of overweight/obesity increased from 21% to 24% from 15 to 17 years. 1141 subjects were NWMH, 138 were NWMU, 237 were OOMH and 259 were OOMU. Subjects who were OOMU had increased PWV (beta 0.11 [95% CI 0.01, 0.21], p=0.038) and reduced carotid distensibility (beta -2.0 [95% CI -3.0, -0.87], $p<0.001$) compared to those who were NWMH. Being OOMH had no adverse effect on PWV at 17 years (p=0.75) and less pronounced changes on carotid distensibility at 17 years (beta -1.55 [95% CI -2.70, -0.43], p=0.01).
Conclusion: We demonstrated, for the first time, that metabolic health status is a significant modifier of the CV risk of overweight and obese adolescents. Metabolic healthy overweight/obese individuals had a more favourable vascular phenotype compared to those who were metabolic unhealthy. These findings suggest that metabolic screening and control should be incorporated in CV preventative strategies of overweight and obese adolescents.

P4419 | BENCH
Extracellular adherence protein of staphylococcus aureus inhibits thrombus resolution

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Background: Venous thromboembolism is the third most common cardiovascular disease with an overall annual incidence of 1-2 per 1000. We have previously shown that bacterial infection is associated with thrombus persistence, and with complicated thrombosis such as chronic thromboembolic pulmonary hypertension. Staphylococcal extracellular adherence protein (EAP) is a broad-spectrum adhesin that inhibits host leukocyte recruitment and angiogenesis. Both processes are involved in thrombus resolution, therefore we hypothesized that EAP may be a key mediator of vascular remodeling subsequent to thrombus infection.
Methods: We induced thrombus in the infrarenal vena cava (IVC) of an established murine model of stagnant-flow venous thrombosis. One day after IVC ligation we tail-vein-injected mice with wild-type EAP-competent Staphylococcus (S.) aureus or EAP-deficient S. aureus. To investigate the influence of EAP without infection, repeated intraperitoneal injections of isolated EAP were performed, and compared with saline injections. Thrombi were harvested at 3, 7, 14 and 28 days after IVC ligation, and (immuno)-histological analyses and real-time PCR were performed.
Results: Thrombus cross-sectional areas and volumes (Figure 1) of EAP-competent S. aureus-infected mice were significantly larger than those of EAP-deficient S. aureus-infected mice on day 7 (n=8, $p<0.05$). Furthermore, between days 3 and 7, thrombus cross-sectional areas and volumes illustrated significantly delayed thrombus resolution in mice infected with EAP-competent S. aureus compared with mice infected with EAP-deficient S. aureus (n=8, $p<0.05$).
Conclusion: Our data confirm that infection with wild-type S. aureus delays thrombus resolution. This effect was significantly attenuated when mice were infected with an isogenic EAP-deficient strain. EAP is one of the S. aureus proteins that are responsible for thrombus persistence and vascular occlusion.

P4420 | BEDSIDE
Temporal endotherial dysfunction due to noctural hypoxemia induce may be preventable by statin treatment

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Background: It has been demonstrated that sleep apnoea syndrome (SAS) is associated with cardiovascular morbidity and mortality. Various mechanisms link SAS to an increase in cardiovascular diseases (CAD). Endothelial dysfunction was considered to be an initiator and promoter of coronary artery atherosclerosis before the emergence of clinical signs of overt CAD. The aim of the present study is to investigate the interaction between endothelial function and mid night hypoxemia caused by SAS.
Methods: We studied consecutive 210 patients who underwent polysomnography in our institutes. Subjects were divided into 2 groups based on polysomonography (SAS group126, NonSAS group84). Endothelial function using hyperaemia-induced flow mediated vasodilatation (FMD) was compared between 2 groups. FMD was assessed before and after polysomnography and serial change of FMD was assessed.
Results: Pre FMD value was significantly lower in patients with SAS. Patients with SAS showed a significantly worsening of FMD after polysomnography (p=0.01). Furthermore, the degree of deterioration in FMD was associated with the hypoxemia degree. In a multivariate analysis, SAS was independent factor explaining worsening of FMD (p=0.011). Contrary, statin therapy (p=0.025; odds ratio 3.92) and young age (p=0.007; odds ratio 5.29) could be the factors of avoiding a worsening of FMD.
Conclusions: In SAS patients, endothelial dysfunction was observed and worsened after sleep. Statin therapy may prevent endotherial dysfunction due to nocturnal hypoxemia and contribute to future cardiac event.

P4421 | BENCH
Early changes in neutrophil morphology predict myocardial damage after myocardial infarction

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Background: Revascularization after myocardial infarction (MI) induces a strong inflammatory response resulting in an increase of circulating neutrophils. Neutrophil quantities have found to be a good predictor for future adverse events. In

this study, we hypothesized that the extent of morphological changes in circulating neutrophils also reflects the myocardial damage after MI and therefore relates to outcome.
Methods: One hundred seven STEMI patients treated between 2009 and 2012 with at least one white blood cell count determined by an automated hematology analyzer within 24 hours after PCI were selected. This analyzer differentiates between leukocyte subsets based on morphological characteristics derived from light scatter patterns. Neutrophil morphology was compared with simultaneously measured creatine kinase (CK). Pigs (n=9) were subjected to left anterior descending artery (LAD) occlusion for 75 minutes followed by 3 days of reperfusion. Blood was collected at baseline, during ischemia and at multiple time-points during reperfusion followed by whole-blood analysis with the same hematology analyzer as above. Cardiac damage was determined by histological infarct size, 3D-echocardiography and Troponin measurements. Coronary blood sampling was performed to determine differences in neutrophil morphology between simultaneously sampled arterial and venous coronary blood.
Results: In STEMI patients, a significant increase in neutrophil axial light loss (ALL) over time was seen ($p<0.001$) correlating with CK levels (R=0.314, $p<0.001$). In pigs, neutrophil ALL increased over time ($p<0.001$). Neutrophil ALL measured at 15 min after reperfusion correlated significantly with infarct size (R=0.760, p=0.017) and Troponin I levels (R=0.810, p=0.015). Neutrophil ALL also negatively correlated with LVEF measured by 3D-echocardiography (R=-0.757, p=0.018). Coronary sinus sampling revealed structural differences in neutrophil morphology between arterial and coronary venous blood (p=0.013), pinpointing the infarcted myocardium as the source of the observed changes.
Conclusion: MI alters the morphology of circulating neutrophils in both patients and pigs in relation to the extent of damage reflected by CK and Troponin I levels. In pigs, neutrophil morphology early after reperfusion predicts infarct size and cardiac function after 3 days. Neutrophil scatter profiles might therefore prove valuable markers for the prediction of cardiac damage after MI.

VASCULAR CELL DYSFUNCTION II

P4423 | BEDSIDE
Correlation between vascular calcification and systemic inflammation markers in hypertensive patients

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Purpose: The RANKL/RANK/OPG complex may mediate valuable connections between the vascular and immune systems. Structural and functional pathophysiological changes in endothelial cells and inflammation of vascular structures conjoin to influence a number of mechanisms responsible for the progression of atherosclerosis. The purpose of the study was to correlate vascular calcification markers osteoprotegerin (OPG) and nuclear factor kappa B ligand (RANKL) with inflammation markers such as high sensitivity C reactive protein (hsCRP) and fibrinogen in hypertensive patients with or without coronary artery disease (CAD).
Methods: This prospective study included 223 hypertensive patients divided based on the presence of CAD in 140 patients with angiographically documented CAD and 83 patients without CAD. The patients were compared with a control group of 74 healthy age-matched subjects (CON). Serum levels of hsCRP, OPG and RANKL were determined by ELISA. The carotid intima-media thickness (carotid IMT) was measured by high resolution B-mode ultrasound imaging according to the Mannheim Consensus. Left ventricular wall thickness (LVWT) and ejection fraction (LVEF) were measured by echocardiography. Aortic pulse wave velocity (PWV) was determined using the Arteriograph device. The Pearson correlation test was used for interpretation of results.
Results: The values of OPG were significantly higher in hypertensive patients with CAD compared to hypertensive patients without CAD and CON (3.9 ± 0.48 vs 2.8 ± 0.62 vs 1.2 ± 0.36 pg/ml, all $p<0.001$). The values of RANKL were significantly lower in hypertensive patients with CAD compared to hypertensive patients without CAD and CON (0.67 ± 0.16 vs 1 ± 0.84 vs 2 ± 0.11 pg/ml, all $p<0.001$). In all groups, OPG values were significantly correlated with cardiac parameters: LVWT ($r=0.862$, $p<0.001$), LVEF ($r = -0.827$, $p<0.001$), inflammatory markers: fibrinogen ($r=0.667$, $p<0.001$), hsCRP ($r=0.857$, $p<0.001$), carotid IMT ($r=0.824$, $p<0.001$) and aortic PWV ($r=0.833$, $p<0.001$). The values of RANKL were significantly correlated with cardiac parameters: LVWT ($r = -0.586$, $p<0.001$), LVEF ($r=0.554$, $p<0.001$), inflammatory markers: fibrinogen ($r = -0.313$, $p<0.001$), hsCRP ($r = -0.445$, $p<0.001$), carotid IMT ($r = -0.454$, $p<0.001$) and aortic PWV ($r = -0.540$, $p<0.001$).
Conclusions: OPG and RANKL are associated with the presence of CAD. Both calcification markers correlate with inflammation and arterial stiffness and may be good indicators of atherosclerotic vascular damage in hypertensive patients.

P4424 | BENCH
Dedicated therapies for calcified vessels: arterial calcification inhibition through local administration of bisphosphonates on arterial wall

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Purpose: Vascular calcification, an independent predictor of cardiovascular mortality, is considered to be an actively regulated process, sharing common molecular mechanisms with bone formation. Bisphosphonates are pharmaceutical compounds, which inhibit calcification and bone resorption. However, systematic administration of those compounds shows several pharmacokinetic restrictions, regarding their dose and their accumulation in vascular wall. In the current study, we aimed to evaluate the safety and efficacy of the local delivery of the bisphosphonate zolendronic acid on inhibition of calcium formation in the arterial wall in an experimental atherosclerotic animal model.
Methods: Sixteen New Zealand rabbits were used for this experiment. The animals were placed on vitamin D enriched atherogenic diet for three weeks. Subsequently, all animals underwent angiography of abdominal aorta and common iliac arteries for the evaluation of their anatomy and their calcification. A mixture containing 500 μg/l zolendronic acid (0.2mg zolendronate diluted in a solution, consisting of 20 ml sterile 0.9% NaCl solution and 20 ml contrast) was delivered on the vascular wall of the target iliac artery, using a dedicated balloon catheter. A placebo mixture (consisting only of 0.9% NaCl solution and contrast) was administered on the contralateral iliac artery of each animal, which was used as control. At 28 days all animals underwent euthanasia; both iliac arteries were collected and sectioned transversely in multiple sections. Histologic sections for morphometric analysis were stained with hematoxylin-eosin and von Kossa. Computer-assisted histomorphometry (Image Pro Plus; Media Cybernetics) was performed for the calcium content quantification of each section from the target and the control iliac artery. Calcium content was expressed as %percentage coverage of the vascular media area.
Results: In all animals the delivery of zolendronic acid and placebo mixtures in both the target and control arteries was successful and uncomplicated. A total of 144 artery segments were microscopically examined from each treatment group. The mean percentage of the calcium content of the media was higher in the control artery segments in comparison to the target artery segments (2.66 ± 0.73 versus 1.08 ± 0.62%, $p<0.01$).
Conclusions: Inhibition of vascular calcification by local catheter-based delivery of bisphosphonate zolendronic acid is safe and effective. These finding and its potential clinical implication remain to be confirmed in human studies.

P4425 | BENCH
Chronic oral intake of the omega 3 optimized formulation EPA:DHA 6:1 protects against angiotensin II-induced hypertension and endothelial dysfunction in rats

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Regular intake of fish products is associated with a reduced risk of cardiovascular diseases. The beneficial effect has been attributed at least in part to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA have been shown to cause endothelium-dependent nitric oxide (NO)-mediated relaxations of isolated blood vessels, with an optimized ratio of EPA:DHA 6:1. The aim of the present study was to determine whether chronic intake of EPA:DHA 6:1 affects experimental hypertension and endothelial dysfunction induced by angiotensin II (Ang II).
Male Wistar rats daily received 500 mg/kg of either EPA:DHA 6:1 (omega 3) or corn oil (control) for 5 weeks. After 1 week, rats underwent sham surgery (sham rats) or surgery with implantation of an osmotic mini-pump infusing Ang II (0.4 mg/kg/d) for 4 weeks. Blood pressure was monitored by tail sphyngomanometry, and the reactivity of second branch mesenteric artery rings using myographs.
Infusion of Ang II to rats induced within 7 days a pronounced increase of systolic blood pressure, which reached 215.6 ± 8.5 mmHg compared to 136.8 ± 6.2 mmHg (n=8) in the control group after 21 days. The hypertensive response to Ang II was markedly reduced in the omega 3 group reaching 169.0 ± 7.8 mmHg whereas the omega 3 treatment alone had no effect (136.0 ± 4.2 mmHg). In second branch mesenteric artery rings, relaxations to acetylcholine (Ach) were markedly reduced in the Ang II group affecting the endothelium-dependent hyperpolarization (EDH)-mediated component to a greater extent than the NO-mediated component. The NAPDH oxidase inhibitor (VAS-2870) improved both the NO and the EDH component in the Ang II group. Pronounced endothelium-dependent contractile responses to Ach were observed in the Ang II group compared to the control group, which were abolished by indomethacin (cyclooxygenase inhibitor). Chronic intake of EPA:DHA 6:1 prevented the Ang II-induced endothelial dysfunction both by improving the NO- and EDH-mediated relaxations and by reducing endothelium-dependent contractile responses to Ach. The present findings indicate that chronic intake of EPA:DHA 6:1 prevented the development of hypertension and endothelial dysfunction induced by the infusion of Ang II to rats. The Ang II-induced endothelial dysfunction involves NADPH oxidase, indicating a redox-sensitive mechanism. The beneficial effect of EPA:DHA 6:1 is mediated by an

improvement of both the NO- and the EDH-mediated relaxations as well as a reduction of endothelium-dependent contractile response most likely by preventing oxidative stress.

P4426 | BEDSIDE
Fibrocalcific commitment of aortic valve interstitial cells via TF expression and signalling

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Purpose: Aortic valve stenosis (AVS) is an atherosclerosis-like process characterized by valve interstitial cell (VIC) commitment to fibrocalcification. Tissue factor (TF) expression was shown to be associated with calcification in human stenotic aortic valves. We investigated TF and downstream signalling pathways in VIC and its role in their pro-fibrocalcification commitment.
Methods: TF expression in control and fibrocalcific human aortic valves was assessed by immunohistochemistry, westernblot (antigen) and colorimetry (activity). Constitutive TF expression in VIC isolated from these valves and grown in culture, was likewise assessed. Inducible TF expression in IL1ß-stimulated (10 ng/mL) VIC isolated from control valves was also assessed. Downstream signalling pathways (ERK, PI3K, Smad2 and ß-catenin) of FVIIa/TF complex in IL1ß-stimulated VIC were assessed by westernblot. Results were expressed as mean (SEM).
Results: TF expression was significantly increased in fibrocalcific vs control aortic valves (antigen TF/ß-actin: 0.6±0.1 vs 0.3±0.08; activity: 253±25 vs 131±20 mU/mg protein, respectively). In both valves, TF expression was colocalized with VIC (neither endothelial cells nor macrophages). Constitutive TF expression in cultured VIC was significantly increased in VIC isolated from fibrocalcific vs control valves (antigen TF/ß-actin: 3.4±2.0 vs 0.7±0.1; activity: 37±6 vs 19±4 mU/mg protein, respectively). Following IL1beta stimulation (10 ng/mL) of VIC isolated from control valves, TF expression was significantly upregulated compared to unstimulated VIC (antigen TF/ß-actin: 1.8±0.4 vs 0.7±0.1; activity: 76±35 vs 19±4 mU/mg protein, respectively).
In a TF-dependant way (inhibition by pre-incubation with a specific anti-TF antibody), FVIIa stimulation of TF-overexpressing VIC induced, when compared to unstimulated VIC, a significant up-regulation of ERK (pERK/ERK 0.8±0.2 vs 0.2±0.1 respectively, 0.3±0.1 with anti-TF antibody) and PI3K (pPI3K/PI3K 4.5±0.9 vs 1.2±0.3 respectively, 1.3±0.6 with anti-TF antibody) signalling pathways. FVIIa stimulation of TF-overexpressing VIC also induced, when compared to unstimulated VIC, a significant up-regulation and nuclear translocation of Smad2/3 (pSmad2/Smad 2/3 0.2±0.02 vs 0.09±0.0.01 respectively, 0.08±0.006 with anti-TF antibody) and of ß-catenin (ß-catenin/ß-actin 1.2±0.07 vs 0.3±0.1 respectively, 0.3±0.1 with anti-TF antibody) signalling pathways.
Conclusions: These results may be in favour of an implication of TF/FVIIa axis in VIC commitment to AVS. Modulation of this pathway may represent a new therapeutic target in AVS treatment.

P4427 | BENCH
Pancreatic tumor-derived microparticles cause excessive venous thrombosis through intrinsically activated TF by excluding neutrophils and platelets

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Background: Pancreatic tumor patients are at an increased risk of developing venous thrombosis (DVT), which is associated with a significant mortality due to pulmonary embolism. However, it is unclear how malignant tumors cause remote thrombosis. One possible mechanism is the shedding of microparticles (MPs) into the blood.
Objective: We assessed the thrombogenic capacity and mechanisms of thrombogenesis of different pancreatic tumor and blood derived MPs in a murine model of DVT caused by flow reduction.
Methods: DVT was induced by flow restriction in the IVC, followed by injection of MPs. MPs were derived from blood of healthy donors (bMP), pancreatic tumor MPs were collected from L3.6pl and FG cell lines. Thrombus formation was assessed by CT, ultrasound, and intravital microscopy. Thrombi were harvested after 48 hrs and thrombus weight and incidence were quantified in C56Bl6, GPIb–/–, lowTF, LysMCreTFflox/flox, P-Selectin–/–, platelet/neutrophil depleted, PCK, ASS, dabigatran, enoxaparin treated mice. L3.6pl MPs were treated with anti-TF and anti-MUC1 antibodies. Thrombus composition was analyzed by immunohistochemistry.
Results: bMPs did not increase thrombus formation compared to control, but FG and L3.6pl MPs significantly increased thrombus weight, while there was no difference between these tumor MPs. However, the highest incidence (100%) was found in the L3.6pl group, which we analyzed in more detail. Using ultrasound and CT, we could show that L3.6pl MP injection markedly augmented DVT formation in vivo. DVT formation in the bMP group was dependent on P-Selectin, whereas it was not affected after L3.6pl MP injection, suggesting that tumor MP induced DVT is independent of leukocyte recruitment to the vessel wall. In addition, leukocyte and platelet accumulation was significantly reduced in the L.3.6pl group. Neutrophil depletion in the L.3.6pl group resulted in significantly increased thrombus weight, in contrast to the control group where thrombus formation was prevented. L3.6pl MP induced thrombosis was independent of platelets and FXII activation, but there was a synergistic effect of intrinsic tissue factor (TF). Thrombus formation could be prevented using anti-TF and anti-MUC-1 antibodies. The comparison of ASS, dabigatran, and enoxaparin showed that heparins are most effective in preventing L3.6pl MP induced venous thrombosis.
Conclusion: Here, we could show that tumor MPs are able to induce excessive DVT through intrinsically active TF by excluding neutrophils and platelets. Thus, the mechanisms of thrombus formation differ depending on the underlying disease.

P4428 | BENCH
Von Willebrand factor as a biomarker of acute changes of blood flow in a rabbit model of reversible supra-aortic stenosis

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Purpose: An acquired von Willebrand factor (VWF) deficiency, with a loss of the high molecular weight (HMW) multimers, is reported in various cardiovascular disorders, mainly aortic stenosis, in which the entire blood volume is exposed to high shear stress during each pass-through. VWF deficiency is corrected after the treatment of the pathological condition but kinetic data about recovery are scarce. We hypothesized that the loss/reapparance of VWF HMW multimers, related to the onset/offset of a high-shear cardiovascular disorder, might be highly dynamic in vivo.
Methods: We investigated the time-course of HMW multimers changes after the onset/offset of a reversible supra-aortic stenosis in 17 rabbits. The ascending aorta was surgically exposed after a median sternotomy under general sedation. An adjustable silicone vascular clamp was placed on the ascending aorta to induce a controlled circumferential stenosis with a reduction in cross sectionnal area >75%. Using this device, aortic stenosis and its reversion were immediate. Blood samples were collected before stenosis (T0), 5 and 30 minutes after induction of the stenosis (T5, T30) and subsequently 5 and 30 minutes after reversion of the stenosis (T35, T60). All measurments were performed on platelet-poor plasma. VWF antigen (VWF:Ag) was performed by ELISA and expressed as a percentage of a standard human plasma. VWF multimer analysis was performed by SDS-agarose 1.5% electrophoresis with loading normalized for VWF:Ag content. The percentage of HMW multimers (>15 mers) was determined using densitometric scanning. At the end of the experiment, rabbits were sacrificed. Results are expressed versus baseline value (mean ± SD). Time points were compared using a Wilcoxon rank test. P values less than 0.05 were considered statistically significant.
Results: A significant decrease of VWF HMW multimers was observed already after 5 minutes (ratio 0.76±0.13; $p<0.01$) and confirmed after 30 minutes (0.74±0.07; $p<0.01$) of supra-aortic stenosis. Conversely, a significant increase of VWF HMW multimers was observed 5 minutes (T35) after the reversal of the stenosis (0.89±0.13; $p<0.01$) with a complete recovery at the end (T60) of the procedure (0.98±0.10; $p<0.01$) (Fig 1). No significant changes in VWF antigen were observed.
Conclusion: Variations in VWF HMW multimers occur within minutes after the induction or the reversion of a supra-aortic stenosis. A prospective study (WITAWI) is currently evaluating VWF as a biomarker of the success of valve implantation performed by transcatheter aortic valve intervention.

P4429 | BENCH
Aging predisposes endothelial cells to increased telomere damage and proinflammatory cytokine expression

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Purpose: Aging is a major factor predisposing for multiple diseases. Endothelial cell dysfunction is a major risk factor in developing cardiovascular disease. The aim of our study was to determine the changes induced by aging on endothelial cells.
Methods: Human umbilical vein endothelial cells (HUVEC) were isolated and cultivated using standard cell culture methods. Aging was simulated by prolonged proliferation in a 1:3 splitting ratio. Proinflammatory cytokines and shelterin complex components and telomere length were determined by quantitative PCR, telomere oxidation was quantified by an enzyme digestion for oxidative DNA sites followed by quantitative PCR. Telomere damage foci were analyzed by fluorescence staining for 53BP1/TRF2.

Results: Aging HUVEC were characterized by a reduced telomere length (relative reduction of 62%, p=0.02) and increased telomere oxidation from 13% to 41% (p=0.01). This increased damage was accompanied by an increase in telomere dysfunction foci formation from 5.5% in young cells to 16.6% in aged cells (p=0.004). This indicated that aging is not only accompanied by a telomere length reduction, but also by telomere dysfunction. Furthermore, members of the shelterin complex, consisting of proteins responsible for protecting telomere integrity, show transcriptional repression in aging cells. Transcriptional reduction caused by aging was observed for TRF1 (33% reduction, p=0.001), TRF2 (43% reduction, p=0.02), POT1 (34% reduction, p=0.0001) and TIN2 (16% reduction, p=0.047). However, reduction in these components was not observed in endothelial cells that were immortalized by overexpressing telomerase, the enzyme capable of elongating telomeres. Still, telomerase did not act directly on shelterin expression, as short term overexpression of telomerase for 48h did not alter TRF1, TRF2, POT1 or TIN2 levels. Telomere dysfunction in aging HUVEC was accompanied by a 40% increased cell size (p=0.03), a 10h increased cell doubling time and an increased proinflammatory cytokine expression including 1.9 fold upregulation of PAI1 (p=0.002) and 2.7 fold upregulation of MCP1 (p=0.03).
Conclusion: Telomere dysfunction is apparent in aging endothelial cells. Furthermore, this telomere dysfunction is accompanied by transcriptional repression of shelterin components fueling telomere damage and probably causing characteristic signs of aging including a basal proinflammatory state and a reduction of proliferative capacity. Rejuvenating endothelial cells might restore telomere stability and reduce disease burden in patients with cardiovascular disease.

P4430 | BENCH
A new method to strengthen native saphenous veins for arterial bypass based on photo-chemical-induced collagen cross-linking

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Purpose: Saphenous Vein (SV) is the most used autograft in patients undergoing coronary artery bypass and the conduit of choice for surgical revascularization in patients with critical limb ischemia. Venous bypass can also find application where arterial revascularization is not possible. However, SV is often not available, due to anatomical or pathological condition (varices), and is frequently limited by age degeneration. With synthetic materials, clinical results at 5-10 years are good for large diameter vessels, whereas graft patency is poor for small-diameter vessels, due to thrombogenicity and neointimal hyperplasia. Thus, recovery of varices and strengthening of vein wall will be desirable. Our aim was SV diameter recovery and wall function restoration, using photo-chemical collagen cross-linking (CCL), according to the clinical protocol currently used to treat keratoconus.
Methods: We used a light source to activate covalent bonds among collagen fibrils. The photo-initiator was riboflavin. Blue light produced by a light-emitting diode at 1.5 cm distance was used as activator. SVs, harvested during bypass cardiac surgery, were stored in saline at 4°C. 1cm vein segment was longitudinally split to create two similar specimens. Treated specimens were pre-incubated in 1% riboflavin for 5, 10, 20 and 30 min. Then, they were maintained in 1% riboflavin and irradiated for same pre-incubation time. For controls, saline was used. Morphology was evaluated by histology, after fixation in formalin, embedding in paraffin and staining with hematoxylin/eosin. Morphometric and mechanical compliance evaluation was also performed.
Results: No significant effect was observed with incubation <30 min. A significant thickening of the sub-endothelial connective tissue and the tunica media of treated SV as compared to control was observed, without endothelial damage. 30 min treatment resulted in 3-time intimal thickening as compared to control, with fibroblast/myofibroblast proliferation and fibrous tissue deposition. Biomechanical changes due to greater rigidity were also clearly evident, with 30 min treated SVs avoiding falling when held with a forceps.
Conclusions: CCL led to a significant shrinking of venous tissue, resulting in compaction and mechanical strengthening. This process is simple, fast and free of toxic chemical cross-linking agents, with no possibility for side effects such as damage of nearby nerves. This method may find application in surgical procedures as peripheral or coronary artery bypass, when native SV are not suitable for arterial implantation, requiring diameter reduction or wall thickening.

P4431 | BENCH
Nitrosonifedipine ameliorates the progression of aortic aneurysms by exerting antioxidative effects

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Purpose: Aortic aneurysms (AAs) are common diseases among the elderly people and rupture of AAs carry a risk of death up to 90%. Even surgical intervention takes large risks of mortality. However, there is currently no medical management to retard the progression of AAs. We reported that nifedipine decomposes under light exposure to a stable nitroso analog, nitrosonifedipine (NO-NIF), which has potential as a novel antioxidant with radical scavenging abilities. We have recently demonstrated that NO-NIF ameliorated the vascular remodeling induced by angiotensin II (Ang II) treatment in mice independent of its blood pressure-lowering effects. In this study, we investigated the effects of NO-NIF on pharmacologically-induced AAs in mice.
Methods: In 10-week–old C57BL/6J male mice, hypertension was induced by Ang II (1000 ng/kg/min) for 6 weeks. β-aminopropionitrile (BAPN) (150 mg/kg/day) was administered for the first 2 weeks by osmotic-pump to induce degeneration of elastic lamina. NO-NIF was intraperitoneally injected at 30 mg/kg/day for 6 weeks. In vitro studies were performed using human umbilical vein endothelial cells (HUVECs).
Results: The combined infusion of Ang II and BAPN induced degenerative aneurysm of the thoracic and/or abdominal aorta (30/41; 73%). NO-NIF significantly reduced the incidence of AAs (19/38; 50%) and thoracic aortic aneurysm (6/38; 15%). Although there was no difference in systolic blood pressure (SBP) between the vehicle- and NO-NIF-treated groups in Ang II and BAPN-induced AAs in mice (SBP; Ang II+BAPN vs Ang II+BAPN+NO-NIF; 135.0±5.2 mmHg vs 134.8±7.3 mmHg). NO-NIF significantly suppressed the degeneration of elastic lamina within the aortic wall associated with aneurysm formation. NO-NIF inhibited reactive oxygen species (ROS) within the aortic wall measured by dihydroethidium staining. The expression of cyclophilin A, which has been reported to enhance vascular ROS and aneurysm formation, is attenuated by NO-NIF treatment in aorta of Ang II and BAPN-treated mice. Also NO-NIF inhibited the expression of vascular cell adhesion molecule 1 (VCAM-1) in the endothelium. Supporting this observation, NO-NIF inhibited TNF-α-induced VCAM-1 expression and NF-κB activation in HUVECs. Hydrogen peroxide-induced p90RSK phosphorylation, which is increased by endothelial cell damage, was also inhibited by NO-NIF treatment in HUVECs.
Conclusions: These findings suggest that NO-NIF prevents aneurysm progression via its antioxidative effects and partly through the protective effects against endothelial cells.

P4432 | BENCH
Different effects of NG-nitro-L-arginine methylester and 7-nitroindazole administered individually and/or together on cardiovascular system of Wistar rats and SHR

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Purpose: Changes in endogenous NO production lead to structural and functional alterations in cardiovascular system. The aim of the study was to evaluated the effect of two NO synthase inhibitors NG-nitro-L-arginine methylester (L-NAME) and 7-nitroindazole (7NI) administered individually and/or together on cardiovascular system of Wistar rats and spontaneously hypertensive rats (SHR).
Methods: L-NAME (50 mg/kg/day in tap water) and 7NI (10 mg/kg/day in pellets) was administered individually or together to Wistar rats and 7NI was administered to SHR from 10th-16th week of age (n=20 in each group). Blood pressure (BP) was measured by the plethysmographic method on the tail artery weekly. For morphological study ten animals were perfused with fixative (120 mmHg) and thoracic aorta, carotid and coronary arteries were processed according to electron microscopic procedure. Cross sectional areas (CSA) of endothelial cells (EC), muscle cells (SMC), and extracellular matrix (ECM) were assigned in coronary wall (intima+media). For functional investigation aortal rings from ten animals from each group were studied in organ bath.
Results: In Wistar rats L-NAME administration evoked BP increase, hypertrophy of the heart and arterial wall (intima+media) of all arteries, increase of CSA of EC, SMC, ECM in coronary artery, and decrease of endothelial dependent relaxation (EDR) to acetylcholine. 7NI administration evoked BP independent hypotrophy of the heart and arterial wall, decrease of CSA of EC and SMC without affecting CSA of ECM, and acetylcholine induced EDR. Administration of 7NI along with L-NAME in comparison to L-NAME (i) decreased BP, trophicity of the heart and arterial wall, and (ii) did not affect EDR to acetylcholine. In SHR 7NI treatment did not evoke any effect on the studied parameters.
Conclusions: The data suggest that L-NAME and 7NI affect different or differently regulatory mechanisms in cardiovascular system of normotensive rats and SHR.
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ENDOTHELIAL FUNCTION: BASIC I

P4434 | BENCH
Microparticles released by replicative senescence in cultured endothelial cells promote premature senescence associated with an impaired NO formation and oxidative stress

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Background: Circulating endothelial microparticles (EMPs) are increased in several age-related vascular diseases such as coronary artery disease, peripheral

vascular disease and allograft rejection following heart transplantation. EMPs, besides being pertinent biomarkers, might most likely also contribute to the development of endothelial dysfunction and vascular damage. This study examined the possibility that the induction of endothelial senescence is associated with EMPs shedding, and that senescence-related EMPs promotes endothelial senescence and prothrombotic changes including (i) enhanced TF expression and activity (ii) reduced endothelial formation of nitric oxide, a potent inhibitor of platelet aggregation.

Methods and results: Replicative senescence was induced by sequential passaging of primary cultures of porcine coronary artery endothelial cells (ECs) up to the third passage (P3). Cells retained phenotypic characteristics of ECs at P1 and P2 whereas they exhibited features of senescence with increased senescence-associated β-galactosidase positive staining and an increased % of cells retained in the G0/G1 phase of the cell cycle at P3. Exposure of ECs at P1 to EMPs (10 nM) collected from the conditioned medium of ECs at P3 increased the % of cells in G0/G1 phase and SA-β-Gal staining after (24-48 h). ECs at P1, which had been exposed to EMPs derived from ECs at P3 for 8 h had an increased expression level of the senescence markers p53, its downstream target p21, and the adaptor protein p66Shc. EMPs derived from ECs at P3 induced oxidative stress in target ECs at P1 as detected using dihydroethidine staining. In addition, EMPs reduced the ability of ECs to inhibit U46619-induced platelet aggregation and induced up-regulation of TF expression in ECs.

Conclusion: The present findings indicate that endothelial senescence is associated with an increased shedding of EMPs, which, in turn, promote premature senescence and prothrombotic changes. This response to senescence-related EMPs involves oxidative stress, the up-regulation of p53 and p21, and a reduced formation of NO. They further suggest that EMPs released by senescent endothelial cells may contribute in an autoamplification loop to the development of an endothelial dysfunction and subsequent thrombogenicity.

P4435 | BENCH
Catecholamines reduced the secreted orosomucoid by epicardial adipose tissue in diabetes and coronary artery disease patients: consequences in endothelial cells

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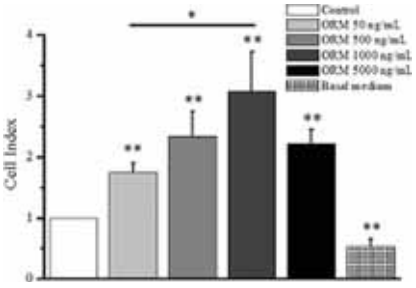
Purpose: Type 2 diabetes mellitus (T2DM) is associated with fat and autonomic dysfunction. Epicardial adipose tissue (EAT), which is highly innervated, plays an endocrine role over the myocardium and endothelial cells. Our aim was to assess the relationship between its secretion profile by EAT and its catecholaminergic regulation in T2DM and coronary artery disease (CAD) patients.

Methods: We obtained EAT, subcutaneous adipose tissue (SAT) and plasma from 55 patients undergoing elective cardiac surgery. The explants were stimulated by isoproterenol (ISO) 1uM for 6 hours. After, the released ORM by fat explants and plasma levels were analyzed by ELISA. mRNA or protein expression was analyzed by real time PCR and western blot, respectively. The endothelial effects induced by ORM were analyzed by impedance and wound healing assays.

Results: We found that ISO was able to increase the ORM secretion by SAT explants ($p<0.05$) but not by EAT. Moreover, in this tissue, the secretion and the content levels of ORM was lower in patients with than those without T2DM (238±131 vs. 405±250 ng/ml; $p<0.01$). The local ORM secretion by EAT was significantly decreased and regulated by b-adrenergic stimulation in T2DM and CAD patients. This effect was not observed in SAT. After testing the ORM effect in endothelial cells, our results revealed that this protein was able to induce the endothelial proliferation and repairing in a dose-dependent manner.



Conclusions: Autonomic system might affect the integrity of the epicardial-coronary barrier by regulation of EAT-released ORM levels. The different secretion profile in EAT from T2DM and CAD patients after the b-adrenergic stimulation could be a link between coronary endothelial and dysautonomia.

P4436 | BENCH
Swimming training improves arterial vasomotor function in spontaneously hypertensive rats: role of reactive oxygen species and nitrogen

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Purpose: Oxidative stress plays an important pathophysiological role in hypertension. Increased vascular superoxide (O-2) has been linked with decreased nitric oxide (NO) and impaired endothelial-dependent vasodilation. Aerobic training (AT) improves endothelial-dependent aortic vasodilation and decrease high blood pressure in spontaneously hypertensive rats (SHR). However, the molecular mechanism of AT on vasomotricity is not completly understood. The aim of this study was to determine if AT decreases O-2, increases NO, leading to an improvement of endothelial-dependent vasodilation in aorta of SHR and diminishing blood pressure (BP).

Methods: SHR and Wistar Kyoto (WKY) rats were distributed in to sedentary (SHRsd, n=7 and WKYsd, n=7) and swimming training (SHRtr, n=7 and WKYtr, n=7), which consisted of 5 days/week, 1 h/day with 4% of body weigth load. After 10 weeks of sedentary or AT period, rats were euthanized and thoracic aorta was removed to evaluated in vitro endothelium-dependent vasodilation to acetylcholine (ACh,10-10 to 10-4M) with and without preincubated N-nitro-L-arginine methyl ester (L-NAME, 10-4M) and endothelium-independent vasodilation to sodium nitroprusside (SNP). Two rings was used to perform proteins levels of endothelial nitric oxide (eNOS) and nicotinamide adenine dinucleotide phosphate-oxidase homologues NOX4 and bioavailability of O-2 and NO measurements. BP was measured by computerized tail-cuff system.

Results: Aerobic training significantly increased maximal vasodilation reponse to ACh in SHRtr compared with SHRsd (85.9±4.3 vs 71.6±5.2%, p=0.03). When the vessels was incubated with L-NAME, were not found the difference in the maximal vasodilation. Maximal vasodilation reponse to SNP were similar in SHRtr vs SHRsd. Also the SHRtr decreased O-2 content (p=0.001), improved NO bioavailability (p=0.007), and decreased NOX4 protein expression (p=0.02) when compared SHRsd. Moreover, BP decreased within SHRtr group (170.3±2.2 vs. 146.8±4.0 mmHg, $p<0.001$) and compared to SHRsd (175.4±3.6 vs. 146.8±4.0 mmHg, $p<0.001$). Interestingly, protein levels of eNOS were similar between SHRtr and SHRsd

Conclusion: In SHR rats, swimming aerobic training decreased vascular superoxide generation and increased NO bioavailability. These results suggest an important mechanism that could explain, at least in part, the improvement aortic endothelial function and decreased blood pressure.

P4437 | BENCH
Role of adenosine triphosphate (ATP) and its bioactive metabolites for impaired vasomotor function in the aorta of caveolin-1 deficient mice

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Caveolin-1 knockout mice develop a severe cardiopulmonary phenotype with left ventricular hypertrophy and a reduced cardiac output. This phenotype was reversed by inhibition or genetic deletion of endothelial NO-Synthase (eNOS). Molecular interactions of eNOS and Caveolin-1 are known for the vascular system. This suggests an involvement of vascular mechanisms in the pathogenesis of the left ventricular phenotype of Caveolin-1 deficient mice (Cav1–/–).

To characterize alterations in the active and passive vessel diameter regulation, isometric force measurements of aorta segments were performed. The internal diameter and the Young's modulus were calculated from resting tension curves assessed in a Mulvany myograph. The internal diameter was significantly larger in Cav1–/– mice (0.77±0.04 mm) compared to wild type controls (0.67±0.01 mm) and the Young's modulus was similar for both groups.

The vascular diameter is also controlled by various humoral factors such as ATP and its metabolites. In mouse thoracic aorta ex vivo application of ATP in a Mulvany myograph resulted in a biphasic response. Following a pre-constriction with phenylephrine, low concentrations (0.3 to 30 μmol/L) resulted in a vasorelaxation while higher concentrations induced a vasoconstriction. The ATP-induced maximum vasorelaxation response was nearly doubled in Cav1–/– mice compared to wild type controls. Combined application of the radical scavenger Tiron and L-NMMA (inhibitor of eNOS) abolished the ATP-mediated relaxation in wild type mice, but not in Cav1–/– mice. These findings suggest that an additional signal transduction pathway for ATP mediated vasorelaxation is present in Cav1–/– mice.

In the circulation, ATP is rapidly degraded to adenosine as evidenced by HPLC measurements. In mouse aorta concentrations of 1-30 nmol/L adenosine induced a minimal vasorelaxation in wild type mice (6%) and this relaxation was not present in Cav1–/– mice. Even more, higher concentrations of adenosine evoked a strong vasoconstrictor response and this effect was more pronounced in Cav1–/– compared to wild type mice. These findings exclude the ATP degradation product adenosine as a mediator of the augmented ATP vasorelaxation.

Taken together, Cav1–/– mice display a major change of metabolic control of vessel diameter in aorta ring preparations. While ATP-mediated vasorelaxation

responses were augmented in Cav1–/– mice independent of nitric oxide and radical production, adenosine, a metabolite of the ATP which usually is a strong vasodilator, acted as a strong vasoconstrictor.

P4438 | BENCH
Activation of RIG-I causes vascular endothelial dysfunction

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Purpose: Atherosclerosis is defined as a chronic inflammation of the vascular system. Number and degree of infections during lifetime are positively correlated with the risk of development of atherosclerosis, also referred to as "infectious burden". Therefore, infections are considered an independant risk factor for atherosclerosis.
Pathogen-associated molecular patterns (PAMP), for example viral or bacterial nucleic acids are detected by pattern recognition receptors (PRR), which are part of the innate immune system and PRR activation results in a proinflammatory immune response. Interestingly, PRR are part of cells that mainly drive the atherosclerotic process, namely macrophages, vascular smooth muscle cells and endothelial cells. Therefore, we tested whether Endothelial Cells and Endothelial Progenitor Cells (EPC) express RIG-I, a PRR known to detect viral nucleic acids, and investigated possible proinflammatory consequences for endothelial biology.
Methods and results: In vitro immunohistochemistry and real-time-pcr experiments show that RIG-I is expressed in Endothelial Progenitor Cells and their progeny Human Coronary Artery Endothelial Cells (HCAEC). Receptor activation leads to enhanced reactive-oxygen species (ROS) formation in both cell types. Additionally, RIG-I stimulation leads to reduced proliferation and migration of HCAECs suggesting impaired endothelial function. Furthermore, HCAEC release proinflammatory cytokines such as IL-6 and IP-10 upon specific RIG-I stimulation.
In vivo systemic RIG-I stimulation in wild type mice leads to enhanced numbers of EPC in the peripheral blood and bone marrow. Additionally, the number of circulating Endothelial Microparticles (EMP) is augmented, organ chamber experiments show impaired endothelial function and ROS production in aortic segments is elevated, indicating activation and endothelial damage. Moreover, re-endothelialization after focal electrical endothelial denudation of the common carotid artery is impaired by RIG-I activation. Interestingly, these effects could not be demonstrated in RIG-I knock out mice, suggesting a possible role of RIG-I in endothelial biology.
Conclusion: Our experiments clearly demonstrate proinflammatory effects in HCAEC and EPC in vitro. In wild type mice specific RIG-I activation causes endothelial dysfunction and impairs re-endothelialization, suggesting a possible role of RIG-I in endothelial function and atherogenesis. A better understanding of innate immune mechanisms might allow the identification of possible new therapeutic options for patients with atherosclerosis.

P4439 | BENCH
Cyclosporine A prevents replicative senescence-related endothelial dysfunction promoting pro-thrombotic and pro-coagulant responses in cultured coronary artery endothelial cells: role of p66 Shc

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Background and aims: During myocardial infarction, clinical studies have indicated a higher incidence of death with increasing age, and that cyclosporine A (CsA) prevents lethal reperfusion injuries. Since aging is associated with the induction of vascular and endothelial senescence, an irreversible cell cycle arrest involving an increased activity of p53 and its downstream target p21, the possibility that CsA prevents endothelial senescence was evaluated.
Material and methods: Replicative senescence was induced by sequential passaging of primary cultures of endothelial cells up to the fourth passage (P4). Senescence associated β-galactosidase (SA-β-gal) activity and the mitochondrial membrane potential were evaluated by flow cytometry using C15-FDG and Dioc6 specific probes, respectively. Endothelial NO formation was evaluated indirectly using washed human platelets. Procoagulant microparticles were measured by multiwell prothrombinase assay following their capture by annexin-5, and the protein expression level by Western blot analysis.
Results: Endothelial cells showed a progressive increase in senescent markers (SA-β-gal activity, p53, p21 an p16), NADPH oxidase subunits gp91 phox and p47 phox and p66 Shc, down-regulation of eNOS and prohibitin, associated with a reduction of the Dioc6 fluorescent signal from P1 to P4. The acquisition of a procoagulant phenotype was characterized by an enhanced expression of tissue factor and the shedding of procoagulant microparticles. Whilst endothelial cells at P1 strongly inhibited washed human platelet aggregation in response to U46619, important platelet aggregation could be evidenced at P3 cells surface. Exposure of endothelial cells at P3 to CsA (0.3 to 30 μg/ml) prevented replicative senescence-induced SA-β-gal activity, and changes in protein expression and of the mitochondrial membrane potential. In addition, CsA restored the inhibitory activity of endothelial cells at P3 on platelet aggregation and reduced the sheding of procoagulant microparticles.
Conclusions: The present findings indicate that replicative senescence is associated with a reduced ability of endothelial cells to inhibit platelet aggregation, and an increased expression of tissue factor and shedding of microparticules. CsA delays the senescence-related impairment of the endothelial function most likely by preventing the upregulation of p66 Shc and NADPH oxidase, and the down-regulation of eNOS and prohibitin. CsA might help to protect the vascular system by preventing endothelial senescence and the subsequent development of prothrombotic and pro-coaguant responses.

P4440 | BENCH
Differential expression of prothrombotic and proinflammatory markers in the human left and right atrial appendage

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Purpose: The most serious complication associated to atrial fibrillation (AF) is the risk of thromboembolic complications such as stroke. Thrombi are more frequently formed in the left atrial appendage (LAA) as compared to the right atrial appendage (RAA). This study was designed to assess the difference between endocardial cells (ECs) of the LAA vs. RAA with respect to expression and induction of pro-thrombotic and pro-inflammatory markers in atrial fibrillation patients.
Methods: Atrial fibrillation patients undergoing coronary artery bypass grafting and/or valve surgery were included in the study. LAA was surgically removed and RAA was resected during insertion of the heart-lung machine cannula tube. To isolate ECs from the other parts of the specimen, appendages were cut open, incubated with collagenase-dispase enzyme solution and then cultured with supplemented DMEM medium. Next, purity of cells was assessed by FACS and protein expression of key thrombotic and inflammatory factors was studied by Western blotting.
Results: Isolated ECs displayed a 98.1% purity for triple positive staining (VEGF-R2, CD31, CD146) as assessed by FACS analysis. Morphology and growth rate of both RAA-ECs and LAA-ECs were similar as compared to commercially available reference human aortic endothelial cells. LAA-ECs showed a significant increase in prothrombotic tissue factor (TF) and plasminogen activator inhibitor-1 (PAI-1) protein expression after stimulation with TNF-α as compared to RAA-ECs. Moreover, expression of proinflammatory vascular cell adhesion molecule-1 (VCAM-1) was significantly higher in stimulated LAA-ECs as compared to stimulated RAA-ECs.
Conclusions: The observed differential increase in protein expression of prothrombotic TF/PAI-1 and proinflammatory VCAM-1 represents an important novel information in the understanding of the molecular mechanisms underlying thrombus formation in AF patients, and may represent one mechanism for the enhanced thrombogenicity of the left vs. right atrial appendage.

P4441 | BENCH
c-Src tyrosine kinase mediates high glucose-induced endothelin-1 expression in diabetes

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Purpose: Endothelin-1 (ET-1), the main effector of the endothelin system, plays an important role in the pathophysiology of cardiovascular disorders associated with diabetes mellitus by inducing vasoconstriction and impaired vascular relaxation, inflammation, oxidative stress, vascular remodeling and metabolic alterations in the vascular wall cells. The molecular mechanisms leading to ET-1 up-regulation in diabetes are not entirely defined. c-Src protein tyrosine kinase regulates important pathophysiological aspects of vascular response to diabetic conditions. In this study, we aimed to elucidating whether a causal relationship among high glucose-activated c-Src and ET-1 up-regulation exists.
Methods and results: Human umbilical vein endothelial cells EAhy926 were exposed to high levels of glucose (16.5-25 mM) for 24 h. Real-time PCR, enzyme-linked immunosorbent assay, and Western blot analysis were used to investigate ET-1 regulation. The c-Src activity and expression were selectively downregulated by pharmacological inhibition and siRNA-mediated gene silencing. High glucose dose-dependently up-regulated ET-1 gene and peptide expression. It also induced significant increases in c-Src phosphorylation. Chemical inhibition as well as silencing of c-Src decreased significantly the high-glucose (25 mM) induced ET-1 expression.
Male C57BL/6 mice were rendered diabetic by intraperitoneal injection of streptozotocin and treated for 5 weeks with either vehicle or Src I1 (1 mg/kg/day), a specific c-Src inhibitor. Circulating ET-1 and the mRNA expression levels of ET-1, VCAM-1, ICAM-1, and MCP-1 were significantly elevated in the aorta of diabetic mice compared to normal animals. Treatment with Src I1 significantly reduced the up-regulated ET-1 peptide, the gene expression of ET-1, as well as the mRNA levels of MCP-1, VCAM-1, and ICAM-1, important pro-inflammatory molecules mediating the recruitment and extravasations of circulation immune cells.
Conclusions: These data provide new insights into the regulation of ET-1 by c-

Src in endothelial cells in diabetes. Since c-Src mediates the signals triggered by numerous diabetic factors including high glucose concentration, cytokines, reactive oxygen species, hormones and vasoactive agents, modulation of c-Src activity may represent a new pharmacological approach to counteract the effects induced by the ET-1 in diabetes and its complications.

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P4442 | BENCH
Hyperosmolarity-enhanced COX-2 expression contributes to high glucose-induced microangiopathy

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Hypothesis: Diabetic hyperglycemia increases plasma osmolarity, leading to adaptive cellular responses. Cycloxygenase-2 (COX-2) plays a role in angiogenesis and plaque stability. We tested the hypothesis that glucose-induced hyperosmolarity promotes angiogenesis through activation of COX-2 expression.
Methods: Human aortic endothelial cells (HAEC) and dermal microvascular endothelial cells (HMVEC) were incubated with 5.5 mmol/L glucose (normoglycemia), high glucose (HG, at 12.5, 25 and 45 mmol/L), or equimolar concentrations of the hyperosmolar control mannitol (HM).
Results: Both HG and HM increased the expression of the water channel aquaporin-1 (AQP1) and of COX-2. HG and HM for 1 h increased the nuclear accumulation of Tonicity enhancer binding protein (TonEBP) and its binding to Tonicity enhancer element at electrophoretic mobility shift assay. HG and HM induced endothelial migration at a fluorimetric assay, and tubulization in Matrigel. Targeting the osmosignaling pathway with small interfering RNAs to AQP1 and to TonEBP both reverted the inducing effects of HG and HM on COX-2 expression, as well as angiogenic activities. Finally, compared with age- and sex-matched C57/BL6 control mice (N=5 wild type, WT), the retina of Ins2 Akita diabetic mice (N=5, male, 1 year-old mice) showed higher vascular density as visualized with CD31 staining (Fig. 1A, B; ONL, outer nuclear layers; OPL, outer plexiform layers; INL, inner nuclear layers; IPL, inner plexiform layers), and increased expression of AQP1 and COX-2 (panel C, D) (**$p<0.01$ by ANOVA and t-test).

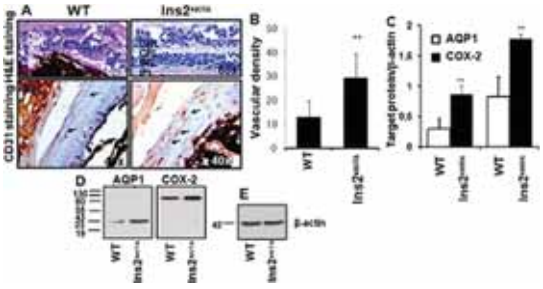

Figure 1. Retinal microangiopathy.

Conclusion: By activating the water channels AQP1 and TonEBP, hyperosmolarity caused by HG or HM induces COX-2 expression and angiogenesis in human endothelial cells, which may be relevant for microvascular complications of diabetes.

P4443 | BENCH
(–)-Epicatechin enhances vascular regeneration

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Purpose: Intake of dietary flavanols is associated with better cardiovascular outcome. (–)-Epicatechin (Epi) one of the major dietary flavanols, has shown to improve flow-mediated vasodilation (FMD) and mobilize circulating angiogenic cells.
Methods and results: To demonstrate the efficacy of Epi to improve conduit artery endothelial vasodilator function, FMD of the femoral artery was measured using ultrasound in male 12 week old C57/Bl6 mice (n=6 per group). Mice received Epi at 0.2–10 mg/kg body weight (BM) orally. Measurements were taken after 30 minutes and 1 week after daily supplementation. To assess vascular regeneration, mice were subjected to hindlimb ischemia (HLI) and recovery of perfusion monitored with laser Doppler perfusion imaging. Perfusion was monitored in relation to the contralateral hindlimb. After baseline perfusion measurements, induction of HLI was conducted through two ligations (proximal and distal to deep femoral artery). In order to test the impact of Epi on vascular regeneration, animals were fed vehicle or increasing daily doses of Epi (1–10 mg/kg) starting 5 days prior to HLI till end of experiments. eNOS knock-out animals served as controls. Similar to humans, consumption of Epi increased endothelial function. Oral application of Epi 0.2–10 mg/kg BW led to u-shaped dose-dependent increases in FMD of the femoral artery after acute and 1 week supplementation indicating efficacy of Epi to improve FMD in mice. Maximal values were achieved at 2 mg/kg. FMD responses were not present in eNOS KO animals and after infusion of a competitive NOS inhibitor. After HLI perfusion decreased in the operated limb to 10–15% and recovered to 54±6% as compared to the contralateral limb in control animals. Epi feeding led to a significant dose-dependent improvement in perfusion recovery with maximal effects observed at 2 mg/kg BW per day (81±7%). In parallel, in morphpmetric analysis we observed a significantly increased number of capillaries in the latter group suggesting enhanced angiogenesis. In eNOS KO animals, hindlimb angiogenesis was impaired as compared to WT animals and L-NAME blocked the Epi related improvements in hindlimb perfusion. In vitro, the incubation of endothelial cells with plasma obtained after consumption of flavanols led to enhanced chemotaxis and tube-formation on matrigel. The cellular responses were inhibited by a NOS inhibitor and a PI3 Kinase inhibitor.
Conclusion: Our data suggest that (–)-epicatechin can improve vascular regeneration by affecting eNOS-dependent cellular functions at amounts that can be achieved with regular diet in humans.

IMAGING FOR PROGNOSIS

P4445 | SPOTLIGHT
Incremental prognostic significance of late gadolinium enhanced magnetic resonance imaging on SYNTAX score in high risk patients

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Background: The purpose of this study was to assess the incremental prognostic value of late gadolinium enhanced magnetic resonance imaging (LGE-MRI) on the Synergy Between PCI With Taxus and Cardiac Surgery Score (SYNTAXsc) in predicting cardiovascular events in high risk patients.
Materials and methods: We studied 280 patients (mean age: 66±13 years) with stable coronary artery disease (CAD). Percentage myocardium affected by MI (%LGE) was calculated. All patients underwent X-ray coronary angiogram and each lesion with ≥50% diameter stenosis in vessels ≥1.5 mm in diameter was scored using the SYNTAXsc algorithm. Major outcome was incidence of cardiovascular events including cardiovascular death, nonfatal MI, unstable angina, ischemic stroke, coronary revascularization, re-hospitalization for heart failure.
Results: During a median follow-up duration of 2.9 years, 37 patients experienced cardiovascular event. When % LGE was added to FRS, EF and SYNTAXsc, the C-statistics for cardiovascular events improved with good global model fit and calibration (C-statistics: FRS 0.57, FRS+%LGE 0.76, FRS+EF 0.61, FRS+EF+%LGE 0.75, FRS+SYNTAXsc 0.72, FRS+SYNTAXsc +%LGE 0.77, FRS+EF+SYNTAXsc 0.73, FRS+EF+SYNTAXsc+%LGE 0.76), indicating the incremental value of %LGE for predicting cardiovascular outcomes.

C-statistics for Cox proportional hazards analysis to predict future cardiovascular events

	C-statistics	95% CI		Increment in C-statistics
		Lower limit	Upper limit	
FRS	0.57	0.51	0.63	
FRS + %LGE	0.76	0.66	0.86	0.21
FRS + EF	0.61	0.52	0.70	
FRS + EF + %LGE	0.75	0.67	0.86	0.14
FRS + Syntax score	0.72	0.63	0.81	
FRS + Syntax score + %LGE	0.77	0.67	0.86	0.04
FRS + EF + Syntax score	0.73	0.65	0.81	
FRS + EF + Syntax score + %LGE	0.76	0.67	0.86	0.03

CI, confidence interval.

Conclusions: Myocardial scar assessed by LGE-MRI significantly correlated with future cardiovascular events. Quantitative evaluation of MI by LGE-MRI improved the risk stratification when added to the FRS, EF and SYNTAXsc.

P4446 | BEDSIDE
Impact of intramyocardial hemorrhage on LV remodeling in reperfused acute myocardial infarction

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Purpose: Left ventricular (LV) remodeling associated with low LV ejection fraction following reperfused acute myocardial infarction (AMI), may occur in some patients. We investigated the prognostic value of infarct size (IS), extent of microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH) as assessed by comprehensive cardiovascular magnetic resonance (CMR).
Methods: Hundred and twelve patients underwent cardiovascular magnetic resonance at 1.5 Tesla with T2-weighted and T2* imaging and late gadolinium enhancement at 4 days ±2 and 6 months follow-up following primary percutaneous coronary intervention for AMI. LV remodeling was defined as an increase >20% of left ventricle end-systolic volume (EDV) at follow-up.
Results: All patients were analyzed. LV remodeling was observed in 38 patients (34%). 53 patients (47%) presented with Anterior AMI, 26 with Lateral (23%) and

33 with Inferior MI (29%). Mean age was 54±12y.o (75% male). Mean delay for reperfusion therapy was 115±100min. Despite identical EDV, patients with LV remodeling had lower LVEF at baseline (45%±7 vs 51±8, p<0.01), a bigger IS (42g±20 vs 32g±20; p<0.01) and MVO extent (p<0.01). By multivariate analysis, IMH (OR=2.8[1.3-6.0]) and IS (OR=3.2[1.8-12.5]) were identified as independent predictors of LV remodeling.
Conclusions: Presence of IMH assessed by T2* CMR significantly influences LV remodeling. IS and IMH are independent predictors of LV remodeling following reperfused AMI.

P4447 | BEDSIDE
Left ventricular global function index assessed by cardiac magnetic resonance imaging is a novel marker for the prediction of cardiovascular events in patients with acute reperfused ST-elevation myoca

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Background: The left ventricular global function index (LVGFI) is a novel indicator of cardiac performance. In healthy individuals, decreased values are strongly associated with major adverse cardiovascular events (MACE). Its role in patients after acute myocardial infarction is unknown and prognostic data are completely lacking. Aim of this study was to investigate the relationship between the LVGFI and infarct characteristics as well as prognosis in a large multicenter ST-segment elevation myocardial infarction (STEMI) population treated with primary percutaneous coronary intervention (PCI).
Methods: We enrolled 795 STEMI patients reperfused by primary PCI (<12 h after symptom onset) in this study at 8 centers. In all patients CMR was completed within one week after infarction using a standardized infarction protocol. Central core lab-masked analyses for the measurement of infarct characteristics (infarct size, myocardial salvage, microvascular obstruction) and the LVGFI were performed. The LVGFI was defined by the ratio of stroke volume divided by LV total volume defined as the sum of mean LV cavity and myocardial volumes. The primary clinical endpoint of the study was the occurrence of MACE within 12 months after infarction.
Results: The mean LVGFI was 31% (interquartile range 26-37). LVGFI was significantly inversely related with infarct size, myocardial salvage and microvascular obstruction (p<0.001 for all). In addition, there was a strong positive correlation between the LVGFI and left ventricular ejection fraction (r=0.86, p<0.001). In adjusted models, the combined clinical endpoint was significantly associated with LVGFI (hazard ratio=0.78, p<0.001). LVGFI had a significant independent predictive value in the multivariable model for MACE (p<0.001).
Conclusions: This large multicenter study demonstrates for the first time that the LVGFI, a novel parameter of cardiac performance, is strongly associated with myocardial damage in patients after STEMI. Moreover, the LVGFI was a powerful independent predictor of hard cardiovascular events and might serve as an important functional parameter of poor outcome in STEMI patients.

P4448 | BEDSIDE
The diagnostic utility and the prognostic implication of cardiovascular magnetic resonance in patients with NSTEMI and no significant lesions in coronary arteries

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Purpose: Non-ST elevation Myocardial infarction (NSTEMI) and no significant coronary artery disease is an important subtype of myocardial infarction. Cardiovascular magnetic resonance (CMR) offers a potential opportunity to clarify the underlying cause in this group of patients. The objective of this study was to investigate the diagnostic value and the prognostic implication of CMR in NSTEMI patients without significant lesions in coronary arteries.
Methods: A retrospective monocentric study enrolling all subsequent patients hospitalized for NSTEMI without significant lesions in coronary arteries (stenosis <50%), between January 2004 and January 2010. All patients underwent cardiac CMR with sequences dedicated for the evaluation of myocardial delayed enhancement. CMR scans were analyzed independently by two experienced interpreters.
Results: CMR provided etiologic diagnosis in 117 patients (84.2%). In the remaining patients (non-contributory CMR), there was no detectable infarction or inflammation and no additional new diagnosis was made. Myocarditis was the most common diagnosis, which was present in 63.2% of the patients. Myocardial infarction was found in 43 patients (36.8%). The limiting factors of CMR to identify the underlying cause were: female sex (63.6% vs 30.8%; p<0.005) and a low level of troponin (0.8±1.0 ng/ml vs 7.1±7.7 ng/ml; p<0.0001). At hospital discharge and after a mean follow up of 55 months, patients with non-contributory CMR had significantly lower rates of secondary prevention therapies prescription compared with the ischemic group (all probability values <0.0001). At long term follow up, MACE (death, non fatal MI and TLR) were significantly higher in the confirmed ischemic patients as compared with non-contributory CMR group (12.2% vs 0%) (p=<0.0001).
Conclusion: Our study demonstrates the interesting role of CMR to identify the underlying cause of NSTEMI patients without significant lesions in coronary arteries. Female sex and low level of troponin were associated with non-contributory CMR. Our study demonstrates also that patients with non-contributory CMR have an excellent prognosis although they received a lower rate of secondary prevention medication prescription. These findings highlight an opportunity to clarify the care of this group.

P4449 | BEDSIDE
Left ventricular remodeling assessed by cardiac magnetic resonance after a ST-elevation myocardial infarction treated with primary percutaneous coronary intervention

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After an acute ST segment elevation myocardial infarction (STEMI), the presence of adverse left ventricular remodeling (LVR) is related to an increase of morbimortality at follow-up. This remodeling is characterized by the presence of left ventricular (LV) dilatation, as well as changes in its morphology and geometry.
The aim of our study is to determine the parameters related to the development of LVR based on cardiac magnetic resonance (CRM) and its incidence, as well as to evaluate the morphological and geometric changes in LV after a STEMI.
This prospective study included 127 consecutive patients with a first STEMI treated with primary percutaneous coronary intervention, and studied with a CMR within the first week and at 6 months. We acquired cine sequences in order to assess LV volumes and ejection fraction, STIR sequences to determine the myocardial area at risk (AAR), and late gadolinium enhancement sequences to assess infarct size (IS), microvascular obstruction (MVO) and the myocardial salvage index (MSI). LVR was defined by an increase of LV end-diastolic volume ≥20%. We also calculated classical parameters of LVR: thinning ratio, expansion index and sphericity index. Among these 127 patients, 40 (31.5%) developed LVR. Mean age was 60 years, 45.6% had an anterior STEMI, and time from symptoms onset to TIMI 3 was 208±65min. At the univariate analysis, we found association (p<0.05) of the following factors with a greater risk of LVR development: IS (32.3% of LV mass in patients who developed LVR vs 21% in non-LVR), AAR (39.5% vs 31.7%), MVO (1.6g vs 0g) and infarct localization (60% of LVR were anterior vs 39% of non-LVR).
However, in the multivariate analysis, IS was the only significant predictor of LVR. With the ROC curve analysis we obtained an AUC of 0.7 (p=0.05), and thus, an IS ≥21% of LV mass has a sensibility of 70% and a specificity of 64% to predict LVR with an OR 3.8 (p=0.001).
Regarding LV morphology in LVR, we found a significant increase not only in LV volumes but also in ventricular diameter and sphericity.
After a STEMI, CMR can improve stratification of the risk of LVR. In our series, 31.5% of patients developed LVR, and infarct size has showed to be a good predictor of such evolution. A threshold of 21% of necrosis over total LV mass could be suitable to predict LVR with a sensibility of 70% and a specificity of 64%.

P4450 | BEDSIDE
Predictor of left ventricular remodeling after acute myocardial infarction: a study of end-systolic wall stress

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Objectives: Investigate whether the end-systolic wall stress is an independent predictor of left ventricular remodeling (LVR) in the aftermath of an acute myocardial infarction after successful reperfusion.
Background: LVR in post myocardial infarction is a poor prognosis outcome associated with a greater number of major adverse cardiovascular events. It remains difficult to predict which patients will remodel.
Methods: We calculate, among other parameters, end-systolic wall stress (WS) by three-dimensional MRI method in the aftermath of a revascularized MI. LVR was defined as a LV end-diastolic volume indexed (LVEDVi) >120 ml/m^2 at 3 months.
Results: Analysis was performed on 169 patients. 13 patients presented LVR, including 11 due to anterior MI. In these 13 patients the data of the initial MRI are more pejorative: WS 25.9±6 vs 16.0±4 103 N·m-2 (p<0.001), a LVEDVi 117.2±20 vs 84.6±16 ml/m^2 (p<0.001), an infarct size 46.6±20 vs 22.8±15 g (p<0.001), a microvascular obstruction size 8.7±1.9 vs 9±3 g (p<0.001) and a LV ejection fraction 31.0±8 vs 49.0±9% (p<0.001). The initial global WS emerges as an independent predictor of LV remodeling (OR 1.298 [1.046 to 1.612], p<0.018) as LVEDVi (OR 1.093 [1.013 to 1.180], p<0.022) and the occurrence of heart failure (OR 9.912 [1.094 to 89.842], p<0.041). LVEF so as infarct and microvascular obstruction size were not independent predictors. Patients with an initial global WS below 20.88 103 N·m-2 will not present LVR in 98.5% of cases (sensitivity and specificity of 84.6%).
Conclusion: End-systolic wall stress is an independent predictor of LV remodeling in post-MI. Patients with an initial global WS below 20.88 103 N·m-2 presented a small risk for LVR.

P4451 | BEDSIDE

Hemorrhagic myocardial infarction assessed by cardiovascular magnetic resonance after primary angioplasty can predict late left ventricular remodeling in patients with acute myocardial infarction

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Background: Recent studies have reported that non-invasive assessment of microvascular obstruction (MVO) and interstitial myocardial hemorrhage by cardiovascular magnetic resonance (CMR) provides a specific biomarker of severe ischemia-reperfusion injury after acute ST-segment elevation myocardial infarction (STEMI). However, the relation between left ventricular (LV) remodeling and hemorrhagic myocardial infarction has not been fully evaluated. The aim of this study was to determine whether the presence of myocardial hemorrhage determined by T2*-CMR can predict progressive LV remodeling in patients with acute STEMI.
Methods: The study population consisted of 107 consecutive patients with a first STEMI successfully treated with percutaneous coronary intervention. T2*-CMR performed within 4 days after primary PCI was used to identify the presence of reperfusion hemorrhage and contrast enhancement was used to detect and quantify MVO. The cine MRI at the baseline and 6 months after STEMI were analyzed to measure LV volume. Late LV remodeling was defined as an increase in end-diastolic volume index (EDVI) >20%. We assessed the association between and hemorrhagic myocardial infarction determined by CMR and late LV remodeling.
Results: Sixty-two/107 (58%) patients had MVO and 43 (40%) of them showed myocardial hemorrhage. Patients with late LV remodeling were more frequently observed in patients with hemorrhagic myocardial infarction compared to those without myocardial hemorrhage (26% vs 3%, p=0.0004). The amount of change of EDVI was larger in patients with hemorrhagic myocardial infarction compared to those without myocardial hemorrhage (2.3±15.7 vs -2.9±10.3 ml/m^2, p=0.038). The total sizes of MVO correlated with the amount of change of LVEDVI (r2=0.09, p=0.0019).
Conclusion: These data suggest that the assessment of myocardial hemorrhage determined by T2*-CMR provides an accurate method of predicting late LV remodeling in patients with STEMI.

P4452 | BEDSIDE

Incremental value of normal adenosine perfusion cardiac magnetic resonance: long-term outcome

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Objectives: To determine the long-term prognostic value of negative adenosine stress cardiac magnetic resonance imaging (CMR) with absent delayed enhancement in patients referred for evaluation of myocardial ischemia.
Methods: We retrospectively reviewed 326 consecutive patients (age 65±11 years, 74% male) with suspected or known coronary disease who had undergone adenosine stress CMR negative for ischemia and delayed enhancement. End-points during a mean follow-up of 6 years (5.9±1.8) were all-causes of mortality and hard cardiac events (cardiac death and nonfatal myocardial infarction). Secondary endpoint: coronary revascularization and hospitalization for angina.
Results: During follow-up, 16 patients died due to various causes (cardiac death in 5 patients). Three patients had nonfatal myocardial infarction. Seven patients were hospitalized for revascularization and 8 for unstable angina medically treated. The annual cardiac event rate was 1.4% (0.9% in the first 3 years and 2.2% between the fourth and sixth year). Predictors of cardiac events in a multivariate analysis model were advanced age [hazard ratio (HR) 1.15; 95% confidence interval (95% CI) 1,02-1,30], diabetes (HR 17.5, 95% CI 2.2-140) and smoking habit (HR 5.9, 95% CI 1.0-35.5). All-causes of mortality rate was 0.8%. Patients with normal stress CMR had excellent outcomes during the 3 years after the study. The cardiac event rate was higher between the fourth and sixth year. Therefore, it may be useful to repeat a new study to reassess the risk status of ischemia after 3 years.

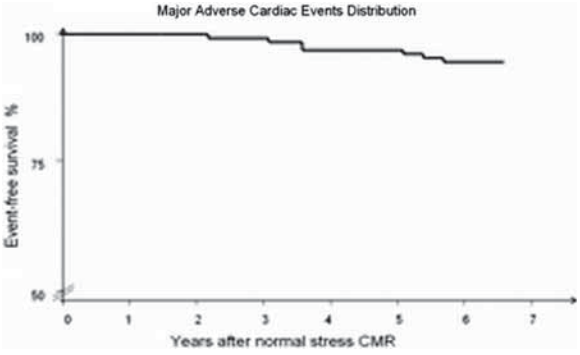

Figure 1. Kaplan Meier curve.

Conclusion: A very low event-rate and excellent prognosis occurred in patients with normal adenosine stress CMR.

P4453 | BENCH

Comparative evaluation of FDG PET and cardiac MRI for prediction of regional left ventricular contractile function improvement after recanalization of chronic occlusion coronary artery

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The aim is a comparison of PET and contrast-enhanced MRI (ceMRI) in predictingof segmental left ventricular (LV) functional recovery in myocardium, subtended by chronic totally occluded (CTO) coronary arteries (CA), after revascularization.
Materials and methods: In 26 patients with coronary artery disease and angiographycally proven CTO coronary arteries cardiac ceMRI and PET were performed before revascularization. Recanalization of CTO CA was successful in 20 patients. An improvement in wall motion at follow-up by at least 1 grade was used as standard for diagnostic accuracy calculation.
Results: Transmurality of scar extension and scar volume values were significantly larger in segments with irreversible dysfunction than in viable myocardium (73,0±37% vs 20,4±33,7%, p<0,0001 and 54,1±33,4% vs 9,8±16,2%, p<0,0001 respectively). Converse tendency was noted for 18F-FDG uptake (51,8±17% vs 67±11,6%, p<0,001). ROC analysis demonstrated that ≤50% of scar extension transmurality predicts significant improvement in local systolic function with a 80,2% sensitivity, 78% specificity and 79,6% accuracy, whereas that values for ≤37,7% of scar volume was 92,7%, 73,2% and 86,9% respectively. The cut-off value ≥56,4% of 18F-FDG uptake and patterns type of myocardial perfusion and metabolism provide 81,1% vs 91% sensitivity, 67,5% vs 75,2% specific, 65,5% vs 83,3% accuracy respectively.
Conclusion: ceCMR has the advantage in accuracy and predictive value in prognosing the segmental LV recovery after endovascular recanalization of CTO CA. In case of contraindications to ceMRI, performance of complex perfusion-metabolism PET imaging seems to be more appropriate. 18F-FDG PET alone is less effective in predicting the segmental recovery.

P4454 | BEDSIDE

Microvascular obstruction versus infarct size as predictors for left ventricular remodeling

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Background and aims: In reperfused acute myocardial infarction, estimation of hyperenhancement volume and microvascular obstruction (MVO) constitutes a dynamic process after contrast administration. Therefore, the prognostic role of these 2 parameters have diverged in different studies. Thus, our aim was to determine the best predictor and the optimal time after contrast injection to predict left ventricular remodeling.
Methods: Subjects were evaluated using CMR within the first week (n=60), 3 months and one year after a STEMI percutaneously revascularized. Cine CMR was performed to measure left ventricular function. Additionally, multi-slice inversion-recovery single shot (ss-IR) images were acquired sequentially at 1, 3, 5, 7, 10, 15, 20, and 25 min after bolus contrast administration to measure the hyperenhancement and MVO (hypoenhancement) volumes. Inversion time was set to null normal myocardium.
Results: The presence of delayed hypoperfusion at each time point after contrast administration results in larger hyperenhancement volumes, end systolic volume (ESV), and reduced ejection fraction (EF) (Table). The hyperenhancement and the hypoperfused volumes at all-time points were significant univariate predictors for ESV during the 3 months and at 1 year. However, in multivariate analysis, the volume of hypoperfusion at 15 min was the only predictor for ESV (r=0.73, p=0.01) and EF (r=- 0.75, p<0.001) at 1 year.

Minutes after contrast	Delayed Hypoperfusion absent			Delayed Hypoperfusion present		
	Infarct size	ESV	EF	Infarct Size	ESV	EF
1	15±11 g	75±21 ml	50±10%	30±16 g	92±32 ml	42±11%
3	17±14 g	77±26 ml	49±11%	33±16 g	97±30 ml	42±11%
5	18±13 g	75±26 ml	49±11%	18±13 g	100±29 ml	41±11%
7	18±13 g	76±25 ml	49±10%	18±13 g	102±30 ml	40±11%
10	19±13 g	78±28 ml	48±11%	19±13 g	101±27 ml	41±11%
15	19±13 g	78±28 ml	48±11%	19±13 g	101±27 ml	41±11%
20	20±14 g	79±27 ml	47±11%	20±14 g	103±29 ml	41±12%
25	20±14 g	79±28 ml	47±11%	20±14 g	103±29 ml	40±7%

Values are mean ± SD. ESV: end systolic volumel EF: ejection fraction.

Conclusion: Infarct size and the area of MVO can predict adverse ventricular remodeling; however, the area of MVO 15 min after contrast is the strongest predictor for ESV and EF at one year follow-up.

P4455 | BEDSIDE

Cardiovascular magnetic resonance characterization of left ventricular reverse remodeling after a first ST-segment elevation myocardial infarction

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Background: Reverse remodeling brings about beneficial consequences in a wide range of cardiovascular scenarios. In ST-segment elevation myocardial infarction (STEMI) an accurate assessment of this process using cardiovascular magnetic resonance (CMR) has not been performed yet.
Methods and results: In two university hospitals we prospectively included 565 STEMI patients in whom CMR was performed 7±1 and 179±8 days post-infarction. Left ventricular ejection fraction (LVEF), LV mass, end-diastolic (LVEDVI) and end-systolic volumes indexes (LVESVI), infarct size (IS) and microvascular obstruction (MVO) were quantified. We focused on those 311 patients (55% of the whole group) with early remodeling (1-week LVESVI >reference normalized values). Reverse remodeling (>10% decrease in LVESVI from 1-week to 6-month CMR) occurred in 139 patients (45% of those with early remodeling). At 1-week CMR, patients with reverse remodeling displayed a smaller extent of IS (23±12% vs. 30±14, $p<0.001$) and MVO (2±3% vs. 5±7, $p<0.001$) but similar values of LVEF, LV mass, LVEDVI and LVESVI ($p>0.3$). LVESVI, LVEDVI, and LV mass decreased and EF improved in patients with reverse remodeling ($p<0.001$); the opposite trend was observed in patients without reverse remodeling. The rate of adverse clinical events (death, re-infarction or re-admission for heart failure) during a 3-year mean follow-up was higher in patients with reverse remodeling (16% vs. 7%, p=0.02). After comprehensive multivariate analyses, the independent predictor of reverse remodeling (0.95 [0.92-0.97], $p<0.001$) and adverse clinical events (1.04 [1.02 – 1.07], $p<0.001$) was 1-week IS.
Conclusions: Reverse remodeling occurs in almost half of STEMI patients with early dilation, it associates with beneficial effects on the most important structural cardiac indexes and on patients' outcome. Infarct size soon after STEMI but not the magnitude of cardiac dilation or dysfunction predicts reverse remodeling.

P4456 | BEDSIDE

Limitation of acute infarct transmurality to predict segmental recovery in STEMI patients: a cardiac imaging study in the PROMISE trial

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Background and aims: In an acute myocardial infarction, the transmurality of the necrosis by cardiac magnetic resonance (CMR) has been considered an excellent predictor of improvement in contractile function. However, different studies suggest that transmurality can be overestimated in the acute phase due to the presence of edema. Thus, our aim was to analyze the accuracy of acute transmurality to estimate the presence of contractile reserve and the recovery of segmental function.
Methods: Ninety-five consecutive patients with an acute STEMI enrolled in the PROMISE trial were studied after a successful primary angioplasty with CMR and dobutamine stress echo during the first week and at 6 months. Infarct transmurality was determined by CMR, the peak longitudinal systolic strain (SS) and strain rate (SSR) were determined basal and after infusion of 10 mcg/kg/min of dobutamine (DBT) in 16 segments per patient (except segment 17).
Results: A total of 1520 segments were analyzed. SS and SSR basal, at 10 mcg DBT and at 6 months follow-up were lower with the increase of infarct transmurality. Infarct transmurality decrease at six months even in transmural infarctions ($p<0.001$). Thus, 80% segments with infarcts 50-75% and 48% segments with infarcts >75% in the acute phase presented contractile reserve and improvement in contractile reserve at follow-up. This improvement was correlated with the decrease of infarct transmurality in these segments at 6 months (table 1).

Table 1. Strain rate versus infarct transmurality

	0–25% at six months		26–50% at six months			51–75% at six months			> 75% at six months		
	Basal	6M	Basal	DBT 10	6M	Basal	DBT 10	6M	Basal	DBT 10	6M
Acute: 50–75%	–0,78	–1,00	–0,67	–0,89	–0,95	–0,67	–0,82	–0,90			
Acute: >75%	–0,86	–0,90	–0,76	–0,77	–0,81	–0,71	–0,75	–0,75	–0,54	–0,64	–0,50

6M: six months. DBT: Dobutamine.

Conclusion: A large proportion of myocardial segments with a transmural infarction in early CMR decrease its transmurality and improve their function at 6 months. Thus, assessment of infarct transmurality in the acute phase can mislead the estimation of functional recovery.

NEW TECHNIQUES IN CARDIOVASCULAR MAGNETIC RESONANCE

P4458 | BEDSIDE

T2 mapping of the human myocardium with an accelerated multiecho spinecho sequence (GRASE) in volunteers -feasibility and reliability-

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Cardiac Magnetic Resonance (CMR) plays an important role in the diagnosis of acute inflammatory myocardial diseases. Since inflammatory foci are accompanied by oedama, they produce an endogenous CMR tissue contrast by changing local T2 relaxation time. At present, T2 weighted MR imaging has several drawbacks (lacking intensity references, subjectivity) and might not be sufficient for detecting acute or low-grade tissue inflammation. Therefore, the purpose of the present study was to validate and investigate reference values of myocardial T2 relaxation mapping with GRASE for the sensitive discrimination between remote and diseased myocardial tissue.
A 1.5 Tesla MRI-System with a 32-chanal coil was used for rapid multiecho image acquisition with GRASE (respiration navigator, (15 T2 echos separated by 10ms, res: 1x1x10 mm^2, 3 short axis slices, TA: 6min). These images were post-processed using software based on the LabView environment for pixel wise T2 generation. In terms of sequence validation and investigation of biological effects on T2 relaxation, phantom experiments were undertaken with muscle tissue ex vivo and in vivo. Healthy volunteers of mixed age and sex (n=62) underwent CMR. In a set of phantom studies, GRASE was validated against a gold standard multiecho spinecho sequence in meat phantoms treated by drying and liquid injections and in non-moving human muscle (upper limb). Due to its quantitative nature GRASE was capable of detecting a 10% loss of global water due to drying and less than 100µl water injected into muscle tissue. The volunteers were divided into 4 groups depended on their mean age. T2 maps could be generated in all cases. Median T2 values of apical short axis slices differed significantly from basal ones (apical: 57.71±2.16ms; basal: 52.89±4.0ms, $p<0.05$). Moreover, there was a significant difference between male and female global myocardial T2 values (male: 55.53±1.8ms; female: 57.83±1.2ms, $p<0.05$). Interobserver variability between to experienced observers was low: The mean difference in T2 time was 0.46±1.5ms (R = 0.94) and the coefficient of variation was 2.2%. Interestingly, increasing age (all volunteers) was correlated with increasing myocardial T2 values (R=0.77).
GRASE derived T2 maps are reliable, highly reproducible and even discriminate between male and female or young and aged myocardium. Phantom studies suggest, that sensitivity and specificity of this novel sequence approach are high enough to discriminate inflammatory foci from remote myocardium.

P4459 | BEDSIDE

Aortic stiffness in the presence of self-limiting and sustained systemic inflammation: comparison of acute myocarditis and chronic inflammatory diseases

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Purpose: Aortic stiffness, measured by pulse way velocity (PWV), is an independent predictor of cardiovascular (CV) events over and above traditional risk factors. Previous evidence revealed moderately raised PWV in the presence of presence of systemic inflammatory diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Changes in aortic stiffness in response to acute systemic inflammation, such as systemic viral myocarditis, remain unknown.
Methods: Ninety-nine subjects with either clinical diagnosis of acute myocarditis (n=44) or chronic systemic inflammatory disease (RA and SLE, n=55) underwent standardized cardiac magnetic resonance protocol for the assessment of PWV. Thirty-eight apparently healthy subjects served as control group. Central PWV was obtained by an inplane phase contrast gradient echo sequence with high temporal resolution (120 phases/cardiac cycle) and foot-to-foot measurement.
Results: Groups were well matched for age and cardiovascular risk factors, with no differences in blood pressure or heart rate between groups. Compared to controls, both patients' groups had significantly raised central PWV (control vs. acute myocarditis vs. systemic inflammation, PWV (m/sec): 5.1±1.0 vs. 8.4±2.4 vs. 8.5±2.6, $p<0.001$, with no significant differences between the two groups of patients on post-hoc analysis. We identified significant relationship between PWV

PWV bivariate correlations

PWV	r	Sign (p value)
Age	0.4	<0.05
Hypertension	0.34	<0.05
Hypercholesterolemia	0.24	<0.05
Smoking	0.22	<0.001
LGE	0.36	<0.001

PWV was significantly correlated with age, with traditional CV risk factors and with the presence of areas of late gadolinium enhancement (LGE) in the CMR study.

and age (controls, r: 0.56; acute myocarditis, r: 0.51; and systemic inflammation, r: 0.3 $p<0.0001$ for all), whereas no other functional index showed significant association.
Conclusion: We demonstrate for the first time that there is increased aortic stiffness in response to self-limiting inflammatory injury, which is comparable in magnitude to sustained systemic inflammation.

P4460 | BEDSIDE
A novel ultra fast CMR approach for the assessment of left ventricular volumes and function in one breath-hold

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Background: CMR is generally accepted as the gold standard for left ventricular (LV) volumes and function assessment. However, conventional cine imaging requires several breath-holds to cover the entire LV during 10-15 min. Compressed Sensing (CS) emerged as a means to accelerate data acquisition.
Purpose: To compare a novel prototype CS single breath-hold, multi-slice cine technique with the standard multi-breath-hold technique for the assessment of LV volumes and function.
Materials and methods: Twelve volunteers (75% male, age 33±8y) and 21 patients (86% male, age 63±14y) were included in the study. The novel prototype single breath-hold multi-slice CS cine sequence was implemented on a 1.5T MAGNETOM Aera (Siemens) MR System. Three long-axis and 4 short-axis slices were acquired in a single breath-hold of 14 heart beats (temporal/spatial resolution: 30ms/1.5 x 1.5mm^2, acceleration factor: 11.0). The CS cine data were analyzed by the Argus 4DVF software (Siemens) which is based on a 3D LV-model that takes the motion of the mitral valve plane into account. For gold standard comparison, a conventional stack of cine SSFP images was acquired (temporal/spatial resolution 40ms/1.2 x 1.6mm 2, slice thickness/gap: 8mm/2mm) and analyzed by the Argus VF software (Siemens). As a reference for the LV stroke volume (LVSV), the aortic flow (AoFlow) was measured by a phase-contrast acquisition (temporal/spatial resolution 40ms/1.8 x 1.8mm^2) in 16 subjects (volunteers and patients without mitral insufficiency on echocardiography). The image quality of the CS acquisitions and the intra- and inter-observer reproducibility were assessed.
Results: The CS acquisition was more accurate than conventional approach for LVSV quantification: LVSV overestimation vs AoFlow was 6.4±6.9ml with CS vs 14.1±11.2ml with the standard approach (p=0.025) with less variability (r=0.91 vs r=0.79, respectively).The CS acquisitions showed an excellent image quality in 94% of the subjects and maintained quantitative accuracy in LV systolic function (CS-LVEF = 48.5±15.9% vs standard LVEF = 49.8±15.8%, p=0.11) with excellent correlation (r=0.96, slope=0.97, $p<0.00001$). The intra-/inter-observer agreement for all CS parameters was good (slopes: 0.93-1.06, r: 0.90-0.99).
Conclusions: Accurate and reproducible measurements of LV volumes and function can be obtained in "one breath-hold" using this novel prototype multi-slice CS cine sequence with significant reduction of the scan time and potential clinical application.

P4461 | BEDSIDE
Non-invasive estimation of the augmentation index at the central aorta using cardiac magnetic resonance imaging

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Purpose: Central aortic blood pressure is measured only using invasive procedures. The present study aimed to estimate the augmentation index (AI) using cardiac magnetic resonance (CMR) imaging, and compare it with the AI obtained in a catheterization study.
Methods: Twenty-two patients who underwent CMR imaging and catheterization study were examined.
Blood pressure change (ΔP) was expressed using Young's modulus (E), vessel wall thickness (h), and the aortic lumen diameter (D) as follows: $\Delta P = \Delta D \times E \times h$. $E \times h$ is almost invariable if the wall thickness of the aorta is assumed to be 1 mm. Under this assumption, blood pressure change is proportional to lumen diameter change. Flow volume and cross sectional area (CSA) were measured by tracing the ascending aorta in phase contrast CMR images (40 frames per cardiac cycle). The aortic lumen diameter (D) was calculated using the CSA as follows: $D = 2\sqrt{}(CSA/pi)$. The image quality score of the waveform was visually assessed as follows: 4, excellent; 3, good; 2, poor; and 1, non-assessable. The CMR-AI was calculated from D0 at minimum lumen diameter, D1 at peak flow and D2 at maximum lumen diameter as follows: CMR-AI = (D2 – D1)/(D1 – D0) × 100.
The AI was calculated from the inflection point identified by the fourth derivative curve of aortic pressure in the catheterization study.
Results: The image quality scores obtained were as follows: 4, 12 patients; 3, 7 patients; and 2, 3 patients. The mean CMR-AI was 33.7±30.8%, and the mean the AI was 25.1±24.9%. Young's modulus was 3.27±1.88 MPa, and the stiffness β was 7.28±4.16. Moreover, CMR-AI was significantly correlated with the AI (R = 0.819, $p<0.001$).

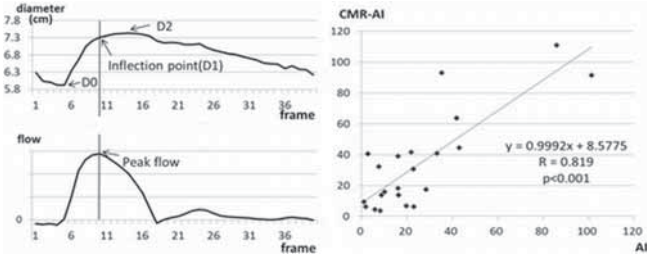

Figure 1

Conclusions: CMR-AI is correlated strongly with the AI. Therefore, the AI at the aorta may be estimated using CMR imaging.

P4462 | BEDSIDE
Discriminating dark rim artifacts from true perfusion defects with fully quantitative perfusion analysis at the pixel resolution of cardiovascular MRI perfusion in humans

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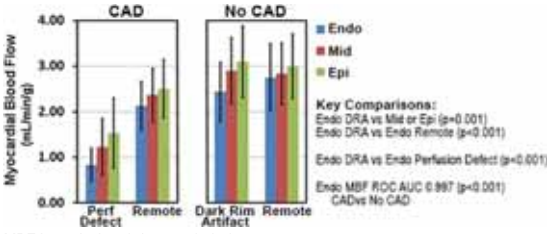
Purpose: A dark rim artifact (DRA) that mimics a perfusion defect is one of the most important limitations in cardiac perfusion MRI (CMR). This study used fully quantitative analysis of myocardial blood flow (MBF) at the pixel resolution to characterize regions of DRA vs. true perfusion defects.
Methods: 199 consecutive patients had a regadenoson perfusion CMR study using a steady state free precession sequence and 0.05 mmol/kg gadolinium. To study DRA, we excluded 139 cases without correlative invasive coronary angiography (CATH) or computed tomography angiogram (CTA) and 18 cases with coronary artery bypass, 3-vessel disease, or technical issues. Classification as a true perfusion defect required CATH with significant coronary artery disease (CAD) (>70% stenosis). Classification as DRA required no significant CAD (<30% stenosis) by CATH or CTA and presence of DRA on CMR. CMR perfusion pixel maps were generated by a model-constrained Fermi deconvolution. Regions of interest were drawn in the subendo-, mid-, and subepicardial myocardium.
Results: Patients (n=42) averaged 55±11 years of age and CAD was present in 23% (n=10). In patients with DRA, MBF in the subendocardium was lower than the midwall and epicardium (Fig 1, p=0.001) as well as remote myocardium ($p<0.001$). However, the endocardial MBF of true perfusion defects was much lower than endocardial MBF in DRA (0.81±0.35 vs 2.40±0.64ml/min/g; $p<0.001$). Endocardial MBF could separate CAD from DRA with an area under the receiver operator curve of 0.997 ($p<0.001$).



MBF in perfusion defects & dark rim art.

Conclusion: Although DRA are present and have statistically lower MBF in the subendocardium than the midwall and epicardium, the endocardial MBF in true perfusion defects is much lower. Thus, fully quantitative analysis of MBF was able to discriminate DRA from true perfusion defects.

P4463 | BEDSIDE
Dynamic changes of T2-Weighted signal intensity magnetic resonance imaging in reperfused myocardial infarction: implications for retrospective area-at risk quantification

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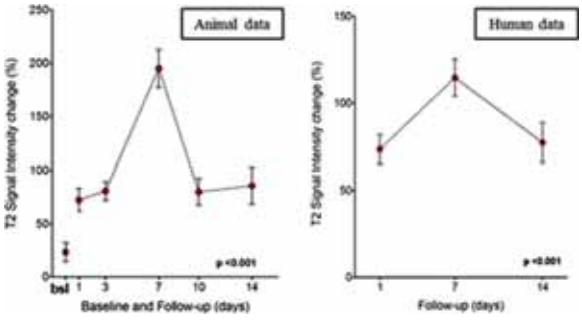
Purpose: The accurate quantification of Area-at Risk (AAR) is of great value in

clinical trials testing therapies aimed at reducing infarct size.Our aims were to serially study post myocardial infarction (MI) signal intensity (SI) on T2-Weighted Cardiac Magnetic Resonance (T2W-CMR).
Methods: Four Large-White pigs underwent 60 minutes LAD artery occlusion followed by reperfusion.T2W-STIR 3T CMR scans were performed pre-MI and on days 1,3,7,10 and 14. In vivo gold standard (GS) for AAR quantification was obtained by selective intracoronary injection of gadolinium using perfusion CMR imaging.Four additional pigs validated this new in vivo CMR-based GS against the classic histopathology GS (negative-Evans blue staining).
T2 prep-SSFP 3T-CMR scans of 20 post-MI patients were also retrospectively analyzed at 3 time points (<24hr; day 5-7 and 14-17).Regions of interest were manually drawn on T2W images to calculate SI change: (SI at the AAR-SI at remote myocardium)/SI at remote myocardium.
Results: Mean T2W SI change (%) in both patients and animals were significantly higher on day 7 than on other days ($p<0.001$ for all comparisons,Figure). There was a highly significant good correlation ($r=0.91$, $p<0.001$) and agreement (mean error 0.91%,limits -7.55% to 9.37%) between the extent of AAR by CMR-based GS and Evans blue.The correlation between AAR quantification by CMR-based GS and T2W-STIR on day 7 was 0.86 ($p<0.001$; mean error-1.33%, limits -10.1% to 7.5%). These values were higher than those at 1,3,10 and 14 days.



T2W signal intensity changes after MI,

Conclusions: After a MI, T2W-SI increases over time, peaking on day 7 with a subsequent decrease both in the pig model and in patients. Similarly, AAR quantification at day 7 better correlated with the GS. These findings may have clinical implications for the best timing to accurately define AAR.

P4464 | BEDSIDE
Diminished myocardial oxygenation response to a breath-hold stimulus in patients with obstructive sleep apnea syndrome

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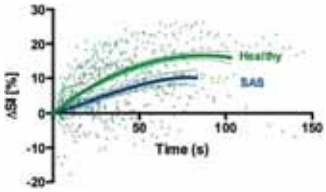
Purpose: Oxygenation-sensitive cardiovascular magnetic resonance (OS-CMR) can non-invasively monitor changes of myocardial oxygenation using a vasodilatory stimulus such as a breath-hold. However, it is unknown how this will affect the regulation of myocardial oxygenation of patients with obstructive sleep apnea syndrome (SAS) who suffer from repeated episodes of hypoxemia.
Methods: In a clinical 3T scanner, 19 healthy participants and 29 SAS patients performed 60s hyperventilation followed by a maximal voluntary breath-hold. During the breath-hold, OS-CMR images were continuously acquired. Signal intensity (SI) was expressed as a %-change from the first image and assessed for the maximum rate of change of SI in the first 25s (Slopemax), the maximum SI (ΔSImax) reached within the breath-hold, and at the end (ΔSIend) when the participant needed to end the breath-hold.
Results: SAS patients had a significantly lower response than healthy volunteers for both ΔSImax (+9.1±7.6% vs. +14.8±6.6%) and ΔSIend (+4.0±11.0% vs. +10.3±7.7%), as well they had a shorter breath-hold duration (51±30s vs. 74±29s, $p<0.05$). Diabetes, hypertension and/or coronary artery disease were present in 13 SAS patients. When accounting for these, ΔSImax and slopemax during the first 25s were significantly different ($p<0.05$), whereas they were not associated with ΔSIend.



The change in OS-SI over the breath-hold.

Conclusions: SAS patients have a delayed and blunted myocardial oxygenation response to a breath-hold stimulus. Furthermore, SAS patients tolerate longer breath-holds with lower oxygenation than healthy volunteers. OS-CMR combined with breathing maneuvers may be useful for verifying SAS-specific alterations of microvascular function in the myocardium.

P4465 | BEDSIDE
Diagnostic accuracy of three different protocols for 3.0 tesla coronary magnetic resonance angiography

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Purpose: The usefulness of coronary magnetic resonance angiography (cMRA) has been reported, although the difference in the diagnostic accuracy of the different protocols has not been established.
Methods: We compared conventional coronary angiography (CAG) and cMRA in 23 consecutive patients who underwent these examinations within six months. We used the standard 15-segment American Heart Association classification system. Stenosis was quantitatively evaluated in segments with a reference diameter of ≥1.5 mm on CAG. Significant coronary artery disease (CAD) was defined as a reduction in the luminal diameter of coronary arteries by ≥50%. The three protocols for cMRA were cMRA1, whole-heart coronary angiography (WHCA) without contrast; cMRA2, WHCA with contrast; and cMRA3, steady-state free precession with contrast at breath-hold by using a 3.0 T scanner. Image quality was graded on a 4-point scale: 1, nonassessable; 2, assessable, fair vessel contrast; 3, assessable, good vessel contrast; and 4, assessable, excellent vessel contrast.
Results: Stenosis was observed in 33 segments, with a prevalence of 10.5%. For cMRA1, cMRA2, and cMRA3, the numbers of assessable segments were 234 (74.3%), 273 (86.7%), and 157 (49.8%), respectively ($p<0.001$ by the McNemar test). For the assessable segments, the mean image quality scores were 2.63±0.67, 3.43±0.77, and 2.23±0.45 with cMRA1, cMRA2, and cMRA3, respectively ($p<0.001$ by the Mann-Whitney U test). The diagnostic accuracy of each protocol is presented in Table. For the assessable segments, the image quality score was better with cMRA2 than with the other protocols.

Table 1

	Sensitivity	Specificity	PPV	NPV
For all segments				
cMRA1 (n=315)	69.7	99.3	92.0	96.5
cMRA2 (n=315)	78.8	98.2	83.9	97.5
cMRA3 (n=315)	42.4	97.2	63.6	93.5
For the assessable segments				
cMRA1 (n=234)	92.0	99.0	92.0	99.0
cMRA2 (n=273)	86.7	97.9	83.9	98.3
cMRA3 (n=157)	87.5	94.3	63.6	98.5
For the assessable proximal segments				
cMRA1 (n=119)	93.3	99.0	93.3	99.0
cMRA2 (n=127)	94.1	96.4	80.0	99.1
cMRA3 (n=99)	91.7	90.8	57.9	98.8

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

Conclusion: cMRA is useful in ruling out CAD, with the cMRA2 protocol showing the highest performance.

P4466 | BENCH
Analysis of myocardial intra and extracellular water. Magnetic resonance studies ex vivo and in situ rat heart model

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Purpose: Myocardial edema (ME) is present in the setting of many heart diseases, including ischemia-reperfusion (IR) injury. Depending on the nature of the insult, distinct patterns of ME distribution have been described, leading to different detrimental effects. The aim of this study was to develop a method to measure myocardial water distribution between intracellular (ICW) and extracellular (ECW) compartments and to analyze its correlation with cardiac magnetic resonance imaging (CMRI) parameters.
Methods: Gadobutrol was used as an ECW marker in a saline perfused isolated rat heart (SPIRH) model. Hearts were perfused with normoosmotic, hyperosmotic or hyposmotic buffer (containing Gd 1mM for the last 5 min) to obtain different patterns of water distribution. At the end of perfusion, hearts were weighed (fresh mass) and sliced; after lyophilization, samples were reweighed (dry mass), thus obtaining total water content (TWC). Gadolinium was extracted from dried samples and measured at 9.4T in a vertical magnet, based on the linear relation between 1/T1 and [Gd]. ECW content was calculated from Gd amount and ICW was calculated by subtraction of ECW to TWC. This method was checked in IR ex vivo protocols and used in in situ rat heart experiments. CMRI study was performed in ex vivo rat hearts previously perfused with Gd-free normosmotic, hyperosmotic or hyposmotic buffer and T2, Diffusion coeffient (B0) and proton density were measured.
Results: Intact rat hearts contained 257±8 of ICW (all data referred as mL of water per 100g of dry tissue, mean ± SE) and 79±10 of ECW. Hearts perfused 40' with normosmotic buffer contained 254±7.7 of ICW and 152±5.6 of ECW.

Hyposmotic perfused hearts contained 300±5 of ICW and 144±5.6 of ECW and hyperosmotic perfused ones had 189±5.3 of ICW and 172±6.5 ECW. SPIRH subjected to 40' of ischemia and 30' of reperfusion showed significant increase of TWC at expense of ECW, but this effect could be prevented when cell death was prevented with blebbistatin administered early during reperfusion and also with hyperosmotic reperfusion. CMRI studies showed a good correlation of proton density with TWC (R2=0.99) while both T2 and B0 had good correlation with ECW (R2=0.99).
Conclusions: 1) The method described to measure ECW and ICW is reliable both in ex vivo and in situ rat models. 2) Proton density correlates with TWC while both T2 value and B0 do correlate with ECW. 3) The protective effect of hyperosmotic reperfusion suggests a contribution of ME to cell death.

P4467 | BEDSIDE
Extracellular volume fraction of cardiac MRI is related to indexes of mitral annuls velocity of tissue Doppler echocardiography

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Purpose: Extracellular matrix expansion and fibrosis are characteristics of adverse myocardial remodeling. Cardiac MRI T1-mapping may quantify the structural change of myocardium. We compared extracellular volume fraction (ECV) with parameters of Doppler tissue imaging indicating stiffness of myocardium.
Methods: Consecutive 51 patients (59±16 years old, 35 men and 16 women) were examined by cardiac MRI T1-mapping and tissue Doppler echocardiography. The subjects included 10 patients of hypertrophic cardiomyopathy (HCM), 10 patients of dilated cardiomyopathy (DCM) and 6 patients of cardiac sarcoidosis (SA). All images for T1-mapping were acquired in mid-diastole phase by saturation recovery single shot acquisition method. We used 2-parameter signal model to determine T1; $S(t) = S(0)*(1 - \exp(-t/T1))$. Myocardial T1 was derived from the average signals of 6 regions of interest placed on a cross-section of mid left ventricle at different saturation delay (0, 300, 600 ms). ECV was calculated by hypothesizing gadolinium contrast (Gd) as an extracellular space marker. ECV = $\lambda*(1 - \text{hematocrit})$; $\lambda = [\Delta R1 \text{ myocardium}]/[\Delta R1 \text{ blood}]$, where $\Delta R1 = 1/T1$ post Gd – 1/T1 pre Gd.
Results: The average ECV (%) was 30±12 (HCM 35±17, DCM 26±6, SA 38±12, respectively). ECV was not associated with end-diastolic volume index, end-systolic volume index, left ventricular mass index and ejection fraction measured from cardiac MRI. However, ECV was positively correlated with septal E/E' (γ=0.320, p=0.022, n=51), lateral E' (γ=-0.363, p=0.010, n=49) and lateral E/E' (γ=0.439, p=0.002, n=49) obtained from tissue Doppler echocardiography. ECV was also correlated with BNP (γ=0.364, p=0.009), HDL-cholesterol (γ=0.357, p=0.010) and body surface area (BSA) (γ=-0.397, p=0.004). In a model of multivariate linear regression analysis adjusted with the backgrounds of the patients, ECV was independently associated with septal E/E' (β=0.279, p=0.033), and BSA (β=-0.364, p=0.006).
Conclusions: Our result suggested that ECV is related to the indexes of left ventricular diastolic function in echocardiography. Cardiac MRI T1-mapping is promising method to evaluate myocardial condition.

CHARACTERISING NON-ISCHAEMIC CARDIOMYOPATHY

P4469 | BEDSIDE
Pathological correlates of left-system intraventricular conduction delay in patients with non ischemic cardiomyopathy

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Background and aims: Pathological correlates of intraventricular conduction delay have been scarcely investigated in patients with non-ischemic cardiomyopathy (NICM). In the current study, we sought to assess left ventricular (LV) structural, functional and tissue abnormalities associated with left-system intraventricular conduction delay in a cohort of NICM patients by cardiovascular magnetic resonance (CMR).
Methods: CMR and 12-lead ECG were performed in 198 consecutive patients with NICM (140 males, age 61±14 years). Late gadolinium enhancement (LGE) technique was used for fibrosis detection and quantification. LV volumes, mass and ejection-fraction were quantified using short-axis cine images. On regional basis, presence and extent of LGE were expressed segmentally according to 16-segment model of the left ventricle. Further, 16 segments were grouped into 1)septum, 2) adjacent and 3)lateral regions. Regional LGE extent was obtained by averaging the segmental values corresponding to each region. According to ECG findings, patients were classified: 1)Left bundle disease (LBD); 2)Right-bundle branch block (RBBB); 3)Aspecific conduction delay (ACD); 4)QRS duration<120ms.
Results: Eighty-five (43%) patients showed LBD (left-branch-block=49 and left-anterior-hemiblock n=36), 11 (6%) had RBBB (10 associated with left-anterior-hemiblock), 17 (9%) ACD and 85 (43%) QRS duration<120ms. Compared to patients with QRS duration<120ms, those with LBD were older (57±15 vs 65±13 years, P=0.003) had greater LV end-systolic volume (77±40 vs 90±40 ml/m^2, P=0.024) and mass (87±21 vs 95±30 g/m^2, P=0.032) but lower LV ejection-fraction (38±11 vs 34±11%, P=0.024). LGE was observed more commonly in LBD than QRS duration<120ms patients (57 vs 25%, P<0.001) and was more often and extensively located in the septum (54 vs 18% and 9±13% vs 3±8%, both P≤0.001). Septal LGE was associated with a higher likelihood of LBD (OR 4.923, 95% CI 2.403 to 10.088, P<0.001) after correction for LV volumes, mass and ejection-fraction.
Conclusions: LBD is the most common form of intraventricular conduction abnormarlity in NICM and is associated with worse LV remodeling and dysfunction as compared to normal intraventricular conduction. Further, fibrosis of interventricular septum yielded a nearly 5-fold increased likelihood of LBD independently of the degree of LV dilatation and systolic dysfunction. This suggests that reparative fibrosis of interventricular septum likely represents the pathological correlate of LBD in patients with NICM.

P4470 | BEDSIDE
Correlation between sphericity index and trabeculation in left ventricular noncompaction and dilated cardiomyopathy

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Purpose: Left Ventricular Noncompaction (LVNC) and Dilated Cardiomyopathy (DC) have classically been described as separate entities. The overlap of their main characteristic (hypertrabeculation) results in an overdiagnosis of LVNC. Adverse ventricular remodeling, characteristic of both entities, is observed as an increase in ventricular volume, diminished systolic function and progressive ventricular sphericity. A positive correlation exists between Sphericity Index (SI) measured by cardiovascular magnetic resonance (CMR) and trabeculation in DC, suggesting that this condition is not exclusive of LVNC and that it could correspond to a more advanced stage of ventricular remodeling. However, the evidence supporting this theory is still limited. The purpose of this study is to correlate SI and trabeculation (segmental and global) in patients with LVNC and DC.
Methods: This is a retrospective, observational and cross-sectional study. The study included 24 patients with DC and 20 with LVNC. Clinical, demographical, echocardiographic and CMR characteristics were compared. SI and the indexes of segmental and global trabeculation (IST and IGT respectively) determined by CMR were measured for both groups.
Results: Patients with LVNC were younger (25.7±13.9 vs 46.4±15.5 in DC, p<0.05) and had a later diagnosis (35 vs. 4 months, p<0.05). Furthermore, they presented a smaller telediastolic volume in the LV (54.7±10.3 vs 67.8±8.8 in DC, p<0.05). LVEF, RVEF and late enhancement was similar in both groups. The IST was larger in LVNC, mainly in the anterolateral segments of the medial and basal thirds, and globally in the apical third. The IGT was also larger in LVNC (2.13 vs 1.1, p<0.05). The apex is of little help in differentiating both conditions. The SI was similar in both conditions (0.72±0.01 vs 0.72±0.12, p=NS). When correlating IGT and SI, none present statistical significance, however, a tendency of direct correlation between IGT and SI exists in DC, which is inverse in LVNC.
Conclusions: Hypertrabeculation in LVNC is found predominantly in the anterior and lateral segments (medial and basal) and globally in the apical third. The tendency of correlation between SI and IGT is direct in DC and inverse in LVNC, which suggests that the hypertrabeculation in LVNC is due to different mechanism than those in ventricular remodeling.

P4471 | SPOTLIGHT
Aortic arch stiffness in fabry disease assessed by cardiovascular magnetic resonance imaging

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Aim: Aortic thoracic remodelling has been recently described in Fabry disease (FD). However, no data was available concerning aortic arch stiffness (AAS) in this rare genetic disease. The aim of this study was to asses AAS parameters in male patients with FD using cardiovascular magnetic resonance imaging (CMR).
Methods: Twenty nine males with FD matched for age with 58 controls underwent CMR using cine and phase contrast velocity sequences.
Thoracic aortic diameter, local (distensibility, β-index stiffness), global (pulse wave velocity) stiffness parameters of the aortic arch and cardiac proprieties were assessed by CMR.
Results: Thoracic aorta was dilated at the different levels except the aortic arch and descending segments and predominates at the level of the sinus of Valsalva (37±5.2 vs 31.9±2.9 mm, p<0.0001).
Aortic arch PWV was significantly increased in FD patients (6.5±3.1 vs 5.0±1.5 m/s, p<0.01).

Compared to control subjects, patients with FD had also markedly decreased distensibility (2.73±1.14 vs 3.45±1.13 10^{-2} kPa^{-1}, $p<0.01$) and increased stiffness index beta (9.4±6.7.10-2 vs 5.9±2.7·10^{-2}, $p<0.001$) in the ascending aorta.
Moreover, descending aortic stiffness parameters were also impaired with a trend for decreased distensibility (2.26±1.15 vs 3.15±1.0·10^{-2} kPa^{-1}, P=0.06) and significant increased β-index stiffness (8.5±3.9·10^{-2} vs 2.9±0.9·10^{-2}, $p<0.0001$).
Conclusion: These data suggest that FD patients exhibited impairment of both local and global aortic arch stiffness parameters.

P4472 | BEDSIDE
Myocardial perfusion reserve is associated with impaired strain and higher disease activity in rheumatoid arthritis: cardiovascular magnetic resonance study

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Introduction: Rheumatoid arthritis (RA) patients develop premature vascular dysfunction and atherosclerosis, with excess mortality mainly attributed to cardiovascular disease (CVD).
Objective: To detect myocardial ischaemia and regional dysfunction in RA using CMR.
Methods: 55 RA patients (39 female, mean age 54±11 years) and 55 matched controls (39 female, mean age 53±10 years) without previously known CVD underwent CMR at 1.5T including cine, tagging, perfusion and late gadolinium enhancement (LGE) imaging; disease activity (DAS28-CRP) and duration were recorded for each subject.
Results: Myocardial perfusion reserve index (MPRI) was lower in RA compared to controls (1.5±0.3 vs. 1.9±0.4, $p<0.001$). Half of RA patients had evidence of non-segmental subendocardial perfusion defects on visual assessment, in keeping with microvascular dysfunction. There was no significant difference in LV size, mass and ejection fraction between RA patients and controls. Peak systolic circumferential strain (-17.0±1.1 vs. -18.7±1.2, $p<0.001$) and peak diastolic strain rate (82±19 vs. 115±21 s^{-1}, $p<0.001$) were impaired in RA. Focal fibrosis on LGE was found in 27 (49%) RA patients compared to none of controls. In RA, MPRI correlated with peak systolic strain (R -0.71, $p<0.001$), peak diastolic strain rate (R 0.63, $p<0.001$) and DAS28-CRP score (R -0.38, p=0.005).

CMR findings

	Control (N=55)	RA (N=55)	P value
LVEDV indexed to BSA, ml/m^2	78±15	79±15	0.92
LVESV indexed to BSA, ml/m^2	22±14	22±8	0.96
LVEF, %	74±4	72±7	0.45
LV mass indexed to BSA, g/m^2	54±11	55±11	0.64
MPRI	1.9±0.4	1.5±0.3	<0.001
Proportion of non-segmental perfusion defects (%)	0	27 (49)	–
Presence of LGE (%)	0	27 (49)	–

Continuous data are mean ± SD unless otherwise indicated. BSA, body surface area; LGE, late gadolinium enhancement; LV, left ventricle/ventricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; MPRI, myocardial perfusion reserve index; RA, rheumatoid arthritis.

Conclusions: MPRI is impaired in RA and is associated with abnormal myocardial deformation characteristics and disease activity.

P4473 | BEDSIDE
Left ventricular global function Index by CMR is more strongly associated to different patterns of myocardial iron overload than the global systolic function

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Purpose: The Cardiovascular Magnetic Resonance by the multislice T2* technique allows to detect different patterns of myocardial iron overload (MIO). The analysis of cine images allows the quantification of the left ventricular global function index (LVGFI). A LVGFI<37% was shown to be strongly predictive of cardiovascular events.
We verified the association between different patterns of MIO and the LVGFI vs the LV ejection fraction (EF) in thalassemia major (TM) patients.
Methods: We considered 812 TM patients (391 M, 30.4±8.6 yrs) enrolled in the MIOT network. The T2* value in all the 16 cardiac segments was evaluated. LVGFI and LVEF were quantified by SSFP cine images.
Results: We identified 4 groups of patients: 138 with homogeneous MIO (all segments with T2*<20 ms), 97 with heterogeneous MIO (some segments with T2*<20 ms, others with T2*≥20 ms) and significant global heart iron (global heart T2*<20 ms), 238 with heterogeneous MIO and no significant global heart iron, and 339 with no MIO (all segments with T2*≥20 ms).
The mean LVFGI was significantly different among the 4 groups (Fig).
Compared to the group with no MIO, all the other 3 groups were significantly more likely to have a LVGFI<37%. Only the groups with homogeneous MIO and with heterogeneous MIO and significant global heart iron had a significant higher risk to have LV dysfunction. The association between different patterns of MIO with a LVGFI<37% was stronger than the association with LV dysfunction (Fig. 1).

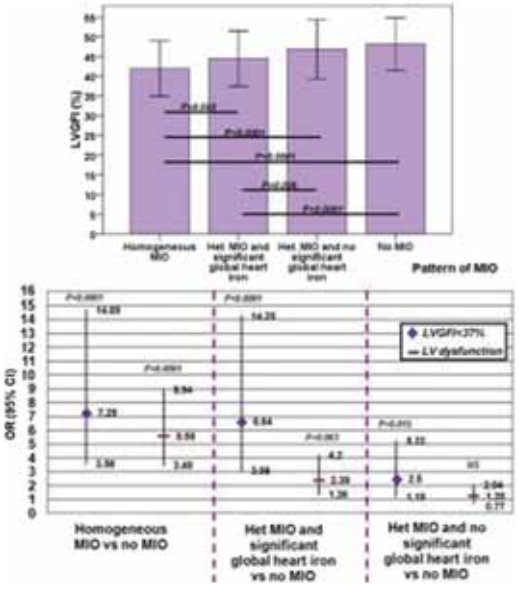

Figure 1

Conclusions: LVGFI is a functional parameter integrating structural as well as mechanical behaviour more stronly associated to different patterns of MIO than the LVEF. Thus, a LVGFI<37% could better identify a significant higher risk of adverse cardiovascular events beyond heart failure in iron loaded patients.

P4474 | BEDSIDE
Effect of splenectomy on cardiac iron and function in different transfusion-dependent patients

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Purpose: The main therapeutic rationale for splenectomy in transfusion-dependent patients with hemoglobinopathies is to decrease blood consumption and transfusion requirement. However, since the spleen is a large physiologic iron depot, splenectomy may have a possible role of in determining extrahepatic iron overload. This study aims to observe retrospectively the effect of splenectomy on cardiac iron and function in different groups of transfusion-dependent patients.
Methods: 1735 transfusion-dependent patients enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) Network were considered. 14 patients had sickle-thalassemia, 23 patients had sickle-cell disease (SCD), 179 had tha-

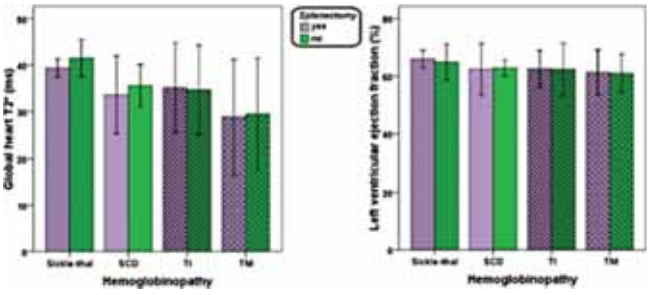

Figure 1

lassemia intermedia (TI) and 1519 had thalassemia major (TM). Cardiac iron was assessed using a multislice multiecho T2* approach. Left ventricular ejection fraction (LV EF) was quantified by cine sequences.
Results: The frequency of splenectomy was: 21.4% in sickle-thalassemia, 65.2% in SCD, 84.9% in TI and 55.1% in TM ($P<0.0001$).
Splenectomized TM patients were older than non-splenectomized patients (34.3±7.9 yrs vs 27.2±7.8 yrs; $P<0.0001$). In each hemoglobinopathy, cardiac T2* and LV EF were comparable between splenectomised and non-splenectomized patients (Fig. 1).
Conclusions: Regardless by the type of hemoglobinopathy, in regularly transfused patients splenectomy was not associated with increased cardiac iron and reduced cardiac function.

P4475 | BEDSIDE
Myocardial fibrosis imaging based on T1-mapping and extracellular volume fraction (ECV) measurement in muscular dystrophy patients: additional diagnostic value compared to conventional LGE imaging

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Background: Cardiac involvement with progressive myocardial fibrosis leading to dilated cardiomyopathy is a major cause of death in muscular dystrophy patients. Extracellular volume fraction (ECV) measurement based on T1-mapping pre- and post-contrast promises the detection of early "diffuse" myocardial fibrosis that cannot be depicted by conventional contrast-imaging based on late gadolinium enhancement (LGE).
Objective: With this study, we evaluated the presence of diffuse myocardial fibrosis in regions of "normal" (LGE-negative) and "diseased" (LGE-positive) appearing myocardium as well as its relation to the extent of left ventricular (LV) dysfunction and the occurrence of arrhythmias in Becker muscular dystrophy (BMD) patients.
Materials and method: Twenty-seven BMD patients (35±12yrs) and 28 matched healthy CONTROLS (33±8yrs) underwent cardiovascular magnetic resonance (CMR) studies including ECV measurement and LGE-imaging. Ambulatory monitoring of arrhythmic events was performed by means of an external event loop recorder.
Results: Twenty BMD patients (74%) demonstrated cardiac involvement as detected by typical inferolateral presence of LGE. Twelve patients (44%) had an impaired LV ejection fraction - all being LGE-positive. Global myocardial ECV was significantly higher in the BMD group (29±6%) compared to the CONTROL group (25±3%, p=0.005). Patients with cardiac involvement demonstrated higher global ECV (31±6%) as well as significantly increased regional ECV not only in LGE-positive segments (34±6%), but also in LGE-negative segments (28±6%) compared to BMD patients without cardiac involvement and to CONTROLS, respectively (24±3% and 25±3%, p=0.01). Global ECV in patients with cardiac involvement substantially correlated to LV ejection fraction (r= -0.629, p=0.003) and to the number of LGE-positive segments (r=0.783, $p<0.001$). On univariable analysis, global ECV – but not the categorical presence of LGE per se – was significantly associated with arrhythmic events (OR 1.97, CI 32.22-1.21, p=0.032).
Conclusion: ECV measurement by CMR is a useful tool in assessing the total extent of myocardial fibrosis as well as in depicting subtle diffuse fibrosis in areas of normal appearing myocardium on LGE-images. Thus, myocardial ECV is a potential additional quantitative tool for accurate detection of cardiac involvement and risk stratification in muscular dystrophy patients.

P4476 | BEDSIDE
Myocardial iron deficiency in non-ischemic heart failure: quantification by cardiac T2-star magnetic resonance imaging

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Purpose: T2* cardiac magnetic resonance (T2* CMR) has been used for the assessment of myocardial iron overload in patients with thalassemia. Although reduction of myocardial iron content was reported to worse cardiac function in experimental models, nothing has been investigated in human subjects. The aim of this study was to utilize T2* CMR to quantify myocardial iron content in patients with heart failure (HF), and to investigate the relationship between iron content, cardiac function, and the etiology of HF.
Methods: CMR data were analyzed from 167 non-ischemic and 31 ischemic HF patients and 50 patients with normal ventricular function. Short-axis T2* imaging was accomplished using 3-Tesla scanner and multi-echo gradient-echo sequence. Myocardial T2* value (M-T2*) was calculated by fitting the signal intensity data for the septum of mid-left ventricle to a decay curve. Non-ischemic HF patients were categorized into patients with ejection fraction (EF) <35% or ≥35%. The relationship between non-ischemic HF with EF <35% and the risk for major adverse cardiac events (MACE) was analyzed by multiple logistic regression analysis using M-T2*and HF biomarkers. ROC analysis was performed to determine the optimal cutoff of M-T2* for the relation to non-ischemic HF with EF <35% or the prediction of risk for MACE. Comparison of M-T2* among the patient groups was performed using Tukey's test.
Results: M-T2* was significantly greater for non-ischemic HF patients (EF<35%: 29±7ms, ≥35%: 26±5ms) than for patients with normal function (22±3ms, $p<0.0001$) or ischemic HF (22±4ms, $p<0.001$). The odds ratio was 1.21 for M-T2* ($p<0.0001$) and were 1.0015 for brain natriuretic peptide ($p<0.0001$) in relation to non-ischemic HF with EF <35%. Further, this value was 0.96 for systolic blood pressure (p=0.012) and 1.02 for M-T2* (p=0.03) in relation to the risk for MACE in patients with non-ischemic HF. ROC analysis revealed on optimal T2* threshold of 26.3ms for identifying non-ischemic HF patients with EF <35% with a C-statistics of 0.78, and this value of 25.1ms for predicting MACE with a C-statistics of 0.66.
Conclusions: T2* CMR demonstrated the robust relationship between myocardial iron deficiency and non-ischemic HF. M-T2* is a biomarker that can predict adverse cardiac function in patients with non-ischemic HF.

P4477 | BEDSIDE
Impact of distribution patterns of myocardial fibrosis on sympathetic nervous dysfunction and long-term cardiac outcome in patients with idiopathic dilated cardiomyopathy

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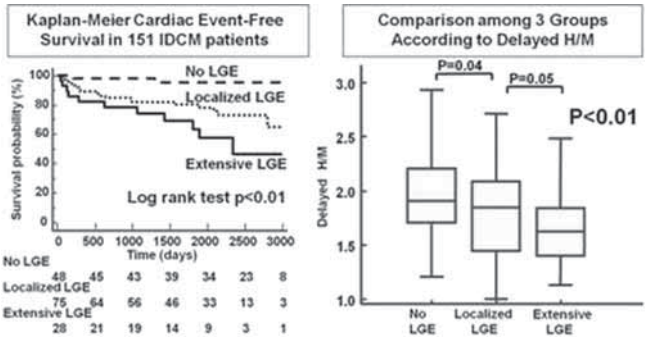
Purpose: Myocardial fibrosis detected by late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) and sympathetic nervous dysfunction detected by 123I-metaiodobenzylguanidine (MIBG) are associated with worse outcome in idiopathic dilated cardiomyopathy (IDCM) patients. We previously reported that combination of LGE and MIBG serves as a strong predictor of cardiac outcome. LGE is observed at various distributions. However, it is not established whether distribution of myocardial fibrosis is associated with sympathetic nervous function or clinical outcome. We sought to investigate clinical impact of LGE distribution on sympathetic nervous function and cardiac events in IDCM.
Methods: We studied consecutive 151 DCM patients (61±15 years, 102 males, LVEF 31±8%) who underwent CMR and MIBG around the same time. Distribution of myocardial fibrosis was estimated by LGE on CMR. Sympathetic nervous function was evaluated by heart/mediastinum ratio in delayed phase (delayed H/M) calculated with MIBG. Cardiac death and heart failure hospitalization were defined as events (follow-up 2150±806 days).
Results: LGE distributed mainly in the inter-ventricular septum, whereas spread more diffusely into other segments in part of patients with IDCM. Patterns of LGE distribution were divided into three groups; no LGE (n=48), localized LGE (localized at septum, n=75), and extensive LGE (spread into other segments, n=28). Among three groups, extensive LGE group was associated with greater prevalence of adverse events ($P<0.01$). Delayed H/M was lowest in extensive LGE group ($P<0.01$).



Conclusion: Extensive LGE is associated with sympathetic nervous dysfunction and long-term adverse events. The analysis of LGE distribution can be useful to stratify the risk in patients with IDCM.

P4478 | BEDSIDE
Degree of left ventricular myocardial trabeculation and non-compaction phenotype do not influence the prognosis of non-ischemic dilated cardiomyopathy

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Background: Increased left ventricular (LV) myocardial trabeculation has been described in several cardiomyopathies, and particularly in non-compaction cardiomyopathy. Yet its prognostic impact remains unknown. Therefore we investigated whether the degree of LV trabeculated myocardium (Trab), assessed by cardiac magnetic resonance (CMR), influences the prognosis of patients with non-ischemic dilated cardiomyopathy (DCM).
Methods: 158 patients (53±14 years, 99 males) with DCM, LV ejection fraction (EF)<40% and without coronary artery disease by angiography or multidector CT, underwent cine and delayed-enhancement (DE) CMR. The amount of Trab was assessed in end-diastole, by 2 methods: 1) as the maximum ratio of Trab/nonTrab

myocardium measured on long axis cine images and 2) as Trab/nonTrab mass measured on short axis cine stacks. Patients were followed for a composite endpoint of cardiovascular death, heart transplantation, left ventricular assist device implantation, resuscitated cardiac arrest and appropriate device choc (MACE). Kaplan-Meier survival and Cox proportional hazards analysis were used to assess the relationship between the degree of trabeculation and MACE.
Results: Mean indexed LV end-diastolic (EDV) and end-systolic (ESV) volumes were 162±51 ml/m^2 and 125±50 ml/m^2 respectively. Mean LV EF was 24±8%. 36% of patients had DE. The mean±SD Trab/nonTrab ratio was 1.95±1.0. Trab/non Trab mass was 23±8%. Trab mass was significantly correlated to Trab/non Trab ratio (r=.60, p<.001). 70 patients had a end-diastolic Trab/non trab ratio>2.3 suggesting non-compaction. Over a median follow-up of 3.2 years, 26 patients had MACE. Univariate Cox analysis identified NYHA class (p=.046), smoking (p=.009) diastolic blood pressure (p=.03), LVEDVi (p=.003), LVESVi (p=.002), RVEDVi (p=.004), RVESVi (p=.001), LVEF (p=.005) and RVEF (p=.001) as independent predictors of MACE. By contrast, the degree of trabeculation, either assessed by Trab/NonTrab ratio or by Trab mass, was not related to outcome. In multivariable analysis, RVEF was the only independent predictor of event free survival [HR=0.95, 95% CI [0.93-0.98], p=0.006].
Conclusion: The strongest predictor of outcome in our patients with dilated cardiomyopathy was right ventricular ejection fraction. In contrast, prognosis was not influenced by the degree of left ventricular myocardial trabeculation. This argues against non-compaction phenotype being a more severe form of dilated cardiomyopathy.

IMAGING, ARRHYTHMIAS AND CHD

P4480 | BEDSIDE
Cardiac sympathetic denervation assessed with iodine-123-metaiodobenzylguanidine imaging predicts cardiac death and ventricular arrhythmias in primary prevention implantable cardioverter-defibrillator

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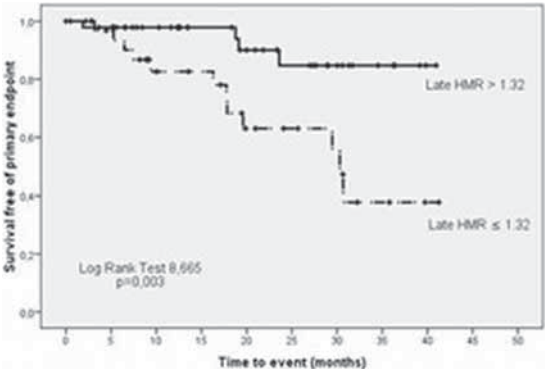
Purpose: Identification of noninvasive prognostic markers of arrhythmic risk in patients with advanced heart failure remains challenging. We examine whether the assessment of cardiac sympathetic activity by 123-Iodine Metaiodobenzylguanidine (123I-MIBG) can improve risk stratification in primary prevention implantable cardioverter-defibrillator (ICD) candidates.
Methods: 84 heart failure patients referred for ICD therapy were enrolled. During evaluation of ICD implantation, patients underwent 123I-MIBG. Early and late 123I-MIBG imaging was performed to assess cardiac innervation (heart-to-mediastinum ratio –HMR- and cardiac washout rate).Endpoint of the study was the composite of appropriate ICD therapy, ventricular tachycardia and cardiac death. A multivariate Cox proportional hazards model was used to analyze the influence of 123I-MIBG in predicting the endpoint.
Results: During a mean follow-up of 18 [6,35-27,65] months, the endpoint was documented in 16 (19%) patients (5 cardiac death, 6 ICD therapy, 2 antitachycardia pacing and 3 tachycardia ventricular). Patients with the endpoint showed heart-to-mediastinum ratio significantly lower (1.26 vs 1.37, p=0.035). Patients with late HMR ≤1.32 (sensitivity 75%, specificity 64%) reached significantly more frequently the endpoint (33.3% vs 3%, p=0.003) than patients with a late HMR >1.32. Late HMR ≤1.32 (HR 7,01; IC 95% 2,06-24,43; p=0,002) and creatinine levels (hazard ratio 6,79; IC 95% 2,651-17,379; p<0,001) were independent predictors for the endpoint.



Conclusions: Heart failure patients referred for ICD therapy have a serious deterioration of cardiac sympathetic activity quantified by 123I- MIBG. Nonetheless, cardiac sympathetic denervation predicts arrhythmic events and cardiac death.

P4481 | BEDSIDE
Early detection of ventricular contraction abnormality in patients with idiopathic ventricular arrhythmias using three-dimensional speckle tracking analysis

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Background: Idiopathic ventricular arrhythmias (VA) possess the risk of VA-related cardiomyopathy. We postulated that VA-related mechanical dyssynchrony during early stage could be identified by using 3-dimensional speckle tracking echocardiography (3DE).
Methods: Thirty patients with VA and normal LVEF underwent catheter ablation were enrolled after excluding structural heart disease. Standard echocardiography and 3DE were performed. The speckle tracking analysis was performed offline with commercial software provided with the Artida Echocardiography, and the results were compared to 60 normal subjects during the same period. Electrophysiological characteristics and electroanatomical properties of substrates were explored.
Results: There was no difference for age and gender distribution between two groups. Both groups had normal LVEF. Speckle tracking analysis with 3DE showed significantly higher standard deviation of time to peak longitudinal strain (LSt_SD) in VA group, while global longitudinal strain, circumferential strain (CS) and radial strain (RS), standard deviation of time to peak CS (CSt_SD) and RS (RSt_SD) were similar. Ventricular substrate analysis for VA group showed small-sized low voltage zone in 15 patients, and no LVZ or scar zone in the remaining 15 patients.

Table 1. Basic characteristics and three-dimensional speckle echocardiography analysis

	Ventricular arrhythmias (n=30)	Control (n=60)	P value
Age, years	43.3±16.7	47.9±14.4	0.293
Gender (male), %	60.0%	50%	0.572
LVEF, %	61.2±7.3	63.8±5.2	0.115
Longitudinal strain, %	–14.9±6.1	–16.2±3.1	0.439
Circumferential strain, %	–28.5±11.1	–26.2±5.7	0.460
Radial strain,%	24.4±14.4	20.7±9.0	0.370
LSt_SD, sec	89.6±49.0	54.5±37.2	0.004
CSt_SD, sec	59.9±42.2	47.9±34.6	0.264
RSt_SD, sec	86.1±40.0	98.7±56.8	0.431

Conclusion: The finding of mechanical dyssynchrony in early stage of VA, irrespective of normal LVEF and fair endocardial substrate, provided better understanding of pathogenesis of VA-related cardiomyopathy.

P4482 | BEDSIDE
Cardiovascular magnetic resonance in patients with MRI-conditional pacemakers: a single centre experience

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Background: While the safety profile of MRI-conditional pacemakers (PPMs) appears good, limited data exists regarding the indications and management outcomes of these examinations and the impact of the device on image quality.
Methods: CMR imaging and pacing data from serial patients with MR conditional PPMs performed at our centre was retrospectively reviewed. Images were acquired using a dedicated 1.5T scanner with an eight-channel phased-array receiver coil. The indication for imaging and any change in management resulting from CMR was recorded. The quality of cardiac cine (SSFP and FLASH sequences) and Gadolinium imaging was rated by an observer blinded to clinical details.
Results: 33 CMR scans of 31 patients, aged 54±14 undertaken between 2011 and 2014 were assessed. All scans were completed successfully with no significant change in lead thresholds or pacing parameters. The CMR data resulted in a new diagnosis in 15 (45%) patients and provided data changing clinical management in a further 7 (21%), Table 1. Cine imaging was performed using SSFP imaging in 14 patients, using SSFP and FLASH in 31 patients and FLASH alone in 2 patients. Non diagnostic cine imaging was significantly less common with FLASH sequences compared to SSFP sequences (18% vs 0%, p=0.004). Gadolinium imaging was performed in 28 patients with artefact resulting in non-diagnostic imaging in only one patient.

Indication for CMR

Indication	n	New diagnosis	Additional data that changes management
Aetiology of syncope/complete heart block	9 (27%)	3 (9%)	
Possible cardiomyopathy	9 (27%)	7 (21%)	2 (6%)
Cardiac sarcoid: diagnosis or follow up	6 (18%)	2 (6%)	
Aortic dimensions (Marfains/post AVR)	4 (12%)		4 (12%)
LV function assessment	2 (6%)	2 (6%)	
Ischaemia/viability	2 (6%)		1 (3%)
Iron loading (Thallasaemia patient)	1 (3%)	1 (3%)	
Total	33	15	11

Conclusions: CMR may be safely performed in patients with MR conditional

PPMs and provides important diagnostic or management-changing information. FLASH sequences improved rates of non diagnostic imaging when compared to SSFP sequences, while gadolinium imaging was less susceptible to artefact.

P4483 | BEDSIDE
Esophageal wall tissue reaction acute after Cryoballoon ablation in patients with paroxysmal atrial fibrillation, a LGE-MRI study

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Background: Esophageal wall thermal injury after Cryoballoon ablation is a potentially serious complication.
Aim: We thought to compare the relationsship of acute esophageal tissue reaction detected using LGE-MRI acute after pulmonary vein isolation (PVI) using both generations of the Cryoballoon in patients with paroxysmal atrial fibrillation (PAF).
Methods and results: Fifty-six patients with PAF (35 male, mean age 59.9±10.5 years old) were included into this study. All patients underwent PVI using the Cryoballoon technique. The "traditional" AF balloon was used in 33 patients (58.9%) whereas the "new" AFA was used in 23 patients (41.1%). LGE-MRI of the left atrium (LA) was performed before and within 24 hours after PVI in all patients. Significant enhancement of the esophageal wall (EWE) as a sign of acute tissue reaction after ablation was found in 22 patients (39.3%). Local tissue reaction was independent from the type of Cryoballoon as EWE was detected in 33.33% in the AF and 47.87% of the AFA group (p=0.275, Fig. 1). EWE was related to the anatomical conditions of the esophagus as EWE was significant higher in those patients where the esophagus was in contact with the left or right inferior pulmonary veins compared to patients where the esophagus was in contact with the posterior wall of the LA (62.5% vs. 8.3%, p=<0.001; Fig. 2).

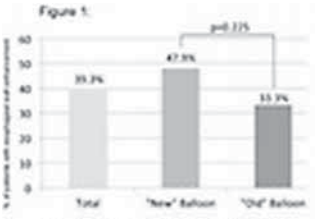

Figure 1: Columns gives % of patients found with esophageal wall enhancement acute after pulmonary vein isolation using the "old" Artic Front or the "new" Artic Front Advanced Balloon

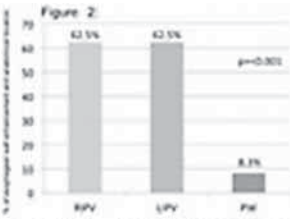

Figure 2: Columns gives % of patients with esophageal wall enhancement acute after pulmonary vein isolation regarding to the anatomical location and contact of the esophagus with the left atrium. RIPV = Right inferior pulmonary vein, LIPV = Left inferior pulmonary vein, PW=Posterior Wall.

Conclusion: From our preliminary data, acute esophageal tissue reaction detected using LGE-MRI after Cryoballoon ablation is correlated with the anatomical relationship of the esophagus and the left atrium and is independent form the used Cryoballoon. Anatomical location of the esophagus can be easily assed with the MRI and should be considered for patients safety during the ablation procedure.

P4484 | BEDSIDE
Late-gadolinium enhanced cardiac MRI defined scar is predominantly located on the left atrial septum and posterior wall in patients with persistent atrial fibrillation

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Purpose: Structural remodelling with fibrotic change is a fundamental determinant of atrial fibrillation (AF) and with electrical remodelling, contributes to the AF substrate. Late-gadolinium enhanced (LGE) cardiac magnetic resonance imaging (CMRI) has been used to detect pre-existent left atrial (LA) scar. LGE-CMRI in the LA has been previously correlated to endocardial voltage. The extent of left atrial fibrosis as determined by LGE-CMRI has been shown to predict clinical outcomes in patients with AF, as well as success following catheter ablation. We sought to non-invasively characterise the distribution of LA scar in patients with persistent AF (PsAF) with LGE-CMRI.
Methods: Patients undergoing first-time ablation procedures for PsAF underwent LGE-CMRI two weeks prior to the procedure with a 1.5T MRI system as described previously. The directly measured LA wall intensities were expressed as multiples of standard deviations (SD) above the mean blood pool intensity (MBPI) to provide a normalised LA wall intensity (NLA). The LA "scar" maps were generated using custom made software written on C++. Maps were imported into a data visualisation application, for manual segmentation into the following LA anatomical regions: septum, anterior wall and posterior wall. The posterior wall was further divided into quadrants. The burden of scar in each region was represented as a percentage of the total area occupied by NLA >2 SD. Statistical analyses were performed using two-tailed unpaired Student's t-test.
Results: A total of 60 patients (age 64±13 yrs, LA size 43±6mm) were analysed. Average LA surface area was 9980±1992mm. Scar as defined by NLA >2SD appears to have predilection to the septum and posterior wall (mean scar burden: posterior wall 17.4±12.2%; septum 16.0±12.6%; anterior wall 10.0±9.9%; p<0.01) with 48 patients having a greater burden of scar on the posterior vs. anterior wall. On a per patient basis there was on average a 4.7±6.8x greater burden of scar on the posterior than anterior wall. On the posterior wall, the left inferior quadrant had the greatest scar burden (mean scar burden, left superior 15.5±16.6%; left inferior 26.5±19.1%; right superior 13.6±11.3%; right inferior 14.4±16.4%; p<0.01).
Conclusions: LGE-CMRI defined scar appears to be predominantly localised to the LA septum and posterior wall. Within the posterior wall, the left inferior quadrant has substantially more scar than other regions. The underlying basis for the distribution of this described LGE is not known and requires further investigation.

P4485 | BEDSIDE
Effect of diabetes on post-infarction remodeling in patients with STEMI receiving primary percutaneous coronary intervention: results of the PROMISE trial

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Background: Patients with STEMI receiving primary percutaneous coronary intervention (PPCI) have a variable evolution of left ventricular ejection fraction (LVEF). The determinants of this evolution are not fully understood.
Objective: The objective of this study was to investigate the evolution of LVEF post PPCI and to identify predictors of its decrease.
Methods and results: 201 patients with STEMI receiving PPCI within 6 hours of symptoms onset with TIMI flow 0-1 were included in the PROMISE trial to investigate the effects of intracoronary adenosine on infarct size. In this population intracoronary adenosine had no significant effect on infarct size (assessed by late enhancement in CMR). Familial and personal history, risk factors, treatments, hemodynamic, angiographic and procedural variables were recorded. In 138 patients a CMR study was performed in the first week and after six months. Adverse LVEF evolution (AEFE) was defined as a negative change of more than 3 percent points. In a first step, the association between the different variables and AEFE was studies by univariate analysis. The contribution of variables significantly associated, or highly relevant, with AEFE was studied by multiple regression analysis.
Results: Of the 138 patients, 79 (57%) patients presented an improvement of the LVEF, however, the LVEF decrease in 59 (43%) patients, fulfilling the criteria of AEFE in 38 (27%) patients. Multivariate analysis identified infarct size (Odds Ratio (OR): 1.07, p<0.001), LVEF in the first week after infarction (OR: 1.1, p=0.004), and diabetes (OR: 3.78, p=0.04) as independent predictors of AEFE. Of note, that the rest of clinical variables, such as, age, sex, risk factors other than diabetes, ischemic time or involvement of the LAD as the culprit artery did not contribute to the prediction of AEFE.
Conclusion: The evolution of LVEF after STEMI is highly variable. In addition to large infarct size and reduced initial LVEF, the presence of diabetes constitutes an independent predictor of AEFE. These results suggest that a more close follow-up of patients with diabetes surviving an STEMI may be necessary, independently of age, sex or infarct localization.

P4486 | BEDSIDE
Cardiovascular magnetic resonance versus echocardiography in measurement of left ventricular wall thickness in paediatric patients with known or suspected hypertrophic cardiomyopathy

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Purpose: Hypertrophic cardiomyopathy (HCM) is a leading cause of sudden cardiac death in the young. Accurate measurement of maximal left ventricular wall thickness (LVWT) is essential for the diagnosis and risk stratification of patients with suspected disease. The use of echocardiography for the assessment of LVWT is common practice, however, cardiovascular magnetic resonance (CMR) provides high spatial resolution imaging and is well suited for this purpose. We sought to compare measurements of LVWT obtained by both CMR and echocardiography in a paediatric population.
Methods: Serial paediatric patients under investigation for known or suspected HCM underwent CMR and echocardiographic imaging a median of 0 days apart. Measurements of LVWT using a 16 segment model were derived from the resulting images, including an estimate of maximal LVWT. The results for both imaging modalities were compared. The data was collected by two operators blinded to the clinical outcome and intra-operator reproducibility was assessed using the co-efficient of variability.
Results: 53 patients with a mean age of 13±3 years (range 3-16 years) were studied. 17% were aged <10 years. 11 patients met the diagnostic criteria for HCM. It was not possible to obtain echocardiographic images of diagnostic quality

for 1 patient. Of the images obtained, 100% of CMR scans and 83% of echocardiograms were of sufficient diagnostic quality for measurement of LVWT using the 16 segment model. Intra-operator reproducibility for maximal LVWT was significantly better for CMR measurements compared to echocardiography (CoV 3.5% vs 22.6%). Overall, CMR produced a lower estimate of LVWT compared to echocardiography (9.4±5.9 mm versus 11.0±6.3 mm; $P<0.003$), with greatest measurement discrepancy in the apical segments ($P<0.003$).
Conclusion: It is clear that CMR can be safely performed in a paediatric population and images of sufficient diagnostic quality are more reliably obtained compared to echocardiography. LVWT measurements derived from CMR images were highly reproducible and CMR was observed to consistently produce a lower estimate of LVWT for all 16 segments, with greatest measurement discrepancy in the apical segments. Overall this may suggest a preferential role for CMR compared to echocardiography in the diagnosis and follow-up of hypertrophic cardiomyopathy in the paediatric population.

P4487 | BEDSIDE
The assessment of the positional change of the amplatzer septal occuluder after transcatheter closure of atrial septal defect -midterm results analyzed by real-time three-dimensional echocardiography-

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Background: Transcatheter closure of secundum atrial septal defect with Amplatzer Septal Occuluder (ASO) has become an alternative to open heart surgery. Althought they are considered safe with a low complication rate, deficient superior rim, oversized ASO and aortic rim absence in multiple views carry the risk of remote cardiac perforation. Whether growing children after ASO are at increased risk is not established yet. Purpose The purpose of this study is to evaluate the position and the progress of ASO devices relevant to adjacent cardiac structures in growing children using three-dimensional echocardiography (3DE) and two dimensional echocardiography (2DE). Subjects Nine patients were selected who underwent ASO at our hospital as well as 3D and 2D echo at right after ASO and at 5 years after ASO. (The age of ASO: 7±2 year, Height: 114±10cm, Body weight: 20±5 kg, device size: 14±3mm.)
Method: The diagnostic apparatus was Philips iE33 with X7-2 probe (Philips medical System).3D volume data from apical four-chamber images were acquired. The full volume data were analyzed by off-line soft ware: QLAB. LV apex and ventricular septum and the device were set to form a straight line both in the for-chamber and two-chamber plane which are made from the 3D reconstruction date. We measured the distance from the edge of the device to the peripheral structure, because it was observable among the mitral valve, tricuspid valve, posterior margin, inferior margin, aorta, and superior and inferior vena cava. We similarly measured these distance by 2DE.We comparatively analyzed the 3DE and 2DE images taken at right after ASO and 5 year after ASO.
Result: The distances in 3D measurement were changed as follows, inferior vena cava (IVC) rim: 10.4→13.7mm Aortic rim: 1.4→0.7mm posterior 30°: 3.9→4.8mm Tricuspid rim (TV): 8.5→10.9mm Mitral valve (MV) rim: 6.1→7.2mm posterior 0°: 4.8→5.9mm posterior 60°:4.0→5.5mm, whlie, in 2D measurement, superior vena cava (SVC) rim 6.5→9.8mm IVC rim: 9.1→11.3mm Aortic rim: 0.8→0.7mm posterior-inferior: 3.7→4.3mm TV rim: 8.5→9.9mm MV rim: 6.5→7.7mm posterior-superior: 4.0→7.0mm. Interobserver agreement was robust in 3D measurement ($p<0.05$).
Conclusion: The aortic root contact had never changed during the growth process, however, the atrial septum surrounding the device had grown in all the areas except for the aortic rim. 3DE was superior in the temporal evaluation of the same cross-section compared with 2DE, and was able to observe the positional relationship with the ASO device in multi-sectional views.

P4488 | BEDSIDE
Intraoperative pericardial real-time three-dimensional echocardiography, a novel technique for guiding intracardiac surgical correction of the congenital heart disease

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Background: Three-dimensional anatomical assessment for the intracardiac surgery in the congenital heart disease would be necessary to elucidate it's complexity. However, real-time three-dimensional esophageal echocardiography cannot be applied for the patients less than 15kg, we assess the impact of intraoperative pericardial real-time three-dimensional echocardiography (PRT3DE) on the surgical correction of the congenital anomaly.
Objectives and methods: 35 patients were enrolled in this study at median age of 2 yrs (5 days-13 yrs, 24 cases with severe atrioventricular valve regurgitation and 11 cases with complex VSD including double outlet right ventricle or transposition of great artery, 2.3-45.6kg median 9.6kg). We performed PRT3DE, immediately after the chest was opened, and put the ultrasound probe directly onto the pericardium which enables us to collect volume data with a high S/N ratio and image resolution. Then, we reconstructed 3D images by online workstation system (QLab) at operating room and use the image as surgical guide. We compared the actual surgical findings to those in the 3D images viewed from surgeon's position and those in the 2D images.
Results: We could reconstructed 3D images of good quality within 15 minutes in 34 of 35 patients (97%). In 34 patients, all of the reconstructed images were well matched surgical findings and provided comprehensive informations for valveloplasty, VSD closure and intracardiac rerouting, when comparing to those of 2D images. The grades of regurgitation after valvuloplasty were improved from 4.0±0.2 to 1.5±0.9. Especially, in common atrioventricular valve with single ventricle, we could evaluate appreciate size and relation of each leaflet and valvular complex accurately and clarify the mechanisms of regurgitation. Moreover, in six cases of complex VSD, we decide to perform VSD rerouting by using 3D guide. All six cases underwent the intracardiac correction successfully.
Conclusions: PRT3DE is one of the most effective methodologies to obtain critical and detail informations on complicated intracardiac 3D structures in congenital heart disease. This approach also enables both cardiovascular surgeons and cardiologists to share the "surgeon's view" in the operating room for planning of cardiac surgery.

P4489 | BEDSIDE
Left ventricular dysfunction, adverse myocardial and aortic remodeling in patients with tetralogy of Fallot without symptoms of heart failure after surgical repair

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Background: Repair of tetralogy of Fallot (ToF) frequently has long-term sequelae of right ventricle (RV) dysfunction, which may also lead to left ventricular (LV) dysfunction due to unfavorable RV-LV coupling. We hypothesized that ToF can lead to adverse left heart remodeling, including LV myocardial extracellular matrix expansion, hallmarks of a cardiomyopathic process.
Methods: Cardiac magnetic resonance (CMR) was performed at 3.0 Tesla in 109 asymptomatic ToF patients, (age: 19.3±12.8 years) after surgical correction (16.6±10.0 years post operation), and 64 age-matched controls. Parameters of LV and left atrial (LA) function and aortic distensibility were obtained from cine CMR. In a subgroup (n=50), T1 mapping was used to determine the myocardial extracellular volume fraction (ECV) as an index of diffuse myocardial fibrosis.
Results: Compared to control subjects, ToF patients had a lower LV ejection fraction (EF) (50.7±8.8 versus 59.0±5.4; $p<0.01$), despite a similar RV EF ($p=0.34$). ToF showed a lower LV mass index, lower LV mass-to-volume ratio, and lower aortic distensibility. LA passive volume and LA total ejection fraction were decreased, and associated with age ($p<0.01$), suggesting an early onset of diastolic dysfunction. ECV was elevated in ToF (0.32±0.05 versus 0.26±0.01 in controls ($p<0.01$), more so in females ($p<0.05$), and was inversely associated with LV mass index ($p<0.05$).
Conclusions: During long-term follow-up after repair of ToF, asymptomatic patients show alterations in LV geometry, function, tissue structure, and aortic distensibility. These findings indicate an early adverse cardiovascular phenotype and underscore the need for life-long follow-ups.

NEW INSIGHTS IN RESTENOSIS

P4491 | BEDSIDE
Safety and efficacy of treatments for in stent restenosis: a network meta-analysis of randomized controlled trials

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Purpose: The optimal treatment for patients presenting with in-stent restenosis remains to be defined, given the large spectrum of alternative strategies. We performed a network meta-analysis of randomized controlled trials to compare safety and efficacy of the different treatments for in-stent restenosis.
Methods: All randomized controlled trials investigating different treatments for patients presenting with in-stent restenosis were included. Major adverse cardiac events (a composite end point of death, myocardial infarction, target lesion revascularization, myocardial infarction and stent thrombosis) were the primary end point, while its components the secondary ones and where appraised within a hierarchical Bayesian model computing odds ratios.
Results: Non compliant/semi compliant balloons were evaluated in 11 studies with 1149 patients, bare metal stent in one study with 224 patients, rotablator in one study with 146 patients, sirolimus eluting stent in 9 with 1017 patients, paclitaxel eluting stent in 7 with 1048 patients, paclitaxel coated balloon in 4 studies with 282 patients, everolimus eluting stent in 1 study with 32 patients, and brachytherapy in 5 with 716 patients. After a median of 12 months (10-14), paclitaxel coated balloon performed not inferior to sirolimus eluting stent, paclitaxel eluting stent and everolimus eluting stent, all of them being superior to non compliant and cutting balloon. This reduction in major adverse cardiac events was

mainly driven by reduction in target lesion revascularization obtained by paclitaxel coated balloon, paclitaxel eluting stent, sirolimus eluting stent when compared to other strategies. Rates of myocardial infarction did not differ between various treatments, as those of stent thrombosis, apart from a reduction of stent thrombosis offered by paclitaxel coated balloon when compared to cutting balloon (odds ratio 0.28: 0.02-0.9, all confidence interval 95%).
Conclusions: Paclitaxel coated balloon performed similar to first generation drug eluting stent for treatment of in-stent restenosis, being superior to cutting and non compliant balloon.

P4492 | BEDSIDE
Dimethylarginine dimethylaminohydrolase 1 gene polymorphisms predict accelerated venous intimal hyperplasia in hemodialysis patients

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Purpose: Venous intimal hyperplasia is a significant clinical problem in patients with hemodialysis arteriovenous fistulas and patients with bypass vein grafts. Although endothelial dysfunction plays a critical role in the development of atherosclerosis, their role in venous intimal hyperplasia is less clear. Dimethylarginine dimethylaminohydrolase 1 (DDAH1) is the major enzyme eliminating asymmetric dimethylarginine (ADMA), a well-known contributor of endothelial dysfunction. The aim of our study is to investigate the effect of genetic variations in DDAH1 gene on venous intimal hyperplasia of hemodialysis patients with venous stenosis of arteriovenous fistulas.
Methods: From May 2010 to January 2012, we assessed the relation between polymorphism in DDAH1 and the development of venous stenosis after a balloon angioplasty of hemodialysis vascular accesses. The cohort comprised of 473 chronic hemodialysis patients who were prospectively followed up for one year after a balloon angioplasty at the outflow vein of hemodialysis vascular access. Eleven single nucleotide polymorphisms (SNPs) of endothelial function related genes, including DDAH1, DDAH2, and endothelial nitric oxide synthetase (ENOS), were analyzed and plasma ADMA levels were determined at baseline. Accelerated venous intimal hyperplasia was defined as more than 50% diameter stenosis at the target venous lesion within three months after a balloon angioplasty.
Results: After adjustment of demographic, vascular access, and cardiovascular risk factors, individuals with high baseline plasma ADMA ($>0.9\mu M$) levels had higher rates of 3-mon target-lesion restenosis at the outflow veins (56% vs. 36%, p=0.05). Among the eleven SNPs, only DDAH1 rs233112, DDAH1 rs1498373, DDAH1 rs2210073 was significantly associated with increased levels of plasma ADMA levels. Compared with patients with rs233112 AA genotypes, those with rs233112 GA or GG genotypes had higher 3-mon target-lesion restenosis rate at the outflow vein. (80% vs. 59%, $p<0.001$). Compared with patients with rs1498373 CC genotype, those with CT or TT genotypes had higher risks of 3-mon target-lesion restenosis at the outflow vein. (74% vs. 57%, $p<0.001$) In the multivariate model, current smokers, graft access, rs233112 GG+GA genotypes (HR 2.302, 95% CI 1.557-3.407), rs1498373 CT+TT genotype (HR 2.070, 95% CI 1.450-2.957) had higher risk of target-lesion restenosis at 3 month.
Conclusions: Our results provide the first evidence that SNPs rs233112 and rs1498373 of DDAH1 are associated with accelerated venous intimal hyperplasia in the hemodialysis patients.

P4493 | BEDSIDE
Angiographic restenosis after percutaneous coronary intervention in HIV-infected patients- incidence and predictors

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Background: Patients infected with human immunodeficiency virus (HIV) are at risk of accelerated coronary arteriopathy. With the success of combinded antiretroviral therapy, HIV infection has become a chronic condition and percutaneous coronary intervention (PCI) in HIV-infected patients has become an important treatment option. However, dedicated angiographic follow-up studies examining anti-restenotic efficacy in PCI-treated HIV-infected patients are lacking.
Methods: Patients with HIV infection who underwent coronary stenting were enrolled in a dedicated registry. Clinical and laboratory data were prospectively collected in an online database. Angiographic follow-up was scheduled at 6-8 months and predictors of restenosis were evaluated.
Results: A total of 47 HIV-infected patients were enrolled. Angiographic follow-up was available in 44 patients (93.6%) with 63 treated lesions. Mean age was 65.5 ± 10.0 year, 86.8% were men, and 72% had multivessel disease. Overall 52 lesions were treated with drug-eluting stents, 11 lesions with bare metal stents. The rate of binary angiographic restenosis was 17.5% (drug-eluting stents: 17.3% vs. bare metal stents: 18.2%). We observed a significant association of binary angiographic restenosis with elevated triglyceride level (P=0.032), therapy with two or more protease inhibitors (P=0.024) and an elevated CD-8 cell count (P=0.029).
Conclusion: The rate of angiographic in-stent restenosis in HIV-infected patients is very considerable. Patients with restenosis had higher triglyceride levels, were treated with more than one protease inhibitors and showed higher CD-8 cell count. Dedicated randomized studies should examine the optimal treatment of this high-risk patient group.

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Evidences of inflammation and oxidative stress implication in the in-stent restenosis evolution

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Aim: Evaluation of the circulatory markers of inflammation and oxidative stress in patients with in-stent restenosis (ISR) developed after coronary angioplasty.
Material and methods: The one year dynamics of blood twelve markers of non-specific inflammation and eleven markers of oxidative stress have been assayed in 68 patients with ISR confirmed by coronarography and exposed to secondary revascularization. Their value was compared with respective indices estimated in 40 healthy persons (control marker).
Results: The obtained outcomes showed a significant rise in a range of 33,3-73,8% of preprocedural levels of TNF-α, IL-6 and IL-8, MCP-1, MIP-1 (macrophage inflammatory protein) soluble SD40 ligand and resistin. The IL-2 and IL-12 elevation was weak in a scope of 8,1-12,7%. On the other hand, heregulin-1β had a decline of 42,6% ($p<0,001$). In first 24 hours after stent stenosis correction all assayed cytokines (excepted heregiline-1β) raised, IL-6 and MIP-1β achieving biggest difference vs control (89,7 and 130,5%). After 6 and 12 months these markers have been remained different to control and indicated an excessive inflammatory response. In regard to oxidative stress it is to note the significant preprocedural elevation of the MAD and advanced oxidized protein products by 44-56,3% while total antioxidant active has fallen doubly. The enzymes of glutathione-redox system did not modified, but AGEs, arginase and fructosamine raised significantly by 23-34,6%. Like inflammation oxidative stress activity augmented postprocedurally (24 h) and maintained elevated even 12 months after secondary revascularization.
Conclusions: (1) Inflammatory response and oxidative stress are boosted in patients with ISR, increase more in first 24 hours after secondary revascularization and do not redress after 12 months. (2) The specific markers of inflammation and oxidative stress may be feasible predictors of in-stent restenosis risk.

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Drug-eluting balloon in 001 bifurcated lesions

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Purpose: In the DES era, the best strategy to treat ostial lesions remains unanswered. This is the first prospective registry assessing the efficacy and safety of second generation of paclitaxel-coated, drug-eluting balloon (PEB), ($3.0\mu g/m^2$ balloon surface area), in patients with 001 bifurcated lesions placed in secondary branches.
Methods and results: After 2.7 years, 51 patients with 001 bifurcated lesion and clinical evidence of myocardial ischemia related to the target lesions were prospectively included in this multicenter (7 center) registry. After optimal dilatation, a PEB was inflated for a minimum of 45 seconds. In 2 patients after predilatation the DEB could not be used and patients were excluded. Left main bifurcated lesions, severe calcification and cardiogenic shock, were the only exclusion criteria. Patients were 62 ± 12 years old, 42% diabetic, 56% ACS as clinical presentation. The most frequent lesion treated was first diagonal (41%). Radial approach was done in most cases (84%). Pre-dilatation was done in all the cases, with cutting balloon in 59%. Angiographic success was 90% (by protocol in 10% of lesions a BMS was implanted because of significant acute recoil (4) or coronary dissection more that type B (1)). At 1 month (follow-up completed in all the patients) there was no adverse event (MACE). At mean of 14.2 ± 2.2 months there was 13.7% cumulative hierarchical MACE (1 MI, 0 cardiac deaths, 7 TLR). There was thrombosis or occlusion. In 4 selected centers at a mean of 7.2 ± 1.1 months, angiographic follow-up was completed in 32/37 (86.4%) patients; reference diameter was 2.2 ± 0.3 mm with a binary restenosis of (5) 16.1%.
Conclusion: We report the first prospective registry assessing 001 bifurcated lesion placed in small vessels (2.2mm). This is a rare type of coronary lesion (inclusion period of 2.7 years) that was observed in a relative young and diabetic population. In this complex setting, second generation of PEB is a safe strategy (no acute thrombosis or cardiac death), technically easier and it seems to be effective at mid-term follow up with a 14% MACE at 1 year.

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Predictors of recurrent restenosis in patients with 2nd generation drug-eluting stent implantation for in-stent restenosis of drug-eluting stent

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Purpose: Recent studies show that 2nd generation drug-eluting stent (DES) is superior to 1st generation DES for the treatment of in-stent restenosis (ISR). However, recurrent restenosis still occurs in some cases and the predictors of recurrent restenosis remain unclear. Thus, we evaluated the predictors of recurrent restenosis in patients treated with 2nd generation DES implantation for ISR of DES.
Methods: From January 2010 to November 2012, 228 consecutive patients with 287 lesions after 2nd generation DES implantation for ISR of DES were enrolled (biolimus-eluting stent, 71 lesions; everolimus-eluting stent 216 lesions). Follow-up coronary angiography at 8 months after procedure was performed in 243 lesions (84.7%), in which small vessel (reference diameter of less than 2.5 mm) was observed in 85 lesions and non-focal type restenosis in 116 lesions.
Results: In the 243 lesions, recurrent restenosis was angiographically documented in 54 lesions (22%) and target lesion revascularization was performed in 39 lesions (16%). Recurrent restenosis was observed in 25 (29.4%) of the 85 small vessel lesions and in 34 (29.3%) of the 116 non-focal type restenosis lesions. A multivariate analysis showed that small vessel (odds ratio 2.21, confidence interval 1.12 to 4.40, p=0.02) and non-focal type restenosis (odds ratio 2.78, confidence interval 1.36 to 5.78, p=0.0048) were independent predictors of recurrent restenosis; however, the type of 2nd generation DES, whether biolimus-eluting stent or everolimus-eluting stent, did not affect the angiographic outcomes (odds ratio 0.80, confidence interval 0.37 to 1.78, p=0.58).
Conclusion: Small vessel and non-focal type restenosis are predictors of recurrent restenosis in patients treated with 2nd generation DES for ISR of DES.

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Characterization of in-stent neointimal tissue components following drug-eluting stent implantation according to the phase of restenosis using a 40-MHz intravascular ultrasound imaging system

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Background and purpose: It is known that drug-eluting stents (DES) are associated with in-stent restenosis (ISR). However, the characteristics of neointimal tissue components according to the mechanism and time course of DES ISR have not been fully examined. The aim of this study was to characterize in-stent neointimal tissue according to the phase of restenosis using radiofrequency signals from 40-MHz intravascular ultrasound (IVUS), called iMAP-IVUS.
Methods: IVUS examinations were performed in 37 angina patients (37 lesions) who underwent repeated PCI for the treatment of DES in-stent restenosis (ISR). The patients were divided into two groups according to the phase of restenosis: the early ISR group (E-IRS; $\leq$1 year) and the late ISR group (L-ISR; $>$1 year).
Results: There were 18 patients in the E-ISR group and 19 patients in the L-ISR group. The mean follow-up period between stent implantation and repeated PCI was 8.02$\pm$2.20 months in the E-IRS group and 40.37$\pm$23.88 months in the L-ISR group. The percentage of lipid components and relative necrotic volume were greater in the L-ISR group than in the E-ISR group (5.77$\pm$1.81% vs. 4.51$\pm$1.71%, P$<$0.05 and 12.20$\pm$2.97% vs. 8.61$\pm$2.33% P$<$0.001, respectively). Furthermore, there was a positive correlation between the follow-up duration after DES implantation in the L-ISR group and the presence of a necrotic plaque component (r=0.49, P$<$0.05).

Fibrotic (%)	73.11±6.31	73.05±6.25	0.98
Lipidic (%)	4.51±1.71	5.77±1.81	<0.05
Necrotic (%)	8.61±2.33	12.20±2.97	<0.001
Calcified (%)	7.06±4.32	5.00±3.40	0.12

Conclusions: There were differences in the neointimal plaque characteristics after DES implantation according to the phase of restenosis. This information may lead to a better understanding of the mechanisms of DES ISR.

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Residual edge stenosis was associated with angiographic outcomes of everolimus-eluting stent in the real world setting

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Objective: The aim of this study was to assess the impact of residual stenosis at edges after everolimus-eluting stent implantation.
Methods: Post marketing study (PMS) Japan is a prospective registry designed to evaluate the safety and efficacy of the Xience V / Promus Stent in routine clinical practice at 47 centers representative of the clinical environment nationwide. Consecutive 2033 patients who underwent PCI using EES were enrolled. Twenty one patients were excluded because of withdrawal of consent, bypass graft lesions, and implantation of other stents. Of these, 1848 lesions of 1546 patients were assessed by means of QCA at post-procedure and 8-month follow-up in the independent corelab.
Results: Seventy six % of patients were male, mean age was 69, 42% had diabetes, 4.7% were hemodialysis patients. Indications for PCI were 28% in ACS and 66% in stable CAD. Lesion was located in RCA 30%, LAD 48%, LCx 18%, LM 3%. Serial QCA was performed in 1306 lesions both at baseline and 8 months (1087 lesions of proximal edges and 1300 lesions of distal edges). De novo lesion was 89%. Complex lesion morphologies were as follows: ACC/AHA type B2 42.5%, type C 38.3%, bifurcation 34.7%, ostial 12.2%, moderate/severe calcification 21.6%, CTO 5.9%. Mean reference diameter was 2.57mm and lesion length was 17.8mm. Mean late loss in-stent was 0.22mm and that in-segment was 0.13mm. Binary restenosis rates were 3.4% in-stent and 6.1% in-segment. ROC curve analysis revealed that 18.5% residual stenosis at proximal edge had 61% sensitivity and 68% specificity and 17.5% residual stenosis at distal edge had 92% sensitivity and 61% specificity for predicting restenosis at follow-up. Therefore, we defined that residual stenosis $>$20% was an inappropriate coverage of the stent edge. Inappropriate coverage group showed higher binary restenosis rates ($>$50% diameter stenosis) than appropriate coverage group in proximal edges (6.6% vs. 1.8%, p$<$0.001), and in distal edges (2.5% vs. 0.2%, p$<$0.001).
Conclusions: Residual stenosis at stent edge was associated with edge restenosis after EES implantation in the real world setting.

P4499 | BEDSIDE

Extracellular RNA and extracellular matrix reorganization in the in-stent restenosis

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Aim: Evaluation of the expression and quantity of extracellular RNA (eRNA) and collagen type I and type III in tissue pattern of in-stent restenosis (ISR) after coronary angioplasty.
Material and methods: The eRNA and collagen turnover have been determined in the tissue pattern of coronary segments with ISR taken postmortem from 19 patients with restenosis. The presence of eRNA was evaluated by immunohistochemical staining, and for quantification the micrometer thick sections stained for SMCs with tetramethylrhodamine iso-thiocyanate–labeled antibody against smooth muscle α-actin, SYTO RNASelect dye and 4′,6-diamidino-2-phenylindole were examined by laser-scanning confocal microscopy (Leica TCS SP2). The TNF-alpha and macrophage number were determined also in RIS, and their correlation to eRNA has been evaluated. Collagen type I and type III have been assayed using specific antibodies (Rockland), and were calculated as percent of positive labeling per tissue area. The markers of collagen type I synthesis (PICP) and degradation (CITP) were determined.
Results: The quantity of eRNA (AU/μm^2) increased in RIS and the estimated rise was proportionally to restenosis degree. A significant elevation of 45% in muscular media was already established in minimal RIS. In moderate and severe ISR degrees eRNA exceeded control (normal coronary segment) index by 2 and 4 times respectively. In adventice eRNA significantly increased only in severe ISR. Related to integral coronary wall to note the significant eRNA elevation by 95-161% in moderate and severe ISR. Remarkably, eRNA positively highly correlated with macrophage (n/mm^2) number (r=+0,8639) and TNP-alpha (AU/μm^2) quantity (r=+0,8838). The collagen turnover exhibited a marked collagen type I degradation while its synthesis was reduced, especially in media zone. Consequently, PICP decreased by 70-92% in moderate and severe ISR, while CITP increased more than 5 times. As a result the ratio CITP/PICP raised 8-fold and more. Importantly, the collagen type III degradation was conspicuously lesser that led to marked increase of the collagen III/I ratio.
Conclusions: (1) eRNA quantity rise associates ISR evolution, correlates with restenosis degree, and may be a predictor of neointima hyperplasia and inflammation boosting. (2) Extracellular matrix reorganization is a hallmark of ISR, and its opportunity refers basically to increased collagen type I degradation while collagen type III degradation is poor.

P4500 | BEDSIDE

Association of epicardial fat measured by 64-multidetector computed tomography with bare-metal stent restenosis

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Background: It has been evidenced that epicardial fat tissue functions as an endocrine organ and secrete pro-inflammatory cytokines. Also, inflammation is known as the mainstay of in-stent restenosis (ISR). However, the role of epicar-

dial fat measured by multidetector computerized tomography (MDCT) in coronary bare-metal ISR has not been evaluated previously. The primary objective of the present study was to investigate the relationship of tomographic epicardial fat thickness (EFT) with bare-metal ISR in stable CAD.
Methods: We enrolled a total of 529 patients (mean age 60.2±10.3 years, 72.4% men) who underwent MDCT for suspected CAD. All the patients underwent BMS implantation and a further control coronary angiography owing to stable or unstable angina pectoris. According to angiographic results, patients were divided into two groups, 230 patients with ISR and 299 patients without ISR. Thickness of the EAT was measured on contrast enhanced multiplanar reformat images with parasternal short axis view at basal, mid-ventricular and apical levels and horizontal long axis view.
Results: The total EFT was significantly increased in patients with ISR compared to those without ISR (95.06±14.6 mm vs 83.45±12.8 mm, $p<0.001$). Using multiple logistic regression analysis, diabetes mellitus, smoking, stent length, stent diameter and preprocedural total EFT (OR: 1.072, 95% CI: 1.053-1.092, $p<0.001$) emerged as independent predictors of ISR. In ROC curve analysis, total EFT >92 mm had 58% sensitivity and 74% specificity (AUC: 0.71, $p<0.001$) in predicting ISR. Patients with a preprocedural total EFT >92mm had a 4.5-fold increased risk of developing ISR.

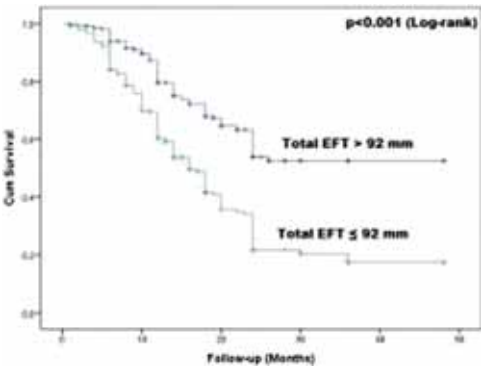

Figure 1

Conclusion: In conclusion, higher preprocedural EFT is a powerful and independent predictor of BMS restenosis in patients with stable CAD.

P4501 | BEDSIDE
Comparison of the efficacy of balloon angioplasty or stent implantation for in-stent restenosis based on analysis by optical coherence tomography

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Purpose: The aim of this study was to investigate the efficacy of balloon angioplasty (BA) or stent implantation (SI) for the treatment of the in-stent restenosis (ISR) based on the restenotic tissue structure analyzed by optical coherence tomography (OCT).
Methods: From January 2010 to January 2013, we evaluated 138 patients with 148 ISR lesions which required revascularization (106 drug-eluting stents (DES) and 42 bare-metal stents (BMS)). Based on their OCT appearance at the minimum lumen area, the lesions were classified as homogeneous and non-homogeneous. We compared recurrent target lesion revascularization (TLR) at 1year follow-up after BA or SI.
Results: By OCT, the restenotic tissue structure was homogeneous in 48 (32%) and non-homogeneous in 100 (68%). In homogeneous group, 27 patients had BA and 21 patients had SI. In non-homogeneous group, 49 patients had BA and 51 patients had SI. Angiographic follow-up after TLR was performed in 104 patients (75%) with 114 lesions (77%) at 1-year. As OCT appeared homogeneous, recurrent TLR was noted in 29.6% of the BA group and in 19.1% of SI group (p=0.4). As OCT appeared non-homogeneous, recurrent TLR occurred in 35% of the BA group and in 13.7% of SI group (p=0.013).
Conclusions: This study suggested that OCT might be helpful to decide the treatment strategies of ISR.

P4502 | BEDSIDE
Local and systemic factors for restenosis after carotid endarterectomy

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Perpose: Restenosis due intimal hyperplasia (IH) is often seen after Carotid Endarterectomy (CEA), but the pathological mechanisms leading to its progression is not totally clear. The progression of intimal hyperplasia after carotid endarterectomy (CAE) is influenced by local hemodynamic factors and systemic factors as well.
Methods: 987 patients (62±5,7 years, 89% of male) undergoing CEA between 2001 and 2011 were included in our study. The mean time of observation was 4,3±1,33 year after operation. We studied the influence of different systemic factors such as age, sex, hypertension, smoking, hyperlipidaemia, gemorheology, diabetes mellitus, lesion characteristics, type of arteriotomy closure and regional flow dynamics on the intimae –media thickness following CEA. Data on the status of 1003 carotid arteries after endarterectomy were assessed with standardized duplex ultrasound and evaluated by univariate and multivariate analysis to identify possible associations.
Results: From systemic factors only increasing level of low-density lipoprotein and platelet aggregation had low, but reliable influence on IMT after CEA. Ages, sex, hypertension, smoking was not significantly associated with the development of intimal hyperplasia following CE. Complicated plaque showed a statistically significant correlation with intimal hyperplasia. There were no significant differences in IMT between patients with eversion CEA versus CEA with patch. From local factors, sheer stress demonstrated a negative association with IMT. Mean shear stress at bifurcation after CEA was 16,7±2,9 dynes/cm^2 and was inversely related with internal diameter of common carotid artery at reconstruction site. Low mean shear stress correlated with low flow volume (r=0,58 $P<0.0001$). IH was inversely associated with shear stress (r=0,39 $P<0.0001$) and flow volume (r=0,37 $P<0.0001$).
Conclusions: Considering the data obtained in this work, we can conclude that the intimal thickening is not uniquely determinate process, and depends on many factors. This study demonstrates that low shear stress leads to progression of IH after CEA. Strong correlation between flow volume and shear stress supports the conclusion that decrease of flow volume can cause intimal hyperplasia.

CORONARY IMAGING: CLINICAL RELEVANCE

P4504 | BEDSIDE
Safety of provocative tests to detect coronary artery spasm. Results from a French registry including 2,430 patients

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Purpose: The use of provocative tests (PT) for the diagnosis of coronary artery spasm (CAS) varies largely within countries, hospitals, and physicians. Potential PT related complications remain the principal reason for not detecting CAS in patients with compatible symptoms.
Methods and results: We report the incidence of complications during and immediately after PT in 2,430 patients with normal or near normal coronary arteries over the last 10 years. Conventional angiography was found normal or near normal before an intra venous injection of methylergometrine maleate 0.4mg was realized after diagnostic angiography, and was followed by another injection in the left and the right coronary arteries 3minutes later. Patients were 55 years old (48-64) and predominantly males (52.3%). Reason for coronary angiography were non-specific chest pain at rest (62.2%), acute coronary syndrome (16.9%), angina at rest and stress (10.2%), silent ischemia (8.9%) and out-of-hospital cardiac arrest (1.8%).
Complications including myocardial infarction (n=1), ventricular fibrillation (n=1), asystoly (n=3), atrio-ventricular block (n=2), persistant CAS (n=3), delayed CAS (n=4), transient ischemic stroke (n=4), migraine (n=2), peripheral spasm (n=1), systemic embolism (n=1), bronchospasm (n=1) were reported in only 0.9% of the total population. Furthermore, complications dropped to only 0.3% in patients with a normal PT. In addition, the majority of the reported complications could be related to the angiography itself rather than to PT. Interestingly, patients with PT related complication were more often hospitalized for acute coronary syndrome and exhibit more often mild atheroma in coronary arteries than those with no complication (47.8% vs 16.6%; $p<0.001$ and 60.9% vs 28.1%; $p<0.01$; respectively).
Conclusion: PT-related complications are extremely rare in selected patients with suspected CAS. The potential severe outcomes in patients with undiagnosed and

Abstract P4501 – Table 1. Clinical outcomes at 1-year follow-up

	Overall (n=148)		p	Homogeneous (n=48)		p	Non-homogeneous (n=100)		p
	Balloon (n=70)	Stent (n=78)		Balloon (n=21)	Stent (n=27)		Balloon (n=49)	Stent (n=51)	
Reccurent restenosis	27 (35.5%)	13 (18.1%)	0.016	9 (33.3%)	4 (19.1%)	0.27	18 (36.7%)	9 (17.7%)	0.031
TLR	25 (32.9%)	11 (15.3%)	0.012	8 (29.6%)	4 (19.1%)	0.4	17 (34.7%)	7 (13.7%)	0.013
All-cause death	1 (1.3%)	3 (4.2%)	0.29	0 (0%)	0 (0%)	NA	1 (2.0%)	3 (5.9%)	0.33
Cardiac death	1 (1.3%)	3 (4.2%)	0.29	0 (0%)	0 (0%)	NA	1 (2.0%)	3 (5.9%)	0.33
Myocardial infarction	1 (1.3%)	0 (0%)	0.33	1 (3.7%%)	0 (0%)	0.37	0 (0%)	0 (0%)	NA
Stent thrombosis	1 (1.3%)	0 (0%)	0.33	1 (3.7%%)	0 (0%)	0.37	0 (0%)	0 (0%)	NA
MACE	26 (34.2%)	14 (19.4%)	0.042	8 (29.6%)	4 (19.1%)	0.4	18 (36.7%)	10 (19.6%)	0.055

Date are presented as n (%). NA, Not available; TLR, target lesion revascularization; MACE, major adverse cardiac event.

untreated CAS, together with the high safety of PT, justify a shift in paradigm toward a more systematic detection of CAS during conventional coronary angiography.

P4505 | BEDSIDE
Coronary torsion contributes to edge late loss after sirolimus-eluting stent and everolimus-eluting stent implantation

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Purpose: We hypothesized that coronary torsion at the stent edge may contribute to edge restenosis.
Methods: The coronary torsion of 31 patients who underwent single sirolimus-eluting stent (SES) or single everolimus-eluting stent (EES) implantation was quantified using IVUS images. The angular velocity was determined using the angle of rotation of the most similar next frame with the least square method. Coronary torsion was defined as the maximum rotated angle in a cardiac cycle and calculated from the integrated curve of the angular velocity. The analysis interest was defined as follows: distal edge segment, 5mm region from stent distal edge; distal in-stent edge, 5mm of in-stent region from stent distal edge; stent center, 5mm region at stent center; proximal in-stent edge, 5mm of in-stent region from stent proximal edge; proximal edge segment, 5mm region from stent proximal edge.
Results: The coronary torsion at the edge was augmented after stent implantation (Table 1). The post-procedural coronary torsions at the distal and proximal in-stent edges were related to edge late loss after both SES (R = 0.625, p=0.013 and R = 0.625, p=0.013, respectively) and EES (R = 0.648, p=0.007 and R = 0.575, p=0.02, respectively) implantations. Multivariate analysis showed that post-procedural in-stent torsion (R = 0.479, $p<0.0001$), post-procedural edge minimum luminal diameter (R = 0.497, $p<0.0001$) and post-procedural mean stent diameter (R = -0.351, p=0.005) were predictors of edge late loss.
Conclusion: The coronary torsion after SES or EES implantation may be one of the mechanisms responsible for edge-restenosis.

P4506 | BEDSIDE
Benefits of using rotational versus conventional coronary angiography in clinical practice

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Purpose: The gold standard in diagnostic imaging of coronary arteries is standard coronary angiography (SCA), a technique that requires multiple static and two-dimensional runs. Dual-axis rotational coronary angiography (DARCA) is a novel angiographic modality to visualize the coronary tree with a single acquisition run with three-dimensional rotation of the gantry around the patient with simultaneous left to right as well as craniocaudal movements. Given that radiation dose and contrast volume (contributors to contrast nephropathy) are negative technical factors, it is interesting to assess whether this new technique allows a reduction of these factors. The aim of this study was to compare DARCA with SCA in an unselected "real world" patient population.
Methods: We prospectively studied 294 consecutive patients undergoing diagnostic coronary angiography with or without angioplasty in our hospital over 3 months. The following variables were studied: dose-area product (Gy/cm^2 DAP), fluoroscopy time (in minutes FT), contrast volume (in ml), procedure time (in minutes) and number of runs.
Results: The overall cohort had a mean age of 68 years with 69% males. We performed 125 rotational angiography (42.5%) with angioplasty in 46% of the overall procedures. DARCA was therefore associated with a 35% reduction in radiation dose (DAP 49.6 vs. 75.2 Gy/cm^2, $p<0.0001$), a 25% reduction in fluorosocpy time (8.47 vs 11.35 min, p=0.008), a 19% in contrast volume (117 vs. 142 ml,p=0.002) and a 54% in numbers of runs (7 vs 15,$p<0.0001$). There was no significant difference in overall procedure time between the two groups. The significant reduction of the DAP and the number of runs was also observed in diagnostic angiograms group and there were no differences of any variable when angioplasty was performed.
Conclusion: The use of rotational angiography allows a reduction of the radiation dose, fluoroscopy time and contrast volume without increasing the length of the procedure. Therefore, DARCA should be promoted in routine coronary angiograms.

P4507 | BENCH
In-vivo evaluation of a novel sirolimus-coated balloon catheter

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Background: Limus-eluting stents are dominating coronary interventions whereas paclitaxel is the only drug on balloon catheters which has shown to reduce restenosis rates in coronary and peripheral artery disease. Few studies indicate neointimal inhibition by limus-coated balloons in animals and none in a clinical trial. It has been shown that a release of sirolimus for a period of 30 days is required for effective inhibition of neointimal proliferations in stent-based local drug delivery. In this study different excipients have been investigated in order to achieve a long lasting sirolimus tissue level. The aim of the present study was to evaluate different prototype sirolimus-coated balloon catheters (SCB) in the porcine coronary model.
Methods: Seventy-two bare metal stents (diameter 3.0 and 3.5 mm; length 16 mm) were implanted in LAD, Cx, and RCA arteries of 24 domestic pigs with different types of balloon catheters: uncoated control, sirolimus-coated balloons with 4 different formulations (AS, Vbn, Vb3, and Vb7), and the paclitaxel coated SeQuent Please balloon (SQP).
Results: Formulations Vb3 and Vb7 resulted in the transfer of 7.3±4.5% and 12.5±2.9%, respectively, to the vessel wall and extraordinarily long persistence time of sirolimus. Quantitative coronary angiography follow-up at four weeks revealed similar angiographic baseline parameters. The Vbn, Vb3, and Vb7 coating caused either reproducible statistically significant or non-significant inhibition of neointimal proliferation assessed by quantitative coronary angiography and histomorphometry.

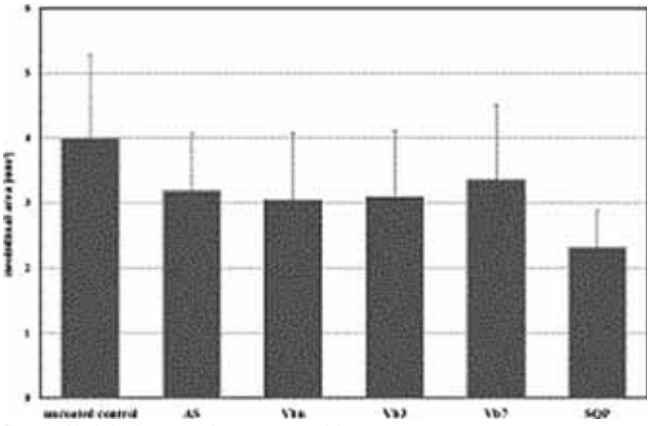

Figure 1. Neointimal area, porcine coronary model.

Conclusion: SCB were found to effectively reduce neointimal proliferation in the porcine coronary model. It has to be determined if this approach will result in a relevant clinical effect.

P4508 | SPOTLIGHT
Feasibility of ulnar artery for cardiac catheterization: AJmer ULnar ARtery (AJULAR) catheterization study

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Purpose: We tried to compare default transulnar access (TUA) with transradial access (TRA) in terms of feasibility and safety.
Methods: We analysed a total of 423 patients (n=423) with normal modified Allen's test, who were scheduled for coronary angiography through TUA with ad hoc percutaneous coronary intervention if necessary. We analysed observed findings with a retrospective cohorts of patients undergoing TRA angiography in a previous study done at our centre. We also performed selective ulnar arteriography of 200 patients (n=200) through radial route to predict the bottlenecks of TUA.
Results: The periprocedural characteristics of the patients are enlisted in the table. There is no statistically significant difference among, no's of attempts made till successful puncture, total procedure time and total fluoroscopy time for either radial or ulnar access angiography by an experienced interventionist ($p>0.05$).

Abstract P4505 – Table 1. Comparison of coronary torsion before and after stent implantation

	Before SES implantation	After SES implantation	p-value	Before EES implantation	After EES implantation	p-value
Coronary torsion at the distal edge segment (degree)	3.2±1.3	2.7±1.3	0.156	3.2±1.7	2.8±0.9	0.051
Coronary torsion at the distal in-stent edge (degree)	3.6±1.6	4.5±1.4	0.038	2.9±1.1	4.0±1.5	0.003
Coronary torsion at the stent center (degree)	4.1±1.5	4.2±1.6	0.558	4.4±2.9	4.6±2.7	0.845
Coronary torsion at the proximal in-stent edge (degree)	3.6±1.1	4.9±1.8	0.001	3.4±2.0	5.8±5.6	0.136
Coronary torsion at the proximal edge segment (degree)	3.5±0.9	2.9±1.1	0.093	2.5±2.1	4.8±5.2	0.117

Table 1. The periprocedural characteristics of the study patients

Parameters	Total (n=423)
Modified Allens test normal (%)	423 (100)
Clinical ulnar pulsation grade	
Low volume (%)	93 (21.98)
Normal volume (%)	292 (69.03)
High volume (%)	38 (8.98)
Failure to cannulate ulnar artery (%)	9 (2.13)
Nos. of attempts made till successful puncture (mean±SD)	3±2
Arterial access time in minutes (mean±SD)	5±2
Total procedure time in minutes (mean±SD)	3.05±1.5
Total fluoroscopy time in minutes (mean±SD)	1.75±1.2
Ulnar artery diameter in mm (mean±SD) (n=200)	2.11±0.49
Ulnar artery anomalies (n=200)	
Ulnar artery spasm/stenosis (%)	16 (8)
Ulnar artery tortuosity (%)	13 (6.5)
High bifurcation of brachial artery at arm level (%)	7 (3.5)
Ulnar artery loops (%)	6 (3)
Ulnar artery atherosclerosis/ calcification (%)	5 (2.5)

However time taken in arterial access is statistically significant in the initial learning curve for the same ($p<0.05$).

Conclusions: For experienced operator TUA is safe and effective alternative to TRA in terms of feasibility and safety. There is a negligible incidence of non-manoeuvrable anatomic obstruction in the real-world scenario in TUA and so fear of the same should not impede the use of this route. Vasospasm in the use of this route is a complication, can be easily tackled to prevent crossover to alternate route.

P4509 | BEDSIDE
Tissue morphology of in-stent ree-restenosis lesions after paclitaxel-coated balloon dilatation and plain old balloon angioplasty for in-stent restenosis lesions: impact of previously implanted stent

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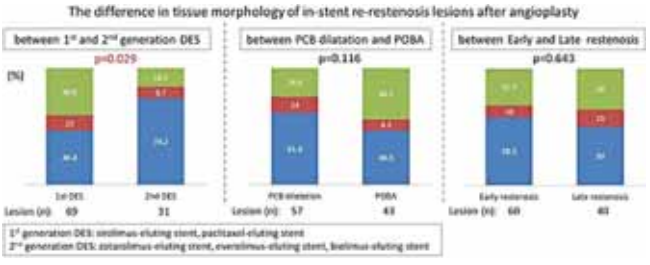
Purpose: It was reported that tissue morphology of in-stent restenosis (ISR) lesions after drug-eluting stent (DES) implantation assessed with optical coherence tomography (OCT) was affected by stent type. Little was known about the re-restenotic tissue morphology after angioplasty using paclitaxel-coated balloon (PCB) dilatation or plain old balloon angioplasty (POBA). The aim of this study was to examine the tissue morphology of in-stent re-restenosis lesions after angioplasty for DES-ISR lesions and to clarify the impacts of previously implanted stent type, treatment modality, and timing of restenosis on it.

Methods: Between January 2009 and February 2014, we performed OCT on 69 in-stent re-restenosis lesions after PCB dilatation and 31 lesions after POBA. Previous stents were 69 first generation DES (sirolimus-eluting stent and paclitaxel-eluting stent) and 31 second generation DES (zotarolimus-eluting stent, everolimus-eluting stent, and biolimus-eluting stent). Early restenosis lesion was defined as lesions less than one year after angioplasty and late restenosis lesion was defined as lesions more than one year after angioplasty. The morphological assessment of neointimal tissue structure (homogeneous, heterogeneous, and layered type) at the minimum lumen area site was performed.

Results: The results are shown in the figure. There was a significant difference in the tissue structure of in-stent re-restenosis lesions after PCB dilatation or POBA between 1st and 2nd generation DES (p=0.029). However, there was no difference in the tissue structure between PCB dilatation and POBA and between early and late restenosis lesions.



Conclusions: The tissue morphology of in-stent re-restenosis may be affected not by treatment modality and timing of restenosis but by previously implanted stent type.

P4510 | BEDSIDE
Severe type-2 diabetes induces reversible alterations of endothelial progenitor cells

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Vascular regeneration is one of the major challenge of future therapeutical approaches. In this regard, endothelial progenitor cells (EPCs) could have a major role in vascular repair after injury. Some studies suggested that EPC number and bioactivity are reduced in patients with type-2 diabetes a pathogenic condition associated to premature and severe vasculopathy. Until now, it is still undefined whether intensive glycemic control can modify EPC bioactivities in type-2 diabetes. In the present study, we investigated whether glycemic control would improve EPC number and function in patients with uncontrolled type 2 diabetes. Forty-five patients with type 2 diabetes and HgA1c $\geq$8.0% were studied. Patients were tested at baseline and after 3 months of glycemic control therapeutic regimem (HgA1c $<$6.5%). The diabetic group was compared to a sex/age matched group (control) of subjects without diabetes. Circulating EPC levels were assessed by flow cytometry for expression of VEGFR2, CD133, and CD34/KDR. The capacity of the cells to form colony-forming units (CFUs), and their migration and viability were quantified after 1 week of culture. Patients with type diabetes (mean age 58.2±5.4 years, 25.6% women, disease duration of 15.4±6.3 years) had a baseline HgA1c of 8.7±0.5%. After the administration of a normoglycemic control regimen, HgA1c decreased to 6.2±0.3%. Interestingly, in our experimental conditions, EPC levels (CD133+ and CD34+/KDR+) increased significantly after the intensive control period (mean of 18%, $p<0.04$ vs baseline). The number of EPC CFUs also increased significantly after glycemic control ($p<0.05$ vs baseline). Nitric oxide (NO) production levels released by EPCs (measured by DAF-2 DA and fluorescent spectrophotometer) improved following the glycemic control ($p<0.05$ vs baseline). Our data are consistent with the hypothesis that a clinical and therapeutical glycemic control is associated with increased levels of EPCs and improvement in some of their bioactivities in type-2 diabetes.

P4511 | BEDSIDE
Impact of the frequency domain optical coherence tomography-based stent sizing on acute results after second generation drug-eluting stent implantation

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Background: Introduction of a frequency domain optical coherence tomography (OCT) allows for rapid imaging with automated quantitative assessments of the coronary artery stenosis. Although intracoronary imaging devices such as intravascular ultrasound (IVUS) and OCT have been used as a guide to achieve optimal stenting, standard method to select stent size based on the pre-intervention imaging has not been established yet.

Purpose: The aim of this study was to investigate impact of OCT based stent sizing on acute results after 2nd generation drug-eluting stent (DES) implantation.

Methods: A total of 103 consecutive patients who underwent OCT-guided DES implantation were studied. Based on the stent diameter to mean reference lumen diameter ratio (S/D ratio), lesions were divided into quartiles (Q1: S/D ratio $<$0.984, Q2:0.984$\leq$S/D ratio$<$1.066, Q3:1.066$\leq$S/D$<$1.166, Q4: 1.166$\leq$S/D ratio). Stent expansion, incidence of incomplete stent apposition (ISA) and stent edge dissection were compared between the quartiles.

Results: Stent expansion as assessed by minimal stent area divided by mean reference lumen area was similar among the quartiles (Q1:0.83±0.15, Q2: 0.83±0.13, Q3: 0.86±0.17, Q4: 0.78±0.13, P=0.31), but post-hoc analysis showed a trend toward better in Q3 than in Q4 (P=0.06). Incidence of stent distal edge dissection showed a trend toward higher in Q4 and incidence of distal ISA was significantly higher in Q1 and Q2 (Figure).

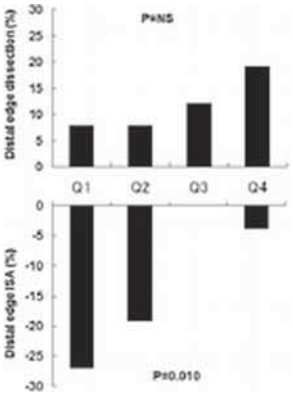

Figure 1

Conclusions: OCT-guided stent sizing affects acute results after DES implantation. S/R ratio may be useful as a guide for stent sizing.

P4512 | BEDSIDE

Scatter radiation reduction during right transradial coronary angiography: a randomized trial using a lead-free shield drape

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Purpose: Transradial approach for coronary angiography has increased due to improved patient comfort and decreased bleeding complications. However, increased radiation exposure remains a significant concern. Our aim was to evaluate the reduction of radiation dose received by staff using a lead-free shielding drape (SD) placed over the patients undergoing transradial coronary angiography in a randomized trial.

Methods: A total of 112 patients who underwent right transradial coronary angiography were randomized to shielding drape use versus no radiation shield protection. Measures of personal dose equivalent Hp (10) were performed by two electronic dosimeters located at the chest of physician and nurse above the lead apron. An additional dosimeter located on the C-arm at axis rotation level was used as control.

Results: We found no significant differences in baseline characteristics or those related to procedure between both groups. Despite similar fluoroscopy time and DAP, a significant reduction in cumulative dose received by operator was found. Mean cumulative dose reduction was up to 70%. The benefit was not apparent at the position of nursing.

Table 1

	All (N=112)	Without SD (N=59)	With SD (N=53)	p
Age (years)	64.4±11.2	63.6±11.1	65.4±11.3	0.394
BMI (kg/m^2)	30.4±4.5	29.9±4.2	30.8±4.7	0.328
Contrast (ml)	134.1±79.1	143.6±86.3	123.7±69.7	0.190
PCI	36 (32.1%)	21 (35.6%)	15 (28.3%)	0.409
Fluoroscopy time (min)	3.21 [2.02–6.03]	3.36 [2.02–6.03]	2.33 [1.81–5.97]	0.487
Number of images	450.50 [353–646]	460 [346–651]	441.5 [354.5–634.5]	0.596
Total DAP	19.08 [14.11–27.21]	18.84 [14.40–31.38]	19.37 [14.06–26.46]	0.943
Operator's Hp (10) (μSv)	6 [3–14]	9 [5–23]	4.5 [2–9]	<0.001
Nurse's Hp (10) (μSv)	3 [1–4]	3 [2–6]	3 [1–4]	0.101
Arc (μSv)	160 [113.5–246.5]	159 [109–248]	175.5 [128–245]	0.744

SD, shielding drape; BMI, body mass index; PCI, percutaneous coronary intervention; DAP: dose-area product; Hp (10): personal equivalent dose; Sv: Sievert. Values are expressed as n (%), mean ±SD or median (25–75th percentile).

Conclusion: Utilization of a lead free shielding drape decreases by up to 70% operator radiation exposure during coronary angiography performed through right radial artery access.

P4513 | BENCH

Possible involvement of adventitial sympathetic nerve in the coronary hyperconstricting responses after drug-eluting stent implantation in pigs in vivo

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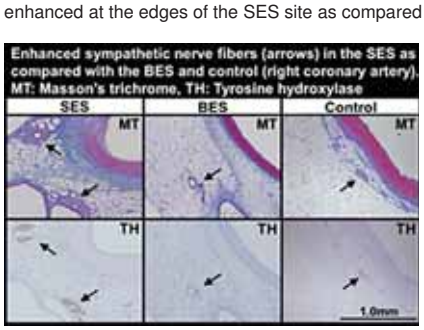
Purpose: The adventitia harbors a wide variety of cells with potent modulation of vascular tone such as sympathetic nerve fibers (SNF). The SNF form a network around the vessels in the adventitia along their entire length. We tested our hypothesis that coronary adventitial SNF is involved in the coronary hyperconstricting responses after drug-eluting stent (DES) implantation in pigs in vivo.

Methods: Sirolimus-eluting stents (SES, 1st generation DES) (n=6) and biolimus A9-eluting stents (BES, new generation DES) (n=5) were randomly implanted into the left anterior descending and circumflex coronary arteries in the same pig. After 1 month, coronary responses were examined by intracoronary serotonin (10 and 100 μg/kg) before and after hydroxyfasudil (HF, a specific Rho-kinase inhibitor: 30 and 100 μg/kg/min). After euthanasia, stented vessels were harvested for immunohistological analysis for the adventitial SNF (tyrosine hydroxylase) and Rho-kinase expressions at the stent edges.

Results: Vasoconstricting responses to serotonin (100 μg/kg) were significantly enhanced at the edges of the SES site as compared with the BES site (P<0.05), and were prevented by pre-treatment with HF. Histological analysis showed that the adventitial SNF tended to be increased at the SES site as compared with the BES site (SES 11.5±1.8/mm^2 vs. BES 6.8±1.4/mm^2, P=0.07). There was a positive significant correlation between the SNF and coronary vasoconstricting responses (R=0.53, P<0.05) and between the SNF and Rho-kinase activities (R=0.49, P<0.05).

Conclusions: These results suggest that the adventitial SNF play an important role in the pathogenesis of DES-induced coronary hyperconstricting responses through Rho-kinase activation in pigs in vivo.



Histology of sympathetic nerves.

P4514 | BEDSIDE

Enhanced expression of hemoglobin scavenger receptor CD163 in accumulated macrophages within filtered debris in acute coronary syndromes

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Background: Coronary intraplaque hemorrhage up-regulates hemoglobin scavenger receptor CD163 expression on macrophages, and have association with vulnerable plaque development. During percutaneous coronary intervention (PCI), mechanical plaque disruption exposes potentially embolic atheromatous contents from culprit plaque. Filter-based distal embolic protection device can retrieve these atherothrombotic debris.

Methods: In 21 patients with stable angina pectoris (SAP, n=12) or acute coronary syndrome (ACS, n=9), atherothrombotic debris were collected using Filtrap (NIPRO). We immunohistochemically determined CD14 (proinflammatory macrophage marker) and CD163 -positive macrophages in filtered debris. We also examined the relation between CD14 and CD163 with culprit plaque volume and components evaluated with ultrasonic tissue characterization (VH-IVUS).

Results: In ACS, both CD14-positive and CD163-positive macrophage counts were higher than those in SAP (CD14: 108.6±65.6 vs 41.9±38.8, p=0.03; CD163: 59.6±25.3 vs 12.8±9.8, P=0.01). In culprit plaque, volume was not different between the two groups, however, necrotic core component (%NC) in ACS were higher than those in SAP (32.7±9.1 vs 21.6±6.9%, P<0.01). Neither CD14 nor CD163 have relation with plaque volume. Both CD14 and CD163 have positive correlation with %NC (CD14: R=0.541, P=0.03; CD163: R=0.806, P<0.01)) and negatively correlated with fibrous components (CD14: R=-0.557, P=0.03; CD163: R=-0.716, P=0.02). Moreover, the CD163 had weak correlation with CRP level (R=0.58, P=0.07).

Conclusions: These findings suggest significant association among intraplaque hemorrhage, necrotic core expansion, inflammation and plaque vulnerability in ACS patients.

P4515 | BEDSIDE

The predictors of cardiovascular events in patients with significant peripheral artery disease and undergoing stress myocardial perfusion imaging

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Objectives: Peripheral artery disease (PAD) has been established as an important factor for poor cardiovascular prognosis. And stress myocardial perfusion imaging (MPI) has been well established as a useful predictor for cardiovascular events. Generally, patients who have normal stress MPI are warranted excellent cardiovascular prognosis that the rate of cardiovascular event is <1%/year. This study evaluates the power of predicting cardiovascular events in patients with obvious PAD and suspected/known coronary artery disease (CAD) who undergoing stress MPI.

Methods: Ninety-seven PAD patients who underwent stress MPI were monitored for 28 months. PAD was characterized by an ankle-brachial index (ABI) <0.9, >1.4 and/or previous revascularization for peripheral artery. Normal stress MPI was defined as summed stress score <3. Cardiovascular events included cardiac death, non-fatal myocardial infarction and Braunwald class III unstable angina requiring hospitalization.

Results: Cardiovascular events were observed in 28 patients (29%). Multivariate Cox regression analysis revealed that familial history of CAD (hazard ratio = 3.03; P=0.029), hemodialysis (hazard ratio = 3.65; P=0.003), left ventricular ejection fraction (hazard ratio = 0.97; P=0.034) and summed stress score of stress MPI (hazard ratio = 1.13; P=0.026) were independent and significant predictors for cardiovascular events. Kaplan-Meier survival curves showed that patients with normal stress MPI had better cardiovascular prognosis than patients with abnormal stress MPI (n=74, 15 events vs. n=23, 13 events; P=0.005 by log-rank). Patients with normal stress MPI could not have excellent prognosis for cardiovascular events.

Conclusions: In PAD patients with suspected/known CAD, stress MPI, hemodialysis, familial history of CAD and left ventricular systolic function can be significant and independent predictors of cardiovascular events. Due to high risk clinical background, normal stress MPI could not show excellent cardiovascular prognosis. To these patients, aggressive strategies (strengthen sub-optimal therapies and careful observation) are needed as early as possible.

PLAQUE MORPHOLOGY: WHAT DOES IT TELL US?

P4517 | BEDSIDE
Coronary atheroma regression and plaque characteristics after aerobic exercise assessed by intravascular ultrasound: a randomized controlled trial

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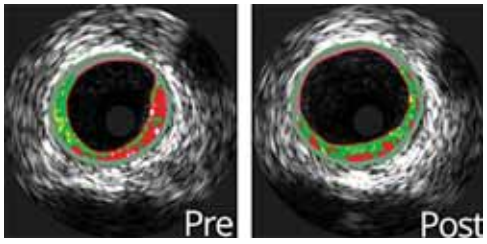
Purpose: To investigate effects of high intensity aerobic interval training (AIT) versus moderate continuous training (MCT) on coronary atherosclerosis in patients with significant coronary artery disease on optimal medical treatment.
Methods: Thirty-six patients were randomized to AIT (intervals at ≈90% of peak heart rate) or MCT (continuous exercise at ≈ 70% of peak heart rate) 3 times a week for 12 weeks following intracoronary stent implantation. Grayscale and radiofrequency intracoronary ultrasound (IVUS) was performed at baseline and follow-up. The primary endpoint was changes in plaque burden and plaque composition. Separate lesions were classified in terms of plaque vulnerability using radiofrequency IVUS criteria. IVUS recordings were analysed off line in an independent CoreLab.
Results: Necrotic core was reduced in both groups in defined coronary segments (AIT -3.2%, MCT -2.7%, both $p<0.05$) and in separate lesions (median change -2.3% and -0.15 mm^3, $p<0.05$). Plaque burden was reduced by 10.7% in separate lesions independent of intervention group (p=0.06). No significant differences in IVUS parameters were found between exercise groups. A minority of separate lesions were transformed in terms of plaque vulnerability during follow-up with large individual differences between and within patients. Figure 1 illustrates the transformation from a thin-cap fibroatheroma to intimal medial thickening in a patient undergoing AIT.



RF-IVUS images pre and post exercise.

Conclusions: Changes in coronary artery plaque structure or morphology did not differ between patients undergoing AIT or MCT. The combination of regular aerobic exercise and optimal medical treatment for 12 weeks induced a moderate regression of necrotic core and plaque burden in IVUS-defined coronary lesions.

P4518 | BEDSIDE
Impact of pre-stenting coronary plaque composition on vascular healing response following implantation of drug-eluting stents

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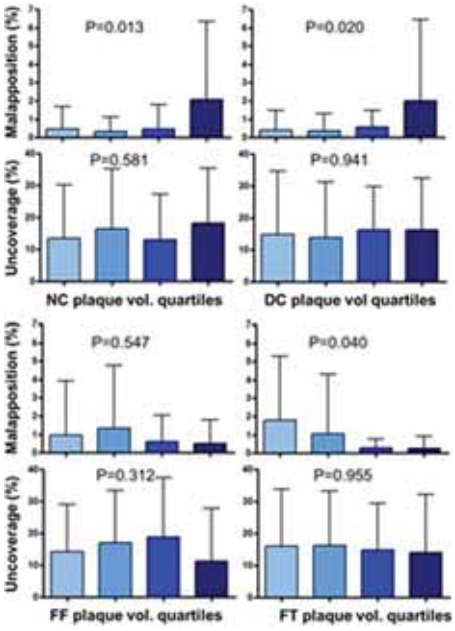
Purpose: We sought to assess the impact of coronary plaque composition assessed by virtual-histology intravascular ultrasound (VH-IVUS) prior to stenting on vascular healing response, strut malapposition and uncoverage, following implantation of drug-eluting stents assessed by optical coherence tomography (OCT).
Methods: We analyzed the OCT images from 121 lesions with 121 patients (age 61±9 years, 88 males) who received pre-stenting VH-IVUS examinations. Pre-stenting plaque composition (dense calcium (DC), necrotic core (NC), fibrotic (FB) and fibro-fatty (FF)) was assessed by VH-IVUS and each component was classified into quartiles. At 6.4±3.2 months after stenting, strut malapposition and uncoverage were evaluated by OCT.
Results: Pre-stenting mean absolute DC, NC, FB and FF plaque volume were 22.9±19.0, 7.9±9.6, 63.8±33.8 and 16.5±12.4 mm^3, respectively. At 6 months after stenting, mean malapposed and uncovered strut percentages were 0.84±2.5 and 15.3±16.7%. Any plaque compositions were not correlated with strut uncoverage. However, pre-stenting NC and DC plaque volumes were positively correlated with the malappsoed strut percentage ($R=0.44$, $p<0.001$ and $R=0.45$, $p<0.001$), although pre-stenting FB and FF plaque volumes were not correlated with the malaapposed strut percentage. Also, the highest NC and DC plaque volume quartiles had significantly greater malapoositions (Figure). Absolute DC volume was an independent preditor for presence of late stent malapposition (beta=1.09, p=0.007)
Conclusions: Pre-stenting plaque composition was not associated with strut uncoverage. However, larger pre-stenting DC and NC plaque volumes were associated with late stent malapposition.



Abstract P4518 – Figure 1. Rate of malapposition and uncoverage.

P4519 | BEDSIDE
Plaque morphology of intermediate coronary lesions and clinical outcomes of an OCT-guided PCI strategy

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Background: An intermediate coronary lesion is a plaque with a vessel narrowing of 30% and 70%. We assessed optical coherence tomography (OCT) features of intermediate lesions in patients with stable angina (SA) and acute coronary syndrome (ACS), and demonstrated the clinical implication of adopting an OCT-based treatment strategy for those intermediate lesions.
Methods and results: Fifty-six patients with SA (30 patients) and ACS (26 patients) undergoing OCT assessment of an intermediate de novo coronary lesion were enrolled. An OCT-guided percutaneous coronary intervention (PCI) strategy based on the presence of thrombus and/or MLA $<3.0mm^2$ was then followed. The primary clinical endpoint was the composite of cardiovascular death, myocardial infarction, and repeated revascularization over 12 months. Patients with SA had larger minimal lumen area (MLA) ($3.5\pm1.5mm^2$ vs $2.7\pm1.3mm^2$; p=0.04) and calcium arc at MLA site as compared to ACS (242±57° vs 114±35°; p=0.0001), while asymmetric index was lower in SA (0.24±0.13 vs 0.33±0.15; p=0.02). Thin cap fibroatheroma (26.9% vs 6.7%; p=0.04) and thrombus (38.5% vs 10%; p=0.01) were significantly higher in patients with ACS. Based on the OCT-guided approach, twelve-month rate of major adverse event rate was not significantly different between the treated and untreated group (p=0.26).
Conclusions: Intermediate coronary lesions showed distinctive OCT features for SA or ACS, respectively. A symmetric vessel narrowing with extensive calcification was found in SA, while a greater prevalence of TCFA and coronary thrombus was imaged in ACS. Twelve-month follow up did not show significant difference in patients treated with PCI from optimal medical therapy only.

P4520 | BEDSIDE
Does longitudinal stent foreshortening occur in balloon expandable coronary stents?

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Purpose: Longitudinal stent foreshortening is a known phenomenon in self-expandable stents, however in balloon expandable stents it needs to be studied. The aim of this study is to measure the length of the balloon expandable stent after deployment and compare with box length.
Methods: The stent length was measured by using IVUS in 95 lesions treated by single stent in 90 consecutive patients. Bare metal stents (BMS) were used in 57 lesions, 60%, and drug-eluting stents (DES) were used in 38 lesions, 40%. By using computer program, the stent length was measured from the longitudinal view between the distal and the proximal stent frames located at one IVUS quadrant (edge-to-edge, E-E) and at two or more quadrants (area-to-area, A-A) using automatic pullback at 0.5 mm/second. The stents were used to treat significant lesions located in the LAD (57.9%), in the RCA (23.2%) and in the LCX (18.9%)

vessels. The box labeled stent length (LL) ranged from 8 mm to 30 mm and the labeled diameter ranged from 2.5 mm to 4.0 mm.
Results: The total measured median E-E stent length was significantly longer then the LL, 18.78 mm (interquartile range, IQR, 15.65 - 23.60) versus 18.00 mm (IQR 15.00 - 23.00), p<0.0001. Moreover, the E-E stent length was significantly different from the A-A length, p<0.0001. Among stent groups, the differences were significantly present in all DES comparisons, p<0.0001, and in BMS, p<0.0001, except the A-A length versus LL, p=0.4. From clinical, laboratory and procedural data the predictors of difference in stent length by multivariate analysis were; the lesion length, p=0.01, pre-intervention lesion minimal diameter of vessel external elastic membrane (EEM), p=0.03, lesions present in the LAD vessel, p=0.03, and the LL, p-0.04.
Conclusions: Longitudinal stent foreshortening is not dominant in balloon expandable stents.The present study revealed important factors (lesion length, minimal diameter of EEM, vessel site and the LL) affecting the true stent length after deployment in human coronary arteries.

P4521 | BEDSIDE
In vivo differentiation of coronary lesions on non-invasive computed tomography angiography and invasive intravascular ultrasound as compared to optical coherence tomography

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Purpose: In vitro studies have shown the feasibility of coronary lesion grading using computed tomography angiography (CTA), intravascular ultrasound (IVUS) and optical coherence tomography (OCT) as compared to histology, whereas OCT had the highest discriminatory capacity. We investigated the ability of CTA and IVUS to differentiate between early and advanced coronary lesions in vivo, OCT serving as the standard of reference.
Methods: Multimodality imaging was prospectively performed in 30 patients with non-ST-elevation myocardial infarction (NSTEMI). A total of 1083 cross-sections of 30 culprit lesions were assessed and co-registered among modalities. Fibrous and fibrocalcific plaque on OCT were defined as early plaque type, whereas lipid rich-plaque on OCT was defined as advanced plaque. To assess associations between each plaque type on CTA and IVUS with early or advanced plaque on OCT, odds ratios (OR) adjusted for clustering were calculated. An OR of >1.0 indicated increased probability of an advanced lesion, whereas an OR of <1.0 indicated an increased probability of an early lesion.
Results: On cross-sectional level normal findings on CTA as well as normal findings on IVUS were associated with early plaque on OCT (OR 0.09; p<0.001 and OR 0.02; p<0.001, respectively). Moreover, non-calcified plaque and napkin ring sign on CTA were associated with advanced plaque on OCT (OR 4.04; p<0.001 and OR 4.54; p<0.001, respectively). Calcified and even more importantly lipid plaque on IVUS were associated with advanced plaque on OCT (OR 2.16; p=0.049, OR 151.93; p<0.001, respectively).
Conclusions: In vivo coronary plaque characteristics on CTA and IVUS are associated with plaque characteristics on OCT. Of note, normal findings on CTA relate to early lesions on OCT, which further supports the use of CTA for exclusion of CAD.

P4522 | BEDSIDE
Percutaneous coronary intervention reduces oxidized low density lipoprotein depending on the vulnerability of plaque in patients with coronary artery disease

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Aim: Oxidized-LDL has a wide range of atherogenic properties, and its plasma levels increases in the patients with acute coronary syndrome (ACS). However, the etiology of plasma oxidized-LDL is unknown. To test the hypothesis that oxidized-LDL is released in part from coronary plaque, we examined serial changes in malondialdehyde-modified low-density lipoprotein (MDA-LDL), one of oxidized LDL particles, before and after PCI in patients with coronary artery disease (CAD).
Methods: Study population consisted of 555 CAD patients undergoing PCI, including 183 ACS and 348 stable angina pectoris (SAP). We made blood sampling before PCI and on the next day of PCI. In 64 patients, blood sampling was performed a mean of 60 minutes after PCI. Same blood sampling was performed in 14 patients undergoing only CAG.
Result: Patients undergoing CAG showed no temporal changes in MDA-LDL value. Baseline MDA-LDL was higher in patients with ACS than those with SAP (148±61 vs. 129±40 U/L, P<0.001). In patients undergoing PCI, MDA-LDL value significantly decreased from baseline to the next day of PCI (136±51 vs. 120±39 U/L, p<0.001). Interestingly, this reduction in MDA-LDL was observed within 60 minutes after PCI procedure (136±63 to 107±45, P<0.01). Multivariate regression analysis documented that baseline MDA-LDL and non-HDL cholesterol values independent factors to predict reduction of MDA-LDL after PCI.
Conclusion: Our data demonstrated that serum MDA-LDL is actively released fromcoronary plaque in patients with CAD, and its clearance is rapid (within 60 minutes). Unstable coronary plaques are likely to release the greater MDA-LDL compared stable plaque. This is the reason why the higher MDA-LDL value is associated with the higher probability of ACS.

P4523 | SPOTLIGHT
Incremental prognostic value of quantitative plaque assessment in coronary CT angiography during 5 years of follow up

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Background: Several characteristics of plaques in coronary computed tomographic angiography (CCTA) are supposed to be indicative of vulnerable plaques and to be particularly prone to plaque rupture and subsequent cardiac events. Nevertheless, plaque characterization is time consuming and technically challenging. Furthermore it is not known if it is better than simple plaque counting. We sought to assess the incremental prognostic value of plaque compositions beyond plaque load and calcium score.
Methods: The study population comprises 1278 consecutive Patients with suspected but not proven CAD. In 387 patients having noncalcified or mixed plaque an automated plaque analysis was performed after manual plaque delineation, calculating low attenuation plaque volume (LAPV, density<30HU), total plaque volume (TPV, <150HU) and remodelling index. In addition the presence of the Napkin sign was assessed. Clinical follow up was performed after a median of 5,6 years. Primary endpoint of the study was a composite of all cause death, myocardial infarction and coronary revascularization later than 90 days after CCTA.
Results: All plaque characteristics correlated well with outcome. Best correlation was found for LAPV (HR 3,36, 95%CI 1,98; 5,70, p<0,0001) and TPV (HR 2,69, 95%CI 1,88; 3,84, p<0,0001). Both parameters showed incremental prognostic value in a stepwise multivariate model including Morise score for clinical risk, calcium scoring and segment involvement score (p=0.032 and p=0.042 resp., see also Figure below).

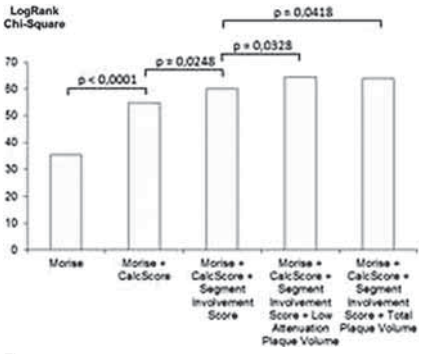

Figure 1

Conclusion: Plaque composition in terms of LAPW, TPV, Remodeling and positive Napkin Sign have a strong correlation with adverse events. LAPV and TPV seem to carry additional prognostic information beyond conventional CCTA analysis and calcium scoring and may improve accuracy of CCTA.

P4524 | BEDSIDE
Optical coherence tomography based study of strut malapposition and uncovered strut with 2nd generation drug-eluting stents at 3 months post-intervention

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Aims: Dual antiplatelet therapy may be discontinued at 3 months after implantation of 2nd generation drug eluting stents (DES). We assessed the mechanism of strut malapposition and coverage with 2nd generation DES by using optical coherence tomography (OCT) at 3 months after percutaneous coronary intervention (PCI).
Methods and results: Fifteen stable and 2 unstable angina pectoris patients who had undergone PCI with OCT were enrolled in this study. Twenty (15 zotarolimus-eluting, 5 everolimus-eluting) stents were deployed. At 3 months after PCI, the percentage of uncovered struts and malapposition were evaluated by OCT. Among a total of 18417 struts in every frame, 603 struts showed malapposition immediately after PCI. Among these, 147 struts (24%) remained malapposed at the 3-month follow-up. At the follow-up, we assessed in the percentage of uncovered struts (8.4±7.7%) by each individual stent. Thrombus was documented in 1 stent. Based on receiver-operating characteristic curve analysis, a strut-to-vessel

distance (S-V distance) ≤160 μm on post-stenting OCT images was the corresponding cut-off point for resolved malapposed struts (sensitivity 79%, specificity 67%, area under curve= 0.80). The S-V distance of persistent malapposed struts on post-stenting OCT images was significantly longer than that of resolved malapposed struts (209±62 vs. 157±45 μm, P<0.001).
Conclusions: A strut-to-vessel distance ≤160μm immediately after PCI predicted well-apposed strut of 2nd generation DES at 3 months after PCI. This distance appeared to be shorter than that previously reported in patients treated with 1st generation DES at 8 months after PCI. These results suggest that discontinuing dual antiplatelet therapy at 3 months after PCI may be unsafe in some patients with 2nd generation DES.

P4525 | BEDSIDE
Fourier-domain optical coherence tomography in the evaluation of the left main coronary artery stenosis. Correlation with fractional flow reserve

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Purpose: Domain optical coherence tomography (FD-OCT) has been used to assess the severity of coronary artery stenosis. However, its value in the evaluation of the left main coronary artery (LMCA) lesions is still unknown. The aim of this study was to assess the safety and diagnostic efficacy of FD-OCT in identifying functional severity of the LMCA stenosis determined by fractional flow reserve (FFR).
Methods: Eighteen patients (15 stable and 3 unstable angina) with an isolated LMCA stenosis (40-80% diameter stenosis by angiographic visual estimation) underwent invasive physiological assessment and FD-OCT imaging of the left main lesion before any intervention.
Results: FFR at maximum hyperemia was≤0,80 in 7/18 (38,8%) patients. Three (16.6%) patients showed ischemic symptoms during OCT image acquisition but none had any major adverse cardiac event. OCT provided optimal visualization of the entire length of the LMCA in 16/18 (89%) patients. Ostial LMCA stenosis was present in 6/18 (33.3%) patients. OCT minimum lumen diameter (MLD), minimum lumen area (MLA), reference lumen area (RLA) (Fig. 1), lumen area stenosis and lesion length were: 1.84±0.30mm, 4.01±1.16mm^2, 12.21±3.29 mm^2, 64.8±12.4%, 5.5±2.99mm, respectively.
FFR values were strongly correlated with OCT derived MLA (r=0.67, p<0.01) and lumen area stenosis (r=-0.76, p<0.001). Receiver-operating characteristic curve suggested an OCT measured MLA<4.1mm (sensitivity 86% and specificity 82%) and lumen area stenosis>67% (sensitivity 86% and specificity 91%) as the best cut-off values for predicting FFR<0.80.

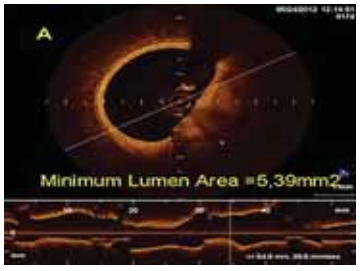

Figure 1

Conclusions: OCT is safe and feasible for the LMCA imaging even in ostial lesions. MLA<4.1mm and lumen area stenosis>67% measured by FD-OCT strongly predict the physiological significance of an LMCA stenosis.

P4526 | BEDSIDE
Impact of inflammatory markers on coronary plaque morphology: virtual histology intravascular ultrasound study

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Background: Recent studies have demonstrated that modifications to LDL such as oxidation have been linked to the pathogenesis of atherosclerosis and one of the cytokines, monocyte chemoattractant protein-1 (MCP-1) has been referred to as a promoter of inflammation.
Purpose: An investigation whether malondialdehyde modified LDL (MDA-LDL) and MCP-1 were associated with the formation of vulnerable plaque in patients with ischemic heart disease was performed.
Methods: 45 patients with stable angina were enrolled. 102 coronary plaques were analyzed by conventional and virtual histology intravascular ultrasound (VH-IVUS). % necrotic core volume (%NCV) of each plaque was measured. We defined thin capped fibroatheroma (TCFA) as having %NC area >15% in multiple slices with a component of the NC in contact with the luminal area. Serum levels of MDA-LDL and MCP-1 were determined. Plaques were divided into two groups based on the presence (A group, 45 lesions) or absence (B group, 57 lesions) of TCFA with a comparison relating to inflammatory markers performed. A further analysis was undertaken to determine the correlation between %NCV and inflammatory markers.
Results: Both MCP-1 value and MDA-LDL value were determined to be significantly higher in the A group (278±82 vs 220±74, p=0.002, and 120±35 vs 100±38, p=0.03). No significant difference was determined between the Hs-CRP value between group A and B (0.19±0.22% vs 0.16±0.20%, respectively, p=0.4). Patients with plaques of high %NCV (defined as %NCV>25%) had significantly higher MDA-LDL to LDL-cholesterol ratio and MCP-1 level than those with low %NCV (defined as %NCV<25%) (1.43±0.52 vs. 1.10±0.36, p=0.02, and 270±84 vs. 217±75, p=0.04, respectively). VH-IVUS analyses showed that MDA-LDL to LDL-C ratio and MCP-1 level positively correlated with %NCV (r=0.424, p=0.004, and r=0.32, p=0.04, respectively).
Conclusion: Both the one type of inflammatory marker, MCP-1, and the oxidation marker, MDA-LDL, was significantly higher in the group having TCFA (A group). These results suggest that the measurement of MDA-LDL and MCP-1 level may be useful for assessing vulnerable plaque in patients with ischemic heart disease. MDA-LDL and MCP-1 level may be important predictors for the risk of cardiovascular disease.

P4527 | BEDSIDE
Association between necrotic plaque volume measured by iMAP and post procedural high sense troponin-T level elevation

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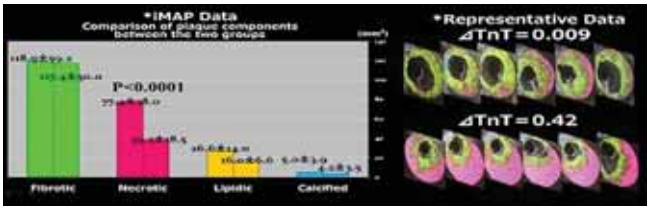
Background: iMAP is a tissue characterization analysis system using the 40-MHz intravascular ultrasound (IVUS). Previous studies demonstrated that plaque morphology measured by other IVUS imaging modalities were associated with elevation in levels of cardiac biomarkers after percutaneous coronary intervention (PCI). However, few data using iMAPTM have been reported.
Methods: From April 2013 to December 2013, 52 consecutive patients with stable angina or silent coronary ischemia who underwent PCI were enrolled. We traced the external elastic membrane cross-sectional area (CSA) and lumen CSA every 1mm axial intervals with in the target lesion. Volume of each plaque component (Fibrotic, Lipidic, Necrotic and Calcified plaques) was evaluated by iMAP analysis software. High sense troponin T (Hs-TnT) was measured before and 24 hours after PCI, and increase level of Hs-TnT was defined as ΔHs-TnT. Patients were divided into two groups in accordance with median of ΔHs-TnT. (Median=0.048, each group: n=26)
Results: There was no significantly difference in patient characteristics between the two groups. In iMAP-IVUS analysis, Necrotic plaque volume was significantly higher in HighΔHs-TnT group (P<0.0001). In Simple regression analysis, Minimum lumen diameter QCA, Lipidic plaque volume, Necrotic plaque volume and %plaque area of target lesion were significantly correlated with ΔHs-TnT. (r=0.28 p=0.04, r=0.45 p=0.0007, r=0.62 p<0.0001, r=0.48 p=0.0004). The Necrotic plaque volume was independently correlated with ΔHs-TnT in multiple regression analysis.(p=0.01)



iMAP data and representative data.

Conclusion: The volume of Necrotic plaque measured by iMAPTM is associated with ΔHs-TnT in patients with stable angina or silent coronary ischemia.

P4528 | BEDSIDE
Deferral versus performance of coronary intervention based on coronary pressure-derived fractional flow reserve: systematic review and meta-analysis

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Introduction: Fractional flow reserve (FFR) has been proposed as the gold standard to assess functional severity coronary artery stenosis and to stratify which lesions should be subjected to coronary intervention (PCI).
Objective: To determine the safety of using FFR as a decision-making tool for deferral or performance of PCI, based on data from published studies.
Methods: Systematic review by independent researchers was performed in PubMed and EMBASE including papers indexed until October 11th 2013 that used FFR (0.75 or 0.80) to determine in which lesions PCI should be performed

or deferred. Outcomes of interest were death, myocardial infarction (AMI) and new revascularization (RV). Comprehensive Meta Analysis Software was used to pool study results and for meta-regression.
Results: After peer review, 60 abstracts remained and 19 papers (12 observational studies and 7 randomized-controlled trials) were included for analysis, totaling 3,097 patients (3,796 lesions). Nine papers had two arms (PCI and Defer) and 10 had only the Defer arm; FFR cut-off was 0.75 in 15 studies, and 0.80 in 4. Weighted mean follow-up time was 21.2 months (6.9 to 53). In indirect comparisons, PCI and Defer groups had similar death: 2.2% (CI95% 0.9 - 5.1%, I2 = 72.7) x 2.0% (1.1 - 3.5%, I2 = 40.5), p=0.86, and AMI rates: 1.9% (0.8 - 4.0%, I2 = 0) x 1.9% (1.1 - 3.1%, I2 = 49.8), p=1.00. RV rates were higher in the PCI group: 14.0% (8.0 - 23.2%, I2 = 87.8) x 4.4% (8.8 - 6.9%, I2 = 58.9), p=0.002. Direct comparisons, including two-arm trials, also showed no differences in death: OR = 1.86 (0.81 – 4.27, I2 = 11.5; p=0.14) and AMI rates: OR = 0.75 (0.21 – 2.69, I2 = 47.1; p=0.66); RV rates were again higher in the PCI group: OR = 3.10 (1.25 – 7.70, I2 = 72.2; p=0.015). Meta-regression suggests influence of the proportion men on the RV rates (β = 0,058, p=0,026). No other co-factors (age, hypertension, diabetes, FFR cut-off) influenced the outcomes.
Conclusion: Based on pooled data, FFR seems to be a safe and useful tool to determine lesions to be treated. Higher RV rates were observed in the PCI groups, speculatively related to restenosis. This data, however, should be parsimoniously interpreted, given the considerable heterogeneity of the studies published so far.

P4529 | SPOTLIGHT
Adenosine-induced maximal coronary hyperemia for myocardial fractional flow reserve measurements: comparison of administration by femoral venous versus antecubital venous access

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Introduction: Over the past decade, FFR measurement has been increasingly used in cardiac catheterization laboratories. It provides a quantitative assessment of the functional severity of a coronary artery stenosis identified during coronary angiography and cardiac catheterization. Achieving maximum hyperemia is a prerequisite for correct measurement of FFR.
Methods: 18 randomly selected patients with coronary artery disease were included. FFR was measured with a pressure monitoring wire and the recording was digitally stored. Hyperemia was successively induced by adenosine via the antecubital vein at a dose of 140 ug kg-1 min-1 (A140), via the antecubital vein at a dose of 180 ug kg-1 min-1 (A180), and via the femoral vein at a dose of 140 ug kg-1 min-1 (F140).
Results: Induction of hyperemia by A140 yielded significantly lower hyperemic responses than compared with A180 (P=0.004) and F140 (P=0.001). No significant difference was seen between adenosine administration by A180 versus F140. Hyperemic stimulation by A140 underestimated lesion severity near the ischemic threshold of FFR more frequently than the other modalities. There were no differences in side-effects between any of the dosages and routes of administration.
Conclusions: The intravenous application of adenosine via antecubital venous access is feasible but slightly less effective than the femoral approach. In this setting, an antecubital dosage of 180 ug kg-1 min-1 is comparable to the standard dosage of 140 ug kg-1 min-1 in the femoral vein. In some patients, this regimen might prevent an underestimation of lesion severity.

CORONARY FLOW VELOCITY

P4531 | BEDSIDE
Estimation of lipid volume in plaque for prediction of slow flow phenomenon during elective coronary intervention

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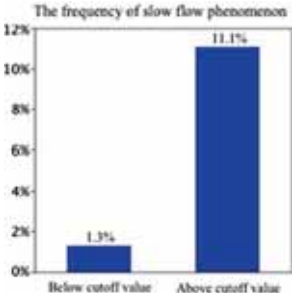
Purpose: Slow flow phenomenon developed unexpectedly during elective percutaneous coronary intervention (PCI) has been reported to worsen the prognosis of patients. One of the causes of slow flow phenomenon is the leakage of lipid component from target plaque for PCI. By the estimation of lipid volume in plaque at the target lesion, we investigated whether it is possible to select high risk patients for slow flow phenomenon during PCI.
Methods and results: We investigated consecutive 356 coronary lesions with elective PCI by using integrated backscatter intravascular ultrasound. Slow flow phenomenon occurred in 17 lesions (4.8%) after procedure and the value of creatine kinase at the next day was significantly higher in the patients with slow flow phenomenon (316±273 vs. 77±65 IU/L, p<0.0001). We defined the estimated lipid volume as the product of the lipid area at the minimal lumen diameter site multiplied by total stent length.The estimated lipid volume was significantly correlated with the true lipid volume that was calculated by integration of every 1mm slice (r=0.865, p<0.0001). ROC analysis revealed that the cutoff value of the estimated lipid volume for slow flow phenomenon was 133.2mm^3 (AUC 0.799). As compared with the group with less than cutoff value, the group with more than cutoff value had a high risk for slow phenomenon (odds ratio, 9.46; 95% CI, 3.01-41.6; p<0.0001).
Conclusion: To predict of the development of slow flow phenomenon, it is important to evaluate the true lipid volume in plaque in the target lesion. However the accurate measurement of the true lipid volume is difficult during PCI. The analysis of the estimated lipid volume by using IB-IVUS is easy during PCI and useful to select patients with high risk for slow flow phenomenon.



P4532 | BEDSIDE
Efficacy of intracoronary nicorandil administration for achieving hyperemia in intermediate coronary lesions with microvascular dysfunction

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Background: Fractional flow reserve (FFR) has been known to underestimate functional severity of coronary stenosis with microvascular dysfunction.
Aim: The aim of this study was to investigate the impact of intracoronary nicorandil (NCR) administration on achieving hyperemia in coronary lesions with microvascular dysfunction.
Method: FFR and coronary flow reserve (CFR) were assessed in 41 patients with 56 intermediate coronary stenoses, using a 0.014-inch Combowire. Hyperemia was induced by injection of intracoronary NCR (2 mg for left coronary artery and 1.2 mg for right coronary artery), following intracoronary ATP (50 μg, 100μg, 200μg for left coronary artery and 30 μg, 60 μg, 120 μg for right coronary artery). Hyperemic microvascular resistance (HMR) was determined as the ratio of mean distal pressure to average peak velocity during hyperemia.
Result: A strong correlation was found between ATP and NCR-induced FFR (R2 = 0.963, p<0.0001). Furthermore, a significant correlation between ATP and NCR-induced CFR was found, but relatively weak (R2 = 0.626, p<0.0001). When we divided 40 lesions showing ATP-induced FFR ≥0.8 into Group A (CFR ≥2.0, n=13) and Group B (CFR <2.0, n=27), NCR-induced CFR was significantly higher than ATP-induced CFR in Group B (1.57±0.42 vs. 1.48±0.30, p<0.05). There were no differences in Group A. HMR in Group B was tended to be higher than in Group A (4.26±2.22 vs. 2.92±1.74, p=0.0683).
Conclusion: Intracoronary NCR administration was more effective than intracoronary ATP administration for evaluating accurate FFR in borderline coronary lesions with microvascular dysfunction.

P4533 | BEDSIDE
Calculation of the residual pressure gradient after stent implantation of the coronary lesions on the basis of 3D coronary angiography and fluid dynamic equations

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Background: The measurement of the fractional flow reserve (FFR) is the most accurate method to determine the hemodynamical importance of borderline coronary lesions. However, after stent implantation the reasons and the prognostic relevance of the residual pressure gradient are not quite clear.
Aims: Fluid dynamic calculation of the residual pressure gradient after stent implantation, comparison of the results with the measured FFR values and determine the reasons of the residual pressure drop.
Method: 18 stented coronary segments were analyzed. FFR measurements by Radi Pressure Wire, St.Jude Medical) were performed just after the stent implantation. The target arteries were reconstructed in 3D using a dedicated 3D QCA software package (QAngio XA Research Edition 1.0 Medis Special by Leiden) from the orifice of the coronary artery to the position of the pressure sensor. The coronary artery volumetric flow during vasodilatation was calculated based on the velocity of the contrast material injected just after the intracoronary adenosine administration. The components of the pressure gradients due to the pre-, and postlesional laminar resistances, as well as the laminar and turbulent gradients of lesions itself were determined by fluid dynamic equations using the morphological data derived by 3D coronary angiography and contrast material velocities after stent implantation.

Results: The measured and the calculated FFR values showed (r=0.79; p=0.0003) statistically significant correlations. The Bland- Altman analysis (mean: -0,04; -0,11-0,03) proved that the calculated FFR was reasonable precise in our model in comparison with the measured values. The difference between the expected perfect results after the stent implantation and the measured FFR was characterized with the "1-poststent FFR" value. The calculated laminar pressure gradient after stent implantation showed strong correlation with the "1-poststent FFR" (r=0.83, p=0.0001). On the other hand, the correlation between the "1-FFR" and the calculated pressure gradients only for the stented segment, as well as the measured collateral indexes, were found to be not significant.
Conclusions: The majority of the non-optimal FFRs measured after stent implantation can be explained not necessarily with the insufficient stent expansion but with the pressure gradient caused by the laminar resistance along the non-significantly diseased segments of the vessel surrounding the stent.

P4534 | BEDSIDE
Combining pressure wire pullback with the instantaneous wave-free ratio permits measurement of the physiological lesion length of stenoses

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Background: Tandem and diffuse coronary disease present an ongoing challenge with longer stents at risk of increased restenosis and adverse outcomes. Pressure wires can limit stenting to ischaemic vessels but face practical difficulties when planning stent length required. The instantaneous wave-free ratio (iFR) is a resting index of lesion severity which can be measured continuously during pressure wire pullback. Computation can identify and measure the length of regions with the greatest pressure loss (pressure drop intensity, ΔiFR/mm). We systematically compared the anatomical length selected for intervention to the physiological length.
Methods: Intracoronary motorized pressure-wire pullbacks were performed under resting conditions in 32 coronary arteries with tandem and diffusely disease undergoing coronary intervention guided by angiography. Automated algorithms plotted ΔiFR/mm for the vessel identifying focal and diffuse disease. The lengths of pressure drop intensity were compared to the anatomical length of the stenosis selected for real-world PCI and the length of real-world stent used. Data shows mean±SEM.
Results: Pre-PCI iFR was 0.79±0.03. The physiological length of the lesions was significantly shorter than their anatomical length by quantitative angiography (12.6±1.5mm vs 23.3±1.3mm respectively, $p<0.001$).
PCI was performed using traditional angiographic guidance to achieve an iFR of 0.93±0.01. The mean stent length used was 27.5±2.3mm, significantly longer than physiological length ($p<0.001$). Computed virtual PCI showed the same physiological result could be achieved by treating only the areas of high pressure drop intensity to produce a significantly larger gain in iFR per mm of stent deployed (1.1±0.3%/mm versus 2.5±0.72%/mm, p=0.005).
Conclusion: iFR pullback can be performed at rest and can plot ΔiFR/mm for the entire vessel. Physiological lesion length is typically shorter than anatomical length. Pullback analysis could demonstrate that shorter stents with focal deployment would achieve similar physiological outcomes as longer stents. Pullback may identify stenting strategies that offer little haemodynamic benefit for the stent length deployed. Co-registration of ΔiFR/mm with angiographic and intracoronary imaging is possible and may provide a tool for interventionalists to plan intervention for complex coronary lesions.

P4535 | BEDSIDE
Prognostic value of refusal of coronary angiography in patients with effort chest pain and high coronary flow velocities in the left main and proximal left anterior descending coronary artery

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Background: Previous studies have demonstrated that transthoracic Doppler echocardiographically (TTDE) derived peak diastolic coronary flow velocities (PDCFV) can accurately identify significant left main (LM) and proximal left anterior descending (PLAD) coronary artery disease. However, the prognoses of patients with effort chest pain and high PDCFV values have not yet been systematically studied. Aim: the purpose of the study was to evaluate the prognosis of patients with high PDCFV in the LM and/or PLAD according to the acceptance or refusal of the coronary angiography.
Methods: The PDCFV in the LM/PLAD segment was assessed by TTDE from modified parasternal and apical 5 chamber views in all patients. All subjects had peak PDCFV ≥140 cm/sec in the LM/PLAD and indication for coronary angiography according to the current guidelines. The study population included 146 patients (89 men, mean age: 68±11 years) and was divided into 2 subgroups. Group "A" consisted of 108 patients (74%) who underwent coronary angiography and Group "B" of 38 patients (26%) who did not (due to the refusal of the patients). Based on the result of the coronarography, 89 patients (82%) in Group "A" underwent clinically driven LM/PLAD revascularization either by PCI or CABG. Participants in both groups were treated by optimal medical therapy. All-cause mortality was the end point for the study.
Results: At enrollment, PDCFV did not differ in the two groups (194±52 vs. 201±49 cm/sec, p=NS). During a median follow-up of 68 months, 76 patients (52%) died. Kaplan-Meier survival estimates showed a significantly better outcome for Group "A" patients compared with Group "B" patients (65% vs. 25% at 6 years of follow-up, $p<0.00001$). In a sequential multivariate Cox model of clinical and resting echo data, independent predictors of all-cause mortality were: refusal of coronary angiography (HR, 2.8; 95% CI, 1.6-4.8), age (HR, 1.05; 95% CI, 1.05-1.08), resting left ventricular ejection fraction (HR, 0.97; 95% CI, 0.96-0.99) and left atrial diameter (HR, 1.07; 95% CI, 1.02-1.13).
Conclusions: Proving of a high flow velocity profile in the left proximal coronary arteries by TTDE identifies patients having high risk for death without invasive coronary artery evaluation. Denial of coronary angiography in this subset of patients has independent and incremental prognostic power to predict long-term mortality over clinical and other echocardiographic data. Therefore, all efforts have to be made to convince these patients for the acceptance of the invasive coronary angiographic evaluation strategy.

P4536 | BEDSIDE
Recanalization within 120 minutes of symptom onset and microvascular integrity assessed by coronary doppler flow velocity measurements in ST-segment elevation myocardial infarction

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Background: The impact of total ischemic time on microvascular obstruction as assessed by coronary flow velocity measurements (MVO-CFV) and clinical outcome has been insufficiently studied. This study investigated the relationship between long-term cardiac events and the incidence of MVO-CFV worsened by primary coronary angioplasty delay in patients with ST-segment elevation myocardial infarction (STEMI).
Methods: Because of the low incidence of microvascular obstruction (MVO) in the presence of normal blood flow before percutaneous coronary intervention (PCI) as previously reported, 34 patients with pre-procedural TIMI 3 flow were excluded. A total of 193 consecutive patients with first anterior STEMI who underwent angioplasty were subjected to CFV measurement with a Doppler guidewire. The CFV spectrum provided the systolic peak velocity and diastolic deceleration time (DDT). We defined the presence of MVO-CFV as a DDT of ≤600 ms and the appearance of systolic flow reversal.
Results: All patients who achieved reperfusion within 120 min after symptom onset were successfully salvaged from MVO-CFV. There was a significant correlation between duration of ischemia and incidence of MVO-CFV ($P<0.01$). There were no changes in the incidence of MVO-CFV beyond 240 min after symptom onset. We classified the patients into three categories according to duration of ischemia: ≤120 min, >120 to 240 min, and >240 min. The major adverse cardiovascular events (MACE) rate was compared among the three groups. Earlier reperfusion was associated with a significantly lower risk of MVO-CFV (0/18 [0%], 29/73 [40%], and 63/102 [62%], respectively; $P<0.01$). Long-term follow-up was performed at a mean of 5.5±3.5 years. The long-term incidence of MACE was lowest in the ≤120 min group and highest in the >240 min group. The stepwise Cox proportional hazards model revealed that MVO-CFV was an independent predictor of long-term cardiac events ($P<0.001$). ST-segment re-elevation ($P<0.001$) and duration of ischemia (P=0.003) were independent predictors of MVO-CFV.
Conclusions: Very early recanalization preserves coronary microvascular integrity associated with clinical outcome in patients with anterior STEMI undergoing primary angioplasty.

P4537 | BEDSIDE
Contrast-induced hyperemia as an alternative to adenosine-induced hyperemia in the evaluation of fractional flow reserve in coronary lesions

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Purpose: Being able to evaluate the functional importance of coronary lesions with a pressure wire without inducing pharmacological hyperemia with adenosine has gained increased interest. Coronary contrast medium allows a hyperaemic stimulus and may be an alternative to adenosine in a significant proportion of patients, as previously showed. We intended to evaluate the diagnostic accuracy of fractional flow reserve after contrast hyperemia (FFRcont), as compared to conventional FFR evaluated after adenosine hyperemia (FFRad).
Methods: 98 lesions (66 patients, mean age 63.9±10.5 years, 46 males) were prospectively evaluated, using a pressure wire. The lesion baseline pressure gradient (Pd/Pa) was measured. FFRcont was evaluated after an intracoronary bolus of 10 cc of contrast medium. FFRad was evaluated after maximal coronary hyperemia with adenosine infusion (central vein).
Results: FFRcont values were strongly correlated with baseline Pd/Pa (R2 0.83, $p<0.0001$) and with FFRad (R2 0.86, $p<0.0001$). The best cut-off point in the

ROC curve to predict a FFRad <0.80 was 0.84 (AUC ROC 0.965, 95CI 0.936-0.994; sensitivity 97.4%, specificity 84.7%, positive predictive value 80.9%, negative predictive value 87.7%, global accuracy 89.8%). All lesions with an FFRcont >0.85 (n=47) had an FFRad>0.80 (negative predictive value 100%); all lesions with an FFRcont<0.80 (n=25) had an FFRad<0.80 (positive predictive value 100%). As a result, "extreme" values of FFRcont (<0.80 and >0.85) allowed a correct prediction of FFRad in 72 lesions (73.5%). In 9 lesions, FFRcont was repeated with a 5 minutes interval, and the observed results were similar (Spearman rho 0.99, p<0.0001).
Conclusions: FFR measured after an intracoronary bolus of contrast medium has a high accuracy to predict FFR values after adenosine hyperemia. This technique allows the correct evaluation of functional severity in more than 70% lesions, obviating the need of adenosine-induced hyperemia in a high proportion of patients. Adenosine can be reserved for patients with intermediate (0.80 to 0.85) FFR values after contrast-induced hyperemia.

P4538 | BEDSIDE
Coronary flow velocity reserve in patients with thoracic aortic aneurysm

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Purpose: Aortic aneurysms (AA) are one of the leading causes of morbidity and mortality. Microvascular dysfunction may contribute to cardiovascular consequences in AA patients. Coronary flow velocity reserve (CFVR) has been considered an important diagnostic index of the functional capacity of coronary arteries noninvasively. The aim of this study was to evaluate, by non-invasive CVFR, whether patients with thoracic AA demonstrate significant coronary microvascular dysfunction in the absence of coronary artery disease (CAD).
Methods: We included 44 patients with thoracic AA in the absence of concomitant CAD (30 men,14 women; mean age 60.2±9.6 years). A total of 26 patients without aortic dilatation were selected as the control group. Coronary flow velocities in the distal left anterior descending artery (LAD) were measured using transthoracic echocardiography. CFVR was calculated as the hyperemic to resting coronary diastolic peak velocities ratio.
Results: Compared with controls, patients with AA had higher baseline LAD peak diastolic coronary flow velocities (28.3±5.8 vs. 25.1±4.5 cm/sec, p<0.05), lower hyperemic LAD flow velocities (54.0±10.3 vs. 58.0±12.5 cm/sec, p=0.160), and consequently lower CFVR (1.9±0.3 vs. 2.3±0.5, p<0.001). Multivariate linear regression analysis showed that CFVR was independently associated with age (β=-0.384, p=0.002), aortic systolic diameter (AoSD) (β=-0.406, p=0.001) and interventricular septum thickness (β=-0.232, p=0.043) in patients with AA.

Coronary flow velocity and hemodynamics

Variables	Patients with AA Baseline hyperemia	Controls Baseline hyperemia
Aortic systolic diameter (mm)	45.3±3.6	32.1±3.5†
Aortic diastolic diameter (mm)	43.6±3.9	29.1±3.7†
Coronary flow velocity reserve	1.9±0.3	2.3±0.5†
Peak diastolic flow velocity (cm/s)	28.3±5.8 54.0±10.3*	25.1±4.5‡ 58.0±12.5*
Systolic blood pressure (mmHg)	135±18 133±17	126±17‡ 122±28‡
Diastolic blood pressure (mmHg)	78±12 77±12	76±14 74±12
Heart rate (beat/m)	73±12 96±14*	74±11 99±16*

AA: Aortic aneurysm. *p<0.001 vs. with baseline; ‡p<0.05 vs. patients with AA; †p<0.001 vs. patients with AA. Values are mean ± std. deviation.

Conclusions: Our study demonstrates that noninvasive CFVR is significantly impaired in patients with AA. AoSD is the most important determinant of impaired CFVR.

P4539 | BEDSIDE
Different ifr and ffr cut-off values tested in a prospective real-life experience

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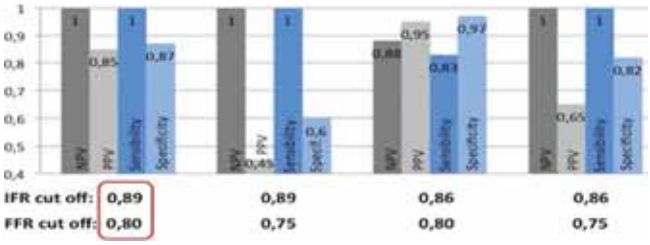
Purpose: The instantaneous wave-free ratio (iFR) is a recent and non-hyperemic pressure-derived severity index of coronary stenosis. Reports regarding its accuracy in comparison to FFR showed discordant results. The aim of this study is to compare the accuracy of different cut-off thresholds for both iFR and FFR assessed in the clinical practice.
Methods: The present investigation is a single-centre, prospective, observational analysis of patients with coronary artery disease showing at least one angiographically intermediate coronary lesion. They underwent both FFR and iFR evaluation in order to interrogate the functional relevance of the stenosis. Receiver operator characteristic (ROC) curves for iFR are used to verify the cut-off points reported in the literature: 0.89 vs 0,86 for iFR and 0.80 vs 0,75 for FFR. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) are determined for all the combinations of iFR and FFR cut-off values.
Results: A total of 35 patients with 53 lesions are analysed. A strong correlation between iFR and FFR is observed (R=0.84; p<0.0001). At ROC analysis the area under the curve approximated the unity for both FFR cut-off value of 0.80 and 0.75 (AUC result respectively 0,98 and 0,96). The differences of diagnostic accuracy are summarized in the figure below.



Diagnostic agreement between iFR and FFR.

Conclusion: This single-centre experience confirms that 0,89 is the optimal iFR cut-off value in compare with an FFR threshold of 0.80. It identifies critical coronary stenosis with sensibility and specificity of 100% and 87% respectively. This value is higher than the cut-off adopted in the ADVISE-study, which was 0.83, but confirm that of the ADVISE-registry.

P4540 | BEDSIDE
The laminar resistance of the coronary segment between the lesion and the sensor of the pressure wire significantly influences the fractional flow reserve

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Background: The determination of the fractional flow reserve can be influenced by the position of the sensor of the pressure wire distal to a coronary lesion.
Aim: Fluid dynamic calculation of pressure gradients restricted to the stenosis and with inclusion of the distal reference segment until the position of the pressure wire. Comparison of the results with the actually measured FFR values.
Methods: A total of 19 de novo lesions of 17 patients were consecutively enrolled. 21 intracoronary pressures measurements were performed by Radi PressureWire™ (in two cases with two different sensor positions). X-ray angiographic images were recorded by flat panel systems. The lumen of the interrogated vessel segments was reconstructed in 3D using a dedicated 3D QCA software package. The coronary artery volumetric flow was calculated based on the velocity of the contrast material in the 3D reconstructed coronary segment. Pressure gradients were determined by fluid dynamic equations using the morphological data derived by 3D coronary angiography and contrast material velocities.
Results: The Bland-Altman analysis showed lower differences between the calculated and the measured pressure gradients when the distal laminar resistances were also incorporated in the model compared to the calculations restricted to the lesions (mean difference: 4 Hgmm vs. 7.6 Hgmm; limits -2 to 11 Hgmm vs. 0.9 to 14.2 Hgmm; range: 13 Hgmm vs. 13.3 Hgmm). Mann-Whitney test proved significant difference between the measured and calculated values only in the latter cases (p=0.07 vs. 0.0016). Similarly if FFR was calculated not only for the lesions but together with the distal resistance then the differences were lower between the measured and calculated values than in cases when the distal resistances were neglected (mean difference: -0.05 vs. -0.09, limits: -0.11 to 0.02 vs. -0.16 to -0.01; range: 0.112 vs. 0.159; p=0.053 vs. p=0.0005).
Conclusions: The FFR reflects not only the pressure gradient of the stenosis, but also the laminar resistance of the poststenotic segment until to the sensor of the pressure wire. Knowing the components of the detected gradients could be important for the clinical considerations of the cases near the cut of value of the FFR.

P4541 | BEDSIDE
Coronary FFR measurement using contrast media: an alternative to adenosine

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Aim: FFR measurement requires to induce coronary hyperemia, usually with adenosine (aFFR). However, adenosine can be contraindicated in some patients, can induce conductive and rhythmic complications and represents an extra cost. Injection of contrast media, routinely performed to validate FFR guidewire placement, also induces hyperemia and could be an alternative method to measure FFR (cFFR) but there is no data defining a threshold value.
Methods and results: This prospective multicentric study included 102 lesions in 74 consecutive patients with stable coronary disease. Patients with acute coronary syndrome, chronic renal failure and contra-indication to adenosine were

excluded. We performed measurements of cFFR and aFFR as follows: 1) baseline pressure value; 2) cFFR after IC contrast injection (Iomeprol or Iodinaxol, 10 ml intracoronary for left coronary artery or 6 ml for right coronary artery); 3) aFFR after IC injection of adenosine (150 μg IC for left coronary artery, 100-120 μg for right coronary artery). The first cohort (cohort A) included 26 patients (age 71±10 years, 70% male) with 35 lesions (51±11% stenosis, LAD n=14, CX n=12, RCA n=8) and was used to characterize the correlation between aFFR and cFFR and to determine the cFFR threshold value that accurately detected significant lesions (defined as aFFR value ≤0.8). Then we studied 48 consecutive subjects (age 68±11 years, 76% male) with 67 lesions (51±9% stenosis, LAD n=36, CX n=18, RCA n=11), (cohort B) as a validation group. From the cohort A, we showed that although cFFR induces slightly lower hyperhemia as compared to aFFR (0.84±0.10 vs 0.82±0.12, p=0.44), it was significantly correlated with aFFR (Pearson's R=0.9; P<0.001). Receiver operator curve analysis revealed that the optimal cFFR threshold value was 0.85 (sensitivity=95%; specificity=73%; area under the curve: 0.92±0.05, p<0.001). We then prospectively tested this cut-off value in the cohort B. We found 27 significant lesion by aFFR (aFFR≤0.80) and 36 significant lesions by cFFR (cFFR≤0.85). Using this threshold, cFFR correctly classified 56/65 lesions. The sensitivity, specificity, positive and negative predictive values were respectively 100%, 76%, 75% and 100%. Significant complications occurred during aFFR: ventricular fibrillation (n=1), atrial fibrillation (n=1) and third degree atrioventricular block (n=2).

Conclusion: cFFR is an easy alternative method to induce hyperemia and to avoid IC adenosine injection. A cFFR threshold value of 0.85 provides excellent sensitivity and negative predictive value.

P4542 | BEDSIDE

Value of TIMI Myocardial Perfusion Frame Count in predicting microvascular dysfunction in STEMI patients receiving reperfusion therapy, evidence from Cardiac Magnetic Resonance

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Background: Several angiographic methods have been established to evaluate microvascular perfusion, e.g., Myocardial Blush Grading (MBG) and TIMI Myocardial Perfusion Grading (TMPG), however, their efficacy were controversial due to the subjective inherence. We have introduced a more objective method named TIMI Myocardial Perfusion Frame Count (TMPFC) to assess microvascular perfusion angiographically, which has shown a good relationship with 30-day and 6-month major adverse cardiovascular events.

Objective: This study aimed to disclose the accurate correspondence between TMPFC and microvascular dysfunction visualized by Cardiac magnetic resonance imaging (CMR) and to determine its optimal cutoff point.

Methods: 140 consecutive STEMI patients who received reperfusion therapy and compatible with CMR were included. TMPFC was calculated using the final angiographic imaging after PCI and defined as frame numbers between myocardial blush appearing and disappearing at infarction zone (30 frame/second). CMR was performed on a 3.0-T scanner using standard protocols 3-8 days after reperfusion (median 4.6 day, depending on individual stability). MD was defined as either the existence of myocardial defect on perfusion scan or on late-enhancement imaging after gadolinium injection.

Results: When CMR was used as the standard reference for MD, value of TMPFC was significantly different between those who had MD (median 85, range 48-135) and those without (median 120.5, range 63-318,p<0.001). When predicting the existence of MD, the area under the receiver operator characteristic (ROC) of TMPFC was 0.871, with the optimal cutoff point 95.5 (sensitivity 84.8%, specificity 0.846, maximal Youden index 0.694). The predictive power of TMPFC for MD was not influenced by gender, reperfusion method, culprit artery, heart rate and infarction size. In a logistic analysis, TMPFC was superior to predict MD against TMPG and MBG (p<0.001, RR for MD with each 1 TMPFC=1.07). TMPFC had a positive relationship with MD size (presented as proportion of microvascular obstruction area to necrosis area in late-enhancement imaging, coefficient=0.425,p<0.001). In patients with TMPFC≥95.5, CMR-based left ventricular ejection fraction was significantly lower than those with TMPFC≤95.5 (45.1±9.14% v.s 57.8±7.26%, P=0.001).

Conclusion: The current study demonstrated: i) TMPFC has a good predictive power for microvascular dysfunction. ii) TMPFC is negatively related to the pump function. These traits make TMPFC a promising tool for prognosis prediction in reperfused STEMI patients

STROKE

P4544 | BEDSIDE

CHA2DS2-VASc identifies heart failure patients in sinus rhythm with high rates of thromboembolic complications: findings in a real-world nationwide cohort

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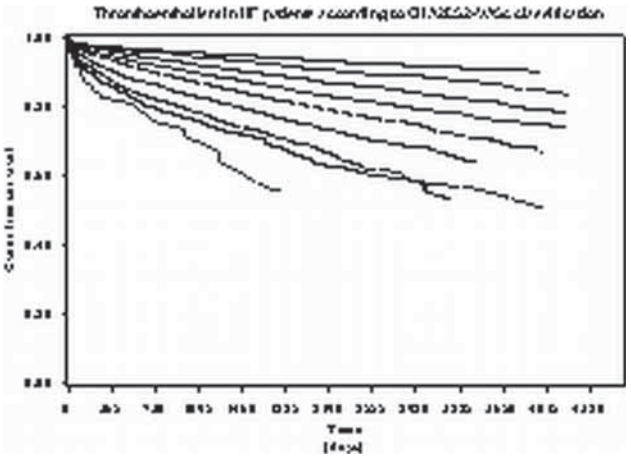
Purpose: Patients with heart failure in sinus rhythm are at an increased risk of thromboembolic complications. Current guidelines state that VKA treatment to heart failure patients in sinus rhythm should be based on an individual risk assessment. To date, a uniform thromboembolic risk stratification system in heart failure is lacking, which may cause an unnecessary risk of both thromboembolism (TE) and bleeding.

Methods: We used a combination of data from the Danish National Patient Registry and The Danish Register of Medicinal Product Statistics to identify patients with heart failure in sinus rhythm and score patients retrospectively according to the CHA2DS2-VASc (Congestive heart failure, Hypertension, Age, Diabetes, Stroke, Vascular disease, intermediate Age, Sex category) risk stratification system.

Results: 93.444 patients were included between 1989-2011. The CHA2DS2-VASc score at the time of heart failure diagnosis identified patients at high risk of TE, as depicted in the figure. To assess the rates of TE over time, we re-classified patients annually from time of heart failure diagnosis and looked at annual rates of TE. Rates during the first year following heart failure were 3.14 - 24.24 events per 100 patient years, dependent on CHA2DS2-VASc class.



Conclusions: The CHA2DS2-VASc score could identify heart failure patients in sinus rhythm with high rates of thromboembolic complications in a retrospective real-world cohort of more than 90.000 patients. The rates presented were much higher than previously reported in randomized controlled trials, and suggests that sub-populations of heart failure patients in sinus rhythm are at a great risk of thromboembolism.

P4545 | BEDSIDE

Troponin T serum level is not associated with the location and volume of acute brain infarction

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Purpose: The cardiac troponin T (cTnT) is frequently elevated in in acute ischemic stroke patients. However, the relationship, if any, between the cTnT level and brain infarction remains to be established. The aim was to investigate the possible correlation between the location and volume of brain infarction and the cTnT serum level in AIS patients.

Methods: The prospective hospital-based study (Clinicaltrials.gov No. NCT01541163) consisted of consecutive AIS patients admitted within 12h of stroke onset. The location and volume of the acute brain ischemic lesion was assessed with magnetic resonance imaging. Standard laboratory tests, including cTnT and repeated electrocardiograms, were performed at admission and after 4h. Correlations between the cTnT level and the location and volume of brain infarction and baseline parameters were tested with a Spearman correlation coefficient. Univariate and multiple logistic regression analysis (LRA) were used to determine the possible predictors of cTnT elevation.

Results: Out of the 200 enrolled patients, elevated cTnT was present in 71 (36%). No correlation was found between the cTnT serum levels and the location (P>0.05) nor volume of brain infarction (P=0.48). LRA identified creatinine (OR: 1.26 per 10 μmol/L increase; 95%CI: 1.043–1.524), NT-proBNP (OR: 1.05 per 100 μg/L increase; 95%CI: 1.018–1.093) and male gender (OR: 3.674; 95%CI: 1.025–13.164) as significant independent predictors of pathological elevation of cTnT.

Conclusions: Although elevated cTnT serum level is relatively frequent in AIS patients within the first 12h of stroke onset, it is not related to the location or volume of brain infarction.

Study was supported by the MHCR grants FNOl 00098892, NT/11046-6/2010 and NT/14288-3/2013.

P4546 | BEDSIDE
Characterization of atrial fibrillation onset in patients with ischemic stroke

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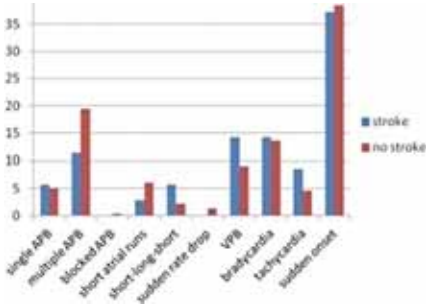
The characterization of onset scenarios of paroxysmal atrial fibrillation (pAF) has recently gained prominence to determine various underlying arrhythmogenic trigger mechanisms. It is hypothesized that there might be specific onset scenarios of pAF in patients with ischemic stroke, however, onset scenarios of pAF have not yet been systematically analysed in a broad patient population without pacemaker indication and especially those patients after ischemic stroke.
Methods and results: From a total of 20.546 consecutive ambulatory 24-hour-Holter-ECG-recordings, 668 episodes of pAF (lasting >1 minute) were identified in 343 patients without previous stroke (155 females; 71±10years) and 35 pAF episodes in 20 patients after ischemic stroke (8 females; 67±15 years). The dominant portion of episodes of pAF was preceded by atrial ectopy [single atrial premature beats (APB), blocked APB, multiple APB, short atrial runs, short-long-short sequences] or heart rate alterations [bradycardia, tachycardia, sudden rate drop, ventricular premature beats (VPB)]. Almost one third of all pAF episodes were not preceded by either ectopy or heart rate alterations (i.e. sudden-onset pAF). There were no significant differences between patients with or without stroke regarding the distribution of pAF-onset patterns. Mean RR-interval during sinus-rhythm tended to be higher in patients after ischemic stroke (866±184ms vs 845±190ms; p=0.1).



Onset scenarios of pAF.

Conclusion: There are no significant differences regarding specific onset-scenarios of pAF patients after ischemic stroke and in patients without stroke. Interestingly, patients with stroke tended to have lower heart rates during sinus rhythm.

P4547 | BEDSIDE
Safety and feasibility of left atrial appendage occlusion by cardiac plug in patients with contraindication to warfarin therapy. a single center experience

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Background: The Protect AF trial demonstrated that LAA closure (LAAC) with the Watchman device was non-inferior to warfarin (warf) therapy. However, published results of LAAC with the Amplatzer Cardiac Plug device in patients (pts) with a contraindication (CI) to warf therapy are limited. These pts are different than pts in Protect AF as they represent with many comorbidities.
Aim of the study: The aim of this study was to investigate the safety and feasibility of LAA closure with the Amplatzer Cardiac Plug device in pts with non-valvular atrial fibrillation (AF) who have a CI to warf therapy.
Methods: From august 2010 until december 2013 in total 67 pts with non-valvular AF underwent LAAC using the Amplatzer Cardiac Plug device. Pts received dual antiplatelet therapy for 6 months after the procedure, no concomitant warf therapy was given. Pts were followed up 6 weeks, 3 months and after one year clinically and by transesophageal echocardiography (TEE).
Results: At our hospital 67 pts (age 76.8±0.87 yrs, 42 m 25 f) underwent LAAC with the Amplatzer cardiac plug. The mean CHADS2 Score, CHA2DS2-VASc score and HAS-Bled score were 3.4±0.18, 4.7±0.19 and 3.8±0.1 respectively. History of bleeding (gastrointestinal n=19 (28.3%) and cerebral n=17 (25.3%) was the major reason for CI to warf therapy.
The procedure was successful in 64 (95.55%) of the pts (in 3 pts the LAA occluder could not be implanted due to a difficult anatomic situation of the LAA). Periprocedural complications were pericardial effusion in 1 pts (1.5%) due to LAA perforation, one pt with fail puncture of the aortic root, CO2 retention due to sedation for performing the TEE and one vascular complication with dissection of the AFC. The presence of mild peridevice leaks was observed in 13 (19.4%) pts. In three patients (4.6%) there were device thrombosis, but none of these patients with device thrombosis developed stroke. During the median follow-up of 454.1±36.8 days three pts (4.6%) suffered from a stroke and 8 pts (11.9%) died (2 cardiovascular deaths, 1 non-cardiac death (severe pneumonia), 2 deaths of unknown cause, one stroke, one carcinoma and one multi organ failure). But the latter patient who died of stroke did not receive LAAC, but was included in the intention to treat analysis.
Conclusion: LAAC might represent a good alternative in pts with a firm CI to anticoagulation, however severe complications can occur. These patients ineligible for warf therapy represent an high risk group with many comorbidities, and therefore longterm –follow up has still to be determined.

P4548 | BEDSIDE
Detection of atrial fibrillation in patients with ischemic stroke by continuous in-hospital cardiac telemetry

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Purpose: Atrial fibrillation (AF) is a common cause of ischemic stroke (IS). However, diagnosing AF can be challenging. So far there is no consensus supporting a certain strategy of heart rhythm monitoring in patients with IS. In-hospital monitoring is a clinical feasible, and to the patient a convenient modality. Therefore, we evaluated the proportion of new diagnosed AF (new AF) in patients with IS and determined the additional benefit of 48 hours continuous in-hospital cardiac telemetry (CICT).
Methods: Patients, admitted with ischemic stroke between August 2008 and January 2014, were enrolled in this study. All patients underwent ECG at admission and additionally patients without known AF, underwent 48 hours CICT. New AF was defined as AF lasting more than 30 seconds and was diagnosed by a cardiologist. The proportion of patients with new AF was determined from ECG at admission and 48 hours CICT.
Results: A total of 1117 patients had IS. Seventy-three patients (6.5%) were excluded because of insufficient CICT. Of the remaining 1044 patients (mean age, 74 years [SD, 12.9 years], 53% males, 79% first-ever stroke), 197 (19%) had known AF and 106 (10%) were diagnosed with new AF, of which 47 (44%) were diagnosed by 48 hours CICT. In general, patients with new AF were older (mean age, 81 years [SD, 10.2 years]) and had suffered severe strokes (mean Scandinavian Stroke Scale (SSS), 36 [SD, 17.2]), than patients in sinus rhythm (mean age, 71 years [SD, 12.9 years], mean SSS, 47 [SD, 13.3]).
Conclusions: Overall, 10% of patients with IS were diagnosed with new AF at admission. Forty-eight hours CICT almost doubles the detection rate of silent AF, and therefore could be a feasible clinical modality for the detection of AF among patients with ischemic stroke.

P4549 | BEDSIDE
Paroxysmal atrial fibrillation in young cryptogenic ischemic stroke: long-term ECG-Holter monitoring study

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Purpose: The cause of ischemic stroke remains often unclear (cryptogenic), especially in younger patients. Cardiac abnormities, particularly atrial fibrillation, represent very frequent known cause, thus undetected paroxysmal AF (PAF) is considered the possible cause in patients with cryptogenic ischemic stroke (CIS). Aim of our prospective study was assess the rates of PAF detected using electrocardiography (ECG) Holter monitoring in young CIS patients and whether prolongation of monitoring (up to 3 weeks) may increase the detection rates.
Methods: The study set consisted of patients ≤50 years with an acute IS enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). In all patients, the brain ischemia was confirmed on CT or MRI. CIS was defined according to the TOAST criteria without presence of any known stroke risk factors and without any ultrasonographic or angiographic signs of atherosclerosis, vasculitis and dissection. Admission ECG, cardiac markers including high sensitive Troponin T (hs TnT) and N-terminal pro-brain natriuretic peptide (NT-proBNP), markers of thrombophilia, CT/MR angiography and ultrasound of cervical and cerebral arteries, transesophageal echocardiography (TEE) and 24-hour ECG-Holter were performed in all patients. In case of negative 24-h ECG-Holter, 3-week Holter monitoring followed.
Results: In total, 526 patients were enrolled in the HISTORY study. Out of 80 enrolled patients ≤50 years, 71 (89%) were identified as CIS (39 males, mean age 38.2±8.5 years). All CIS patients had a normal admission ECG. Mean time from stroke onset to 24-h ECG-Holter was 5.1±2.7 days and to 3-week ECG-Holter 42.1±12.8 days. In total, PAF was detected in 6 (8.5%) patients (4 males, mean age 40.1±3.9 years); in two patients during 24-h ECG Holter and in next 4 patients during 3-week Holter monitoring. Mean time from start of 3-week monitoring to first detection of PAF was 11.5±3.4 days. Patent foramen ovale with evident right-left shunt was detected on TEE in all PAF patients and four (60%) of them had elevated admission hs TnT and NT-proNBP.
Conclusion: PAF was detected in 8.5% of young CIS patients using ECG-Holter monitoring. Prolongation of Holter monitoring may increase the detection rates of PAF. Supported by the IGA MH CR grants NT11046-6/2010, NT14288-3/2013 and by the RVO FNOL 00098892.

P4550 | BEDSIDE

Surface expression of P-selectin glycoprotein ligand-1 on CD14++CD16- monocyte in patients with cardiogenic cerebral infarction

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Aims: It is well known that monocytes in peripheral blood are heterogeneous. Monocytes are recruited to systemic circulation after cerebral infarction (CI), and play an important role in pathogenesis of CI through innate immune responses. CI is generally classified into three entities according to their causes; atherothrombotic, lacunar, and cardiogenic infarctions; however, it remains unclear whether monocyte subsets are related to each clinical entity.

Methods: This study consisted of 52 patients who came to our hospital within 12 hours after CI onset. The diagnosis of CI was performed by neurosurgeons, and patients were classified into three groups 1) atherothrombotic (AT; n=13), 2) lacunar (LA; n=17), and 3) cardioembolic infarction (CA; n=22), according to their comprehensive physical findings including MRI images. Peripheral blood sampling was performed on admission, and measured by flow cytometory. Three monocyte subsets (CD14++CD16+, CD14++CD16-, and CD14+CD16+), and surface expression of P-selectin glycoprotein ligand-1 (PSGL-1) on each subsets were measured.

Results: There were no significant differences in age and gender. Total monocyte counts were AT: 322±156, LA: 321±108, and CA: 339±130 cells/μl (p=0.87), and CD14++CD16- monocyte counts were AT: 283±128, LA: 281±100, and CA: 293±107 cells/μl (p=0.82), respectively. Similarly, no significant differences were observed in CD14++CD16+, and CD14+CD16+ monocyte counts (p=0.75, p=0.81). Surface expression of PSGL-1 on CD14++CD16- monocyte was significantly increased in CA group (AT: 89±67, LA: 94±58, and CA: 164±43 cells/μl, $p<0.05$), while no significant differences were found in surface expression of PSGL-1 on other subsets.

Conclusions: Surface expression of PSGL-1 on CD14++CD16- monocyte is preferentially increased in patients with cardioembolic infarction, suggesting that strong interaction between specific monocyte subset and platelets may be a key pathogenesis of cardioembolic infarction.

P4551 | BEDSIDE

Clinical characteristics and one-year outcomes of atrial fibrillation patients with versus without a previous stroke: From one-year follow-up of the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) is a common arrhythmic disorder, and leads to a substantial increase in mortality and morbidity, particularly from stroke events. The purpose of this study is to investigate clinical characteristics of AF patients with versus without a previous stroke.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Kyoto, Japan. Fushimi-ku is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. At present, we have enrolled 3,821 patients (1.3% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013. We divided the entire cohort into two groups, group of patients with a previous stroke (n=573, 19.3% of total) and others (n=2,393), and compared the clinical backgrounds and one-year outcomes between them.

Results: Patients with a previous stroke were older (77.2 yrs. vs. 73.1 yrs.; $P<0.01$), and more lightweight (body mass index 22.2 vs 23.2; $P<0.01$), and had higher mean CHADS2 score (3.79 vs. 1.64; $p<0.01$). Asymptomatic and chronic AF patients were more in patients with a previous stroke (62.7% vs. 47.9%; $p<0.01$, and 55.0% vs. 43.0%; $p<0.01$, respectively). Patients with a previous stroke experienced more episodes of major bleeding (5.6% vs. 1.2%; $p<0.01$), and received higher warfarin prescription (64.6% vs. 46.8%; $p<0.01$). During one-year follow-up, the incidence of stroke was higher in patients with a previous stroke (5.2% vs. 1.9%; $p<0.01$), but that of bleeding (3.3% vs. 4.5%; p=0.25) or hospitalization for heart failure (4.0% vs. 4.1%; P=1.0) was comparable. After adjustment for age, hypertension, diabetes mellitus, and heart failure, previous stroke was associated with a higher risk of stroke at 1 year (adjusted odds ratio 2.49, 95% confidence interval 1.54-4.00). All-cause death was more in patients with a previous stroke (13.3% vs. 4.1%; $p<0.01$). Among patients with previous stroke, those with oral anticoagulants have a tendency to experience less stroke and bleeding events than those without, but there was no significant difference (4.6% vs. 6.4%; p=0.43, and 3.0% vs. 3.9%; p=0.63, respectively).

Conclusions: AF patients with a previous stroke have higher risk profiles for stroke as well as bleeding. They received higher warfarin prescription, but showed higher incidence of stroke, and no significant increase in bleeding, perhaps due to under-treatment of oral anticoagulants in the real-world clinical practice.

P4552 | BEDSIDE

Impact of obstructive sleep apnoea on cardiac organ damage in patients with acute ischemic stroke

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Purpose: Obstructive sleep apnea (OSA) is indicated as an independent risk factor for hypertension and other cardiovascular disease frequently associated with stroke, but its relation with the presence of target organ damage at cardiac level in acute stroke patients is still poorly explored.

Methods: A total of 130 consecutive patients with acute ischemic stroke were enrolled. Patients underwent full multi-channel 24h polysomnography for evaluation of OSA, and echocardiography to evaluate left ventricle (LV) mass index (LV mass/BSA, LV mass/height), thickness of interventricular septum (IVS) and posterior wall (LVPW), LV ejection fraction, left atrium (LA) size.

Results: 61.9% (67) of patients, mostly males (67.1%) with acute stroke had OSA (ODI>10). Patients with acute stroke and OSA showed a significant increase ($p<0.05$) of LV mass index (LV mass/BSA, LV mass/height), IVS and LVPW thickness and a significant LA enlargement as compared to patients without OSA. LV ejection fraction was not significantly different in patients with stroke with and without OSA and was within normal limits.

Conclusions: Acute stroke patients with OSA had higher LV mass and LV mass index and showed LA enlargement as compared to patients without OSA. The present study confirms the high prevalence of OSA in stroke patients, supporting the pathogenetic link between these conditions. The finding of structural LV abnormalities in acute stroke patients with OSA supports the role of OSA as a risk factor for both cerebrovascular and cardiac damage, and is in line with the suggestion that OSA may contribute to a less favorable outcome in stroke patients.

TOPICS IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION

P4554 | BEDSIDE

Safety of intravenous adenosine infusion during emergency PCI for ST-elevation myocardial infarction: experience from a regional primary PCI centre

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Purpose: On 20 November 2013, the U.S. Food and Drug Administration (FDA) issued a safety announcement on the risk of myocardial infarction (MI) and death in patients receiving adenosine or regadenoson for stress testing. The warning was based on reports of 6 MIs and 27 deaths in the FDA Adverse Event Reporting System (FAERS) database and the medical literature between May 18th 1995 and April 10th 2013. The FDA recommended that "health care professionals should avoid using these drugs in patients with signs or symptoms of cardiovascular instability". Concurrently, we have undertaken a prospective cohort study of coronary microvascular physiology in STEMI patients in which intravenous (IV) adenosine was administered to induce systemic hyperaemia (NCT01717573). We report the haemodynamic effects and clinical experience with IV adenosine.

Methods: A prospective cohort study of near consecutive STEMI patients treated with primary or rescue PCI. At the end of the procedure, IV adenosine (140 mcg/kg/min) was administered using an ante-cubital vein. Patients' symptoms and changes in invasively measured haemodynamics were prospectively recorded. All patients were assessed for adverse cardiac events (MACE).

Results: 292 STEMI patients (mean age 59, 73% male) were prospectively included (11 March 2012 - 21 November 2012). Patients had evidence of cardiovascular instability at presentation (prior to adenosine): 11% had a systolic blood pressure (BP) <90 mmHg, 7% required cardioversion for ventricular fibrillation (VF) and 2% required intra-aortic balloon pump insertion (IABP) and/or inotropes. At the end of PCI, TIMI flow grades of 0/1, 2 or 3 were 1%, 5% and 94%, respectively. The mean (SD) aortic systolic BP was 120 (22) mmHg before and 106 (22) mmHg during the adenosine infusion, [95% CI for difference 10, 19] $p<0.0001$. The respective figures for aortic diastolic BP were 68 (13) mmHg vs. 61 (14) mmHg [95% CI for difference 5, 10] $p<0.0001$. During adenosine infusion 88% of patients reported symptoms including chest discomfort and dyspnoea, all which resolved after stopping the infusion. No adverse events occurred.

Subsequently, within the following 24 hours, a MACE event occurred in 3 (1%) patients. Reflecting the natural history of STEMI after emergency PCI, one patient experienced a stent thrombosis, one patient died from myocardial rupture, and one patient with severe left ventricular dysfunction experienced ventricular fibrillation in CCU.

Conclusion: Our experience supports the safety of IV adenosine for patients with unstable coronary artery disease in the cardiac catheter laboratory.

P4555 | BEDSIDE

Glycemic variability with continuous glucose monitoring is associated with infarct size in patients with ST-elevated myocardial infarction

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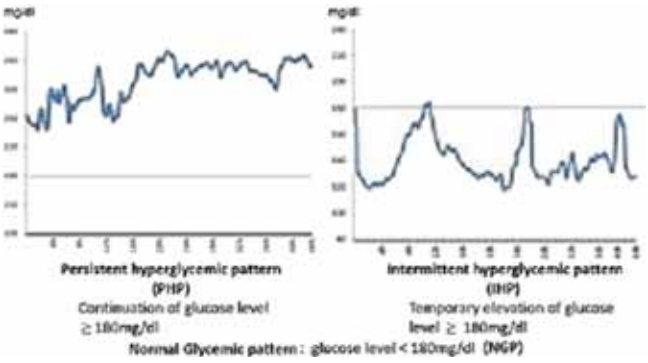
Background: It remains unclear whether acute glycemic variability is associated with an increased risk of cardiac events in ST-elevated myocardial infarction (STEMI) patient.
Therefore, this study aimed to evaluate the effects of enzymatic infarct size and cardiac events given to the variability of glucose levels by a continuous glucose monitoring system (CGMS).
Methods: This prospective study enrolled 51 patients (Mean age was 70±13 years, male was 73%) with STEMI. All patients were inserted CGMS on admission and were measured at least 48-hours. CGMS provide with glycemic excursion displayed at 5-minutes intervals, 576 points during 48 hours. Peak creatine kinase and cumulative lactate dehydrogenase (LDH) were examined during 48 hours. Enzymatic infarct size (LDHQ48) was assessed by the area under the LDH release curve.
Primary end point was the incidence of major adverse cardiac events (MACE) at 1 year, including cardiac death, MI, and heart failure. Secondary endpoint was LDHQ48.
Results: We found 3 patterns regarding to the change of glucose wave (figure). The three patterns were defined persistent hyperglycemic pattern (PHP), intermittent hyperglycemic pattern (IHP), normal glycemic pattern (NGP).
The elevated LDHQ48 was significantly lower in IHP,NGP patients (10788 ±8397U/L, 4542±2683U/L, and 5074±2594U/L in PHP, IHP, and NGP, respectively p=0.0001).
The MACE incidence rates were 100%, 29%, and 8% in PHP, IHP, and NGP, respectively, (p=0.002).



Glycemic pattern.

Conclusion: Glycemic variability is significantly associated with an increased risk of myocardial infarct size during 48 hours after coronary intervention. A significant relationship was also observed between cardiac events and the variability of hyperglycemic levels, included PHP, even IHP.

P4556 | BEDSIDE

The development of no-reflow after primary PTCA can be predicted by impaired brachial artery flow-mediated dilatation at admission

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No-reflow after primary PTCA is associated with a worse prognosis and has been shown to be an independent predictor of death, myocardial infarction (MI), and impaired left ventricular function in patients (pts) after acute MI. New devices for its prevention failed to improve prognosis in all MI pts but may be effective in high risk population. The aim of our study was to determine early predictors of no reflow by investigating endothelial function in patients (pts) with recent acute MI.
151 patients with ST elevation MI were investigated. All patients were admitted during the first 12 hours after symptoms onset and treated according to current guidelines. Endothelium - dependent flow-mediated brachial artery dilatation (FMD) was measured using high-resolution ultrasound at admission. Myocardial Blush Grade (MBG) was used for angiographic assessment of myocardial reperfusion.
Pts with recent ST elevation MI had initially reduced brachial artery FMD – 6.4±0.5%. 59.6% of pts with recent ST elevation MI had relatively preserved brachial artery FMD (>5%), and paradoxical reaction to FMD test (FMD≤0%) was detected in 16.6% of pts. The results of FMD test at the day of admission were not associated with any of the major risk factors or MI characteristics. Patients with preserved endothelial function significantly often had complete recovery of coronary microcirculation (MBG 3) after primary PTCA (83.7% of pts with FMD >5% vs 6.7% of pts with FMD≤5%, p=0.032). The highest rate of no reflow (MBG 0-1) was detected in pts with paradoxical reaction to FMD test (2.3% of pts with FMD >5% vs 17.7% of pts with FMD≤0%, p=0.012). Impaired reactive hyperemia (FMD≤5%) was associated with complicated index hospitalization (death, acute heart failure, left ventricular dilatation and dysfunction) and the worst hospital outcomes were seen in patients with FMD≤0%.
The development of no-reflow after primary PTCA may be predicted by impaired brachial artery flow-mediated dilatation at admission, suggesting the importance of endothelial function for its evolution.

P4557 | SPOTLIGHT

In-hospital mortality of patients presenting with suspected acute coronary syndrome with new or presumed new left bundle branch block compared to known left bundle branch block

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Introduction: In suspected ACS (sACS), new or presumed new LBBB (n/pnLBBB) is considered as acute STEMI equivalent. At our large academic medical center, we sought to compare the in-hospital mortality (IHM) of patients presenting with sACS and having n/pn LBBB verses known LBBB (kLBBB).
Methods: We reviewed records of all patients with suspected ACS who had LBBB on presentation between 1/12001 and 12/30/2010. Clinical characteristics, angiographic data and in-hospital outcomes were compared between those with n/pnLBBB and kLBBB.
Results: Out of 3908 patients with sACS, 127 (3.3%) had n/pnLBBB and 85 (2.2%) had kLBBB (see table). IHM (n/pnLBBB: 14.2% vs kLBBB: 10.6%, p=0.30) of LBBB with sACS is higher than the literature report of in-hospital STEMI mortality of about 4%. On multivariable logistic regression, the independent predictors of IHM were: cardiac arrest on presentation (OR: 5.4, 95% CI: 1.47-19.9, p=0.011) and left ventricular ejection fraction (OR: 0.950, 95% CI: 0.91-0.99, p=0.02). Acuity of LBBB, age, gender, risk factors, creatinine, emergent angiography and revascularization (whether emergent or later during index hospitalization) were not predictors of IHM.

Baseline data and clinical outcomes

	New or presumed new LBBB (N=127	Known LBBB (N=85)	p value
Clinical characteristics, coronary angiography and revascularization			
Age (yrs), mean±SD	70±12	67±15	0.17
Male gender, N (%)	48 (56.5%)	65 (51.2%)	0.27
History of coronary artery disease	39 (30.7%)	43 (50.6%)	0.003
Cardiac arrest on presentation	21 (16.5%)	9 (10.6%)	0.16
Cardiogenic shock on presentation	20 (15.7%)	6 (7.1%)	0.048
Left ventricular ejection fraction (%)	42±18	38±16	0.156
Emergent coronary angiogram	67 (52.8%)	37 (43.6%)	0.12
Emergent coronary revascularization	20 (15.7%)	22 (25.9%)	0.051
Total coronary revascularization	27 (21.2%)	26 (30.6%)	0.09
Clinical outcomes			
In-hospital mortaliy	18 (14.2%)	9 (10.6%)	0.30

Conclusion: In this study, IHM was high in patients with suspected ACS and LBBB, but comparable among n/pnLBBB and kLBBB. Our data should be considered when management decisions are made in suspected ACS patients with n/pnLBBB on presentation.

P4558 | BEDSIDE

Spontaneous reperfusion rate in patients with ST elevation myocardial infarction treated with a loading dose of prasugrel or clopidogrel

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Background: Prasugrel and clopidogrel have proven efficiency in ST-elevation myocardial infarction (STEMI) management.
Objective: The aim of this study was to compare spontaneous reperfusion rate in STEMI patients (pts) treated with a loading dose of prasugrel or clopidogrel.
Methods: We analyzed data from the "Observatoire Régional Breton sur l'Infarctus", a prospective registry of STEMI patients admitted within 24h of symptoms onset between May 2010 and July 2012. We retrospectively included patients with STEMI presenting within six hours of symptom onset and undergoing percutaneous coronary intervention (PCI). There were two groups of patients depending on the loading dose treatment (60mg of prasugrel versus 300mg or 600mg of clopidogrel). The endpoint was Thrombolysis In Myocardial Infarction (TIMI) flow grade in culprit artery prior to primary percutaneous coronary intervention (PPCI).
Results: We included 1125 pts: 696 received clopidogrel, 429 received prasugrel. Pts treated with prasugrel were younger (57,7±10 years vs 65±14, p=0,001). The sex ratio was 75,3% in the clopidogrel group and 86,2% in the prasugrel group (P<0,001).
There was no significant difference in pre-PPCI TIMI flow grade 3 in the two groups (18,4% in the prasugrel group versus 22,7%, p=0,39), and no significant difference in pre-PPCI TIMI flow grade 0 (59,7% in the prasugrel group versus 58,8%, p=0,25).
In the subgroup presenting with STEMI in the first three hours, similar rate of TIMI flow grade 3 was observed (18,4% in prasugrel group versus 23,2%, p=0,37), and similar rate of TIMI flow grade 0 (58,3 in prasugrel group versus 55,3%, p=0,4).

There was no significant difference in the two groups for pts with or without pre-hospital use of glycoprotein IIb/IIIa inhibitors.
Conclusion: In patients with STEMI presenting within six hours of symptom onset undergoing PCI, there were no more pre-PCI TIMI flow grade 3 in those who received prasugrel loading dose compared with clopidogrel, suggesting no better myocardial reperfusion.

P4559 | BEDSIDE
Effect of inhibitors of renin-angiotensin system on long-term clinical outcomes in ST-segment elevation acute myocardial infarction patients with preserved left ventricular ejection fraction

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Background: It has been known that the inhibitors of renin-anigotensin system (RAS) is effective on long-term survival after primary percutaneous coronary intervention (PCI) in ST-segment elevation acute myocardial infarction (STEMI) with depressed left ventricular ejection fraction (LVEF <40%). However, the benefit on clinical outcomes in STEMI with preserved LVEF (≥40%) has been not evaluated.
Methods: We investigated the 316 patients (pts) presented with STEMI with LVEF≥40%. We compared 2-year clinical outcomes of pts treated with (n=229) and without (n=87) RAS inhibitor at discharge. To adjust potential confounders, the statistical analysis was performed using the logistic regression model.
Results: There were no significant differences in baseline clinical characteristics except age (age was younger in the group with RAS inhibitor; mean±SD, 59.12±12.28 vs 62.72±12.69, p=0.024). There was no difference in the incidence of binary restenosis, Q-wave myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR), TLR-major cardiovascular event (MACE), and TVR-MACE between the two groups. However, the incidence of total mortality (6.0% vs. 12.0%, p=0.037) and cardiac death (6.0% vs 0.6%, p=0.010) was higher in the group without RAS inhibitor. In multivariate logistic regression analysis, the non-use of RAS inhibitor was a predictor for cardiac death (OR, 9.859; 95% CI, 1.047-92.834; p=0.045). In Kaplan-Meyer Curve, the incidence of cardiac death was higher in the non-use group of the RAS inhibitor (figure).

Figure. Kaplan Meyer Curve has shown that there was difference in incidences of cardiac death between use and non-use group of RAS inhibitor.

Conclusion: In our study, the inhibitor of RAS at discharge may be associated with lower cardiac death up to 2-year clinical outcomes following primary PCI in STEMI pts with preserved LVEF.

P4560 | BEDSIDE
"Reperfusion delay" involves new onset atrial fibrillation in ST elevated myocardial infarction: a retrospective clinical study in STEMI patients undergoing primary PCI

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Purpose: New Onset Atrial Fibrillation (NOAF) has low incidence in Acute Myocardial Infarction with ST elevation (STEMI), but was associated with a poor prognosis also in patients undergoing primary PCI. Total Ischemic Time and Door to balloon time (DTBT) are indicators of quality of care in STEMI management because the delay of coronary reperfusion is associated with worse outcomes. We aimed to evaluate a link among clinical, coronary intervention times and NOAF in a large STEMI population undergoing primary PCI.
Methods: We studied retrospectively 1456 consecutive STEMI patients admitted to our Heart Care for primary PCI from April 2006 to September 2012. We analyzed Total Ischemic Time and DTBT, angiography coronary culprit lesion, and TIMI grade flow after coronary intervention. Moreover we evaluated cardiovascular risk factors, laboratory markers, echocardiographic Left Ventricular Ejection Fraction. Regarding the outcomes we analyzed in-hospital and at one year mortality, incidence of reinfarction or new hospitalization at one year follow up. NOAF was identified as atrial fibrillation occurred for the first time during hospitalization (24-48hours).
Results: NOAF was observed in 100 patients with STEMI (7%; mean age 74.6±10.3 years; men 64%). The delay of coronary intervention resulted significantly longer (DTBT and total ischemic time) in NOAF group respect to patients with synusal rhythm (p=0,049). No differences were found in the two groups concerned the culprit lesion, t NOAF patients had a worse angiographic result after coronary intervention (TIMI grade flow <2, p=0.033). Moreover the NOAF group was older (p<0.001), presented more often hypertension (p=0.002), diabetes (p=0.03), kidney disease (p<0.001), lower LVEF (p<0. 001), previous AMI (p=0.018), cardiogenic shock on admission (p<0.001), higher level of BNP (p<0.001), fibrinogen (p<0.001) and troponine (p<0.001), in agreement previous data. In-hospital mortality was higher in NOAF patients and at one year follow up they had higher risk of reinfarction, new hospitalization for all causes (p=0.004) and mortality (p<0.001).
Conclusions: Reperfusion delay is associated with higher risk to develop NOAF in STEMI patients undergoing primary PCI. A timely reperfusion can prevent both atrial ischemia with pressure overload that trigger the arrhythmia, and inflammatory-remodelling myocardial response, involving adverse outcomes.

P4561 | BEDSIDE
Circadian variation of infarct size and neurohormonal activation in patients with acute myocardial infarction

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Aim: We aimed to investigate the circadian variation of infarct size and neurohormonal activation in patients with ST-segment elevation myocardial infarction (STEMI).
Methods: This study included 455 STEMI patients who underwent primary percutaneous coronary intervention within 6 h of symptom onset. Time of onset over a 24-hour period was divided into 6-h intervals. Plasma aldosterone concentration (PAC) and plasma renin activity were measured at admission. Infarct size was estimated by the peak creatinine kinase (CK) level.
Results: Infarct size and PAC showed significant circadian variation. Patients with onset between 0:00 and 05:59 showed the largest infarct size and highest PAC (Peak CK level: 3318 vs. 2198 vs. 2776 vs. 3066 IU/L, p=0.038; PAC: 13.0 vs. 8.4 vs. 7.8 vs. 9.9 ng/dL, p=0.005). Killip class also exhibited a clear circadian variation (1.8 vs. 1.5 vs. 1.4 vs. 1.8, p=0.004). When daytime was defined by the time interval of 06:00–17:59, patients with nighttime onset had significantly higher peak CK and PAC levels (peak CK level: 3182±3769 versus 2428±2699 IU/L, p=0.014; PAC: 11.4±14.3 versus 8.2±6.8 ng/dL, p=0.003). Multiple regression analysis adjusted for nighttime onset, time to admission, final TIMI flow grade, systolic blood pressure, and anterior infarct indicated that nighttime onset positively correlated with peak CK level and PAC.

Predictors for peak CK value

Explanatory variable	Regression coefficient (95% confidence interval)	P value
Nighttime onset	606.3 (20.7 to 1191.8)	0.042
Time to admission	9.2 (–186.4 to 204.8)	0.926
Final TIMI flow grade	–150.0 (–952.2 to 652.3)	0.713
SBP on admission	–23.4 (–32.5 to –14.4)	<0.001
Anterior infarct	1414.7 (837.5 to 1991.8)	<0.001

Conclusion: Infarct size and PAC level showed a significant circadian variation based on the time of onset. Time of onset between 0:00 and 5:59 hours was related to a larger infarct size and higher PAC level.

P4562 | BEDSIDE
Left main angioplasty in the context of non-st elevation acute myocardial infarction: impact in morbidity and in-hospital mortality

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Purpose: To determine the prevalence of Left Main (LM) disease in non-ST elevation acute myocardial infarction (NSTEMI) and to evaluate the impact of LM angioplasty on morbidity and in-hospital mortality.
Methods: We evaluated 3173 patients (P) submitted to coronary angiography for NSTEMI, and we studied all P that showed LM stenosis ≥50%. We considered two groups: Group 1 - P who underwent LM angioplasty and Group 2 – P who not performed LM angioplasty. We recorded age, gender, cardiovascular and non-cardiovascular co-morbidities, Killip-Kimball class (KK) at admission, coronary angiography, number of diseased vessels undergoing angioplasty and type of implanted stent. We evaluated left ventricular ejection fraction (EF) and the following in-hospital complications: re-infarction, stroke, major bleeding, sustained ventricular tachycardia and high grade atrioventricular block. We compared the in-hospital mortality and performed multivariate analysis to identify the predictors for performing LM angioplasty in NSTEMI.
Results: LM disease was found in 10.4% (331 P), of these 17.5% (58P) underwent LM angioplasty. Baseline characteristics of the 2 groups were very similar with no differences in cardiovascular and non-cardiovascular co-morbidities. Patients of group 1 had higher grades KK classes at admission (KK class ≥2:

37,9% vs 26,1%, p=0,015) and received more therapy with clopidogrel (100,0% vs 91,2%, p=0,021), glycoprotein IIb/IIIa inhibitors (24,1% vs 8,1%, p<0,001) and heparin (29,8% vs 14,1%, p=0,004). In addition to LM, P of group 1 had less right coronary artery (RCA) (58,9% vs 76,5%, p=0,007) and circumflex artery disease (62,5% vs 76,1%, p=0,035), however there weren't differences in total of vessels with disease. Group 1 performed more angioplasty of the left anterior descending artery (48,3% vs 17,1%, p=0,003), less RCA angioplasty (17,2% vs 51,4%, p<0,001) and implanted more coated stents (86,2% vs 28,6%, p<0,001). There were no differences in the EF neither in any of the complications considered between the 2 groups. In-hospital mortality was similar (Group 1: 1,7% vs Group 2: 4,8%, p=0,43). By multivariate analysis the most relevant predictor to performed LM angioplasty was the presence of isolated LM disease on coronary angiography [OR: 5.07 (2.05 to 12.5), p<0.001]

Conclusions: In NSTEMI, LM disease is presented in 10.4% patients. LM angioplasty in the context of acute NSTEMI appears to be safe and not associated with an increase in in-hospital mortality or complications. Isolated disease of LM appears to be the most important predictor for performing LM angioplasty.

P4563 | BEDSIDE
Transradial versus transfemoral intervention for acute myocardial infarction: bleeding complications and short term outcome - data of the Berlin Myocardial Infarction Registry

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Background: Transradial intervention is used more commonly in the last years and is recommended for treatment of MI patients (Hamon EuroInterventions Jan 2013; ESC 2012 STEMI guidelines). We analysed the situation in Berlin under daily circumstances.
Methods: The Berlin Myocardial Infarction Registry prospectively collects data on hospital treatment of MI patients. 4287 patients with primary PCI from 16 hospitals were included in the study (1.4.11-31.12.12). Bleeding complications were collected with GUSTO criteria.
Results: (see Table) 1785 patients were treated transradial (41.6%), 2502 transfemoral (58.4%).
Even after adjustment for significantly influential factors on hospital mortality the transfemoral approach showed an OR=1.59 (95%CI: 1.06-2.39) compared to transradial. Transfemoral intervention caused more moderate to severe bleeding complications after adjustment OR=1.89 (95%CI: 1.09-3.28).

Table 1. Differences between patients treated with transradial versus transfemoral intervention

	Transradial intervention	Transfemoral intervention	p
Age in yrs.	63.9	65.3	<0.001
Women in %	24.9	28.8	0.005
STEMI in %	53.2	50.7	0.098
Diabetes mellitus in %	24.9	30.3	<0.001
Renal failure in %	10.4	15.3	<0.001
CHF in %	8.0	15.6	<0.001
Previous MI in %	14.4	21.7	<0.001
Previous PCI in %	16.8	25.3	<0.001
Cardiogenic shock on admission in %	2.3	10.4	<0.001
IABP in %	1.2	5.3	<0.001
Hospital mortality in %	2.9	7.6	<0.001
Bleeding mild (Gusto) in %	2.0	3.2	
Bleeding moderate (Gusto) in %	0.8	1.7	<0.001
Bleeding severe (Gusto) in %	0.4	0.7	

Conclusions: Transradial intervention is used in 41.6% of patients. Bleeding occured significantly less often with the transradial approach even after adjustment. Our registry data show that hospital mortality is higher for MI patients after transfemoral intervention. A randomized clinical trial is warranted.

P4564 | BEDSIDE
Influence of smoking habit on the circadian rhythm of ST segment elevation myocardial infarction (STEMI). Findings from the ARIAM Registry

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Purpose: A circadian rhythm has been described in acute cardiovascular events with a more frequent time of presentation during morning hours. We analyze the effect of smoking habit on circadian rhythm of patients admitted with ST segment elevation myocardial infarction (STEMI).
Methods: The data were taken from the ARIAM-Andalucia registry, which involves 49 hospitals in Andalucia, Spain, from 2001 to 2012. It is a prospective observational multi-center cohort study that analyzes patients admitted with acute coronary syndromes. We classified patients with STEMI in 2 groups: active smokers (AS) or non-active smokers (NAS) which included past smokers and non-smokers, and we analyzed the time of onset of symptoms in a 24-hour clock divided into 4 groups [Group 1 (G1), 00:00 h.- 05:59 h.; Group 2 (G2), 06:00 h.-11:59 h.; Group 3 (G3), 12:00 h.-17:59 h.; and Group 4 (G4), 18:00 h.-23:59 h.] according to their smoking status.
Results: We included 25 633 patients with STEMI (mean age 63,41 + 12,92 years, 24% women). The most frequent group of presentation was Group 2 (G1: 19,7%; G2:31,0%; G3: 27,2% and G4: 22,0%; p<0,001), with a peak of symptoms onset between 10:00 h. and 10:59 h. (6,8%; p<0,001). Patients in G1 had more often diabetes, obesity, previous myocardial infarction (MI) and peripheral vascular disease. Patients in G2 were older, had less often dyslipidemia and obesity. Patients in G3 were more often males and patients in G4 had more often dyslipidemia. We found no statistical differences in gender, prevalence of diabetes, hypertension or previous stroke among the groups. Of all the study population, 9921 (39,7%) were AS. The hourly distribution of onset of symptoms was significantly different between AS (G1: 20,8%; G2: 28,3%; G3: 28,1%; G4: 22,8%) and NAS (G1: 19,0%; G2: 32,7%; G3: 26,7%; G4: 21,6%); p<0,001. In a logistic multivariate regression analysis including variables that showed a significant difference in time intervals such as age, dyslipidemia, obesity, peripheral vascular disease and smoking habit, we found that active smoking (AS) status decreased the probability of having an onset of symptoms in Group 2 interval (OR=0,84; 95% CI [0,79-0,90]; p<0,001).
Conclusions: Smoking habit modifies circadian rhythm in patients with ST segment elevation myocardial infarction (STEMI) with a less frequent time of presentation during morning hours.

P4565 | BEDSIDE
Index of microcirculatory resistance as an early predictive factor of LV remodeling after reperfused myocardial infarction

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Purpose: In the setting of successfully reperfused acute myocardial infarction (AMI) we hypothesized that thermodilution-derived index of microcirculatory resistance (IMR) measured after primary percutaneous coronary intervention (PCI), may be useful to predict LV remodeling 6 months after treatment.
Methods: We prospectively enrolled 62 patients (age 52±9 years; 86% male) with anterior STEMI. All patients were successfully treated by PCI with establishment of Thrombolysis In Myocardial Infarction (TIMI) 3 flow after PCI. The thermodilution-derived index of microcirculatory resistance (IMR) was thereafter measured by using the pressure-temperature sensor-tipped coronary wire at the left anterior descending artery (LAD). Angiographic parameters such as TIMI flow and blush grade were also recorded. Baseline comprehensive cardiovascular magnetic resonance (CMR) was performed before discharge and at 6 months follow-up. Comprehensive CMR included cine, T2-weighted, and late gadolinium enhancement (LGE) imaging. Infarct size (IS) and microvascular obstruction (MVO) were correlated to IMR measurements. LV remodelling was defined as a >20% increase of LV volume at 6 months.
Results: LV remodelling was observed in 35.4% of the patients (22/62). TIMI flow and blush grade after PCI was not different between patients with and without LV remodeling (3 for TIMI flow and 2 for Blush grade respectively, p=0.952). IMR level markedly differed between patients with and without LV remodelig (73,95 vs. 27,23 p=0,0293). After multivariate analysis IMR>40 was the strongest angiographic parameter to predict LV remodeling (OR 15 (1,030-218,4), p=0,03). Regarding CMR, patients with LV remodeling had lower LVEF (43% vs. 48%; p=0.01), larger IS (51 mg vs 32 mg; p=0.002) and greater MVO extent (4.5seg vs. 2seg; p=0.03) when compared to patients with no LV remodeling.
Conclusion: IMR assessed by coronary angiogram after PCI is a strong predictive factor of LV remodeling 6 months after succesfull reperfused AMI.

TOPICS IN STEMI

P4567 | BEDSIDE
Easily available predictors of myocardial infarction mass in ST-elevation myocardial infarction, validated by cardiac magnetic resonance imaging

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Introduction: The gold standard for assessing myocardial infarction mass, which carries a high prognostic value, is the magnetic resonance imaging (MRI), a time-consuming and not always available technique. We aimed to determine easily available predictors of myocardial infarction mass in ST-elevation myocardial infarction (STEMI).
Methods: We prospectively recruited STEMI patients that underwent primary angioplasty in the first 12 hours of myocardial infarction (MI) onset, with no previous MI or major comorbidities, and with a CPK peak >1000U/L. Clinical data, Killip class, laboratory tests and angiographic and procedural data were assessed. A

MRI and a transthoracic echocardiogram were performed in all, between the 2nd and 4th days of MI. Left ventricular ejection fraction (LVEF), infarction mass and left ventricle mass were calculated by MRI and the relative infarction mass (RIM) was obtained by dividing the last two parameters. The global longitudinal strain (GLS) was obtained by the 2D semiautomatic method (average of all segments regional strain). We assessed the association between categorical variables and the RIM by the t-Student test, and the correlation between continuous variables and the RIM by Pearson correlation. The independent predictors of RIM were determined by linear regression.
Results: In the 43 patients included (52±10 years, 90% male) the myocardial infarction mass was 44.0±27.7g and the RIM was 26.6±19.0%. There was no association between the RIM and the cardiovascular risk factors (16% diabetes, 54% hypertension, 49% dyslipidemia, 65% smokers), Killip class (6% II-III), multivessel disease (49%), culprit coronary segment (49% proximal) or angiographic result (100% final TIMI 3). The culprit right coronary artery was associated with lower RIM (18±8% vs 29±16%, p=0.036). The RIM was correlated with the CPK peak (3103±2464U/L, r 0.48, p=0.001), troponin I peak (100±50ng/mL, r 0.37, p=0.036), brain natriuretic peptide level (184±141 ng/L, r 0.44, p=0.030), LVEF (50.9±7.4%, r -0.65, p<0.001) and GLS (-14.5±4.0%, r 0.49, p=0.002), but not with time to angioplasty (366±306min). The independent predictors of RIM were the LVEF (β -0.94; 95%CI -1.55, -0.33; p=0.004) and the GLS (β 1.10; 95%CI -0.03, 2.22; p=0.045). This model (88.8 -0.94xLVEF + 1.10xGLS) had good accuracy for predicting the RIM: r 0.64, ANOVA p<0.001.
Conclusion: In addition to LVEF, the GLS is a new independent predictor of RIM in STEMI. They are both more available and faster tools than CMR, and together have good accuracy for predicting the RIM in the acute fase of STEMI.

P4568 | BEDSIDE
Long-term predictors of death and incident myocardial infarction in cardiology patients assessed for coronary artery disease

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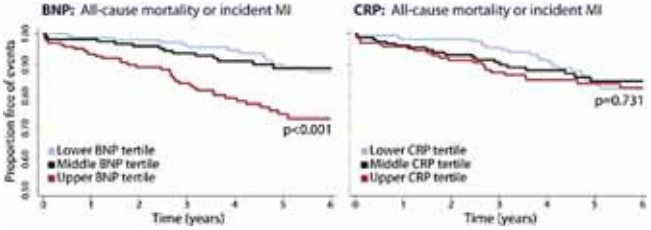
Purpose: Simple clinical markers of long-term adverse outcome are poorly described in cardiology patients with extensive risk factor modification. We sought to investigate the use of B-type natriuretic peptide (BNP), high-sensitivity C-reactive protein (CRP) and conventional risk factors during a five-year period following diagnostic coronary angiography.
Methods: The ARM-CAD Study is a prospective, multi-centre, observational cohort of patients recruited prior to elective angiography. 517 out of 539 participants (96%) were successfully followed-up. Cox regression models included all baseline conventional risk factors, left-ventricular systolic dysfunction (LVSD) and angiographic coronary disease.
Results: At baseline, mean age was 65, 67% were male and 18% had LVSD. Angiography identified ≥50% stenosis in 61% of the cohort. Patients were well treated with appropriate anti-hypertensive (80%), lipid-lowering (63%) and antiplatelet therapy (74%), with 28% undergoing percutaneous intervention and 17% coronary artery bypass grafting. Only three variables were independently associated with the primary outcome of all-cause mortality or incident myocardial infarction (MI) over a mean follow-up of 4.3 (SD 1.9) years: BNP (adjusted hazard ratio [HR] 2.22 comparing BNP above and below 100pg/mL, 95% CI 1.22-4.10, p=0.01), age (HR 1.96 per 10 years, 95% CI 1.38-2.78, p<0.01) and prior MI (HR 1.84, 95% CI 1.01-3.35, p=0.05). CRP and other conventional risk factors were not associated with adverse outcomes.



Kaplan Meier analysis for BNP and CRP

Conclusion: BNP is a strong and independent predictor of death or MI, irrespective of LVSD, risk factor modification and invasive intervention. Even in contemporary, well-managed cardiology patients, a BNP over 100pg/mL should highlight those requiring more aggressive management.

P4569 | BEDSIDE
ST-segment elevation myocardial infarction: which is the best way to identify low-risk patients?

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Purpose: Despite the excellent results of reperfusion therapies for ST-segment elevation myocardial infarction (STEMI), there still is a considerable range of event rate among STEMI patients (P). Identification of the low-risk subset of P is an attractive way to reduce hospitalization and costs. Several scores have been introduced as tools for risk stratification, such as TIMI, GRACE, Zwolle and PAMI scores. We aim to compare these scores for their accuracy to identify P at a lower risk for MACE at 30 days after STEMI.
Methods: The study included P admitted to our CCU for STEMI who underwent primary percutaneous coronary intervention, along 3 years. P that died until the 3rd day were excluded. For each score, P were classified as low risk vs medium/high risk, according pre-established cutoffs: TIMI≤2, Grace<120, PAMI≤2 and Zwolle≤3. Follow-up (FU) regarding MACE at 30 days after event was performed.
Results: From a population of 406 P with STEMI, we included 266 P: 64.6±13.9years-old, 72.9% male, 19.9% KK class>1, and 42% with an anterior STEMI. At 30 days of FU: the percentage of MACE was 9.0% and the mortality rate was 4.1%.
Zwolle score classified a higher percentage of P as low risk (66.9%), compared with PAMI (39.8%), TIMI (27.8%) or Grace (23.3%) scores. Whatever the score we chose, the prevalence of MACE at 30 days was significantly lower in the low risk group: Zwolle (5.1% vs 17.0%, p=0.001), PAMI (2.8% vs 13.1%, p=0.004), TIMI (1.4% vs 12.0%, p=0.007) and Grace (1.6% vs 11.3%, p=0.020).
When comparing the scores on their capacity to correctly classify P with lower event rate as low-risk P, we found that Zwolle had the best performance (AU 0.663, p=0.008), followed by PAMI (AU 0.651, p=0.015) and TIMI (AU 0.631, p=0.035). GRACE score proved to be a worse predictor of low risk (p=0.09).
Conclusions: In this population, Zwolle, PAMI and TIMI scores showed a good capacity to identify STEMI-P with a lower risk of short-term events. Zwolle score sticks out because classifies a higher percentage of P as low risk, still retaining its discriminatory capacity. The application of these scores in clinical practice allows a more accurate identification of P in which an early discharge is safe.

P4570 | BEDSIDE
Serum albumin levels on admission are associated with angiographic no-reflow after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction

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Background: Low serum albumin (SA) levels are associated with increased cardiovascular mortality. We investigated whether baseline SA levels are associated with no-reflow following primary percutaneous coronary intervention (pPCI).
Methods: A total of 536 patients (aged 60±13 years; 74% men) who underwent pPCI were enrolled. The patients were divided into 2 groups: no-reflow and normal-reflow. No-reflow was defined as Thrombolysis In Myocardial Infarction ≤2 flow.
Results: Admission SA levels were significantly lower in the no-reflow compared with the normal-reflow group (3.55±0.44 vs 4.01±0.32 mg/dl, P<0.001). Also, high-sensitivity C-reactive protein (hsCRP), creatinine, creatine kinase MB isoenzyme, troponin-T were significantly higher while hemoglobin, left ventricular ejection fraction (LVEF) were significantly lower in the no-reflow group. In multivariate analysis, SA level remained an independent predictor of angiographic no-reflow (OR 0.114, 95% CI 0.032-0.405, P=0.001) together with LVEF, hsCRP and baseline culprit artery patency.
Conclusions: Admission SA level was an independent predictor of no-reflow after pPCI.

P4571 | BEDSIDE
The volume of percutaneous coronary intervention procedures did not associate with in-hospital mortality for ST-segment elevation myocardial infarction in our metropolitan area

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Background: Performance of percutaneour coronary intervention (PCI) should be restricted to high-volume PCI hospitals. However, there are many low-volume PCI hospitals in our city. A large number of PCI hospitals may contribute to the shortening of door-to-balloon time and improvement of prognosis in our city.
Methods: We analyzed the therapeutic managements and in-hospital mortality of

1975 patients with STEMI from our city CCU network registered cohort database in 2011. All 67 hospitals participating in our city CCU network can perform PCI within 60 minutes from arrival at hospital. All hospitals were divided into 2 groups (562 patients, 38 hospitals; <300 PCI procedures per year and 1413 patients, 29 hospitals; >300 PCI procedures per year) based on their annual all PCI volume.
Results: High-volume centers had shorter median door-to-balloon time than low-volume centers [51 (IQR 30-83) vs 62 (IQR 40-98) minutes, p<0.001]. Killip 1, 2, 3, and 4 were 75.9%, 10.7%, 6.7%, and 6.7% for high-volume centers, vs 79.1%, 9.8%, 4.7%, and 6.4% for low-volume centers, respectively (p=0.150). The max CKs were similar between 2 groups (2702±2891 IU/L vs 2738±3053 IU/L, p=0.074). Coronary artery bypass grafting (CABG) in high volume centers were performed more frequently than those in low-volume centers (5.3% vs 2.4%, p=0.006). The usage rate of drug eluting stent were similar (31.7% vs 35.4%, p=0.138), and aspiration catheter in high-volume centers were used less frequently in low-volume centers (67.9% vs 78.0%, p<0.001). There was no significant difference in in-hospital mortality between 2 groups (7.1% vs 7.1% p=1.000)
Conclusions: In our metropolitan area, though high-volume PCI centers have shorter door-to-balloon time and performed CABG more actively, in-hospital mortality was similar between 2 groups. Primary PCI is mandatory in patients with STEMI. Therefore, the regional balance of PCI hospitals rather than concentrations of PCI hospitals should be considered as therapeutic strategy for STEMI in highly-populated regions.

P4572 | BEDSIDE
Effect of ischemic postconditioning on myocardial strain measured by two-dimensional speckle tracking in primary PCI-treated STEMI patients

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Purpose: Effect of ischemic postconditioning (IPost) on reperfusion injury has been evaluated both in experimental and clinical trials in patients with acute ST elevation myocardial infarction (STEMI). We have recently reported no significant effect of IPost on infarct size measured after 4 months in the randomized POSTEMI trial. The aim of this study was to study the effect of IPost on reperfusion injury and early myocardial recovery measured by myocardial strain.
Methods: Patients with first-time STEMI, symptom duration <6 h, TIMI flow 0-1 in the infarct related artery (IRA) and successful opening (TIMI 2-3) were included. Patients were randomized to either IPost or control and treated by primary PCI. IPost was performed by 4 cycles of 1 min balloon occlusion of IRA, starting 1 min after opening and separated by 1 min reperfusion intervals Global longitudinal peak systolic strain (εSYS, peak negative strain in systole) and peak strain (εPEAK, peak negative strain in diastole) were measured by two-dimensional speckle tracking echocardiography at a median of 2.4 (range 1-5) days after PCI. Post-systolic index (PSI) as a measure of postsystolic shortening, was calculated manually, PSI = (εPEAK - εSYS)/ εPEAK x 100.
Results: A total of 100 patients, median age 61 (range 38 – 87) years, 85% males and 56% with anterior wall infarction were included in the strain analysis, 45 in the IPost and 55 in the control group. Peak systolic strain was reduced to – 13.1 (IQR -16.3, - 11.2). Postsystolic shortening was present in 98 out of 100 patients. No significant between-group differences were found in myocardial strain or post-systolic shortening (measured as εSYS, εPEAK, or PSI) in the IPost group compared to control.

Relationship between myocardial strain measurements and IPost

Strain measurements	IPost group (n=45)	Control group (n=55)	p-value
Peak-systolic strain (ε_{SYS})	–12.9 (–16.5; –11.0)	–13.1 (–16.0; –11.3)	0.80
Peak-strain (ε_{PEAK})	–15.1 (–18.0; –12.8)	–15.2 (–17.0; –13.5)	0.86
Post-systolic index (PSI)	9.1 (5.8; 14.9)	10.0 (4.7; 18.5)	0.83

Data are median values (25 and 75 percentiles).

Conclusion: Ischemic postconditioning did not influence early myocardial recovery, measured as peak systolic strain or postsystolic shortening.

P4573 | BEDSIDE
Influence of the infarct-related artery in delay, treatment and prognosis in a contemporaneous real life population submitted to coronary angioplasty: data from a national registry

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Purpose: Patients with acute myocardial infarction involving the left anterior descendent (LAD) artery are more easily identifiable due to the typical EKG changes and the same is true for right coronary artery (RCA). Myocardial infarctions related to left circumflex (LCx) have usually atypical presentations that can possibly delay diagnosis. Our objective was to analyse, in a population included on a national registry, if diagnosis, treatment and short-term prognosis is different according to the culprit artery.
Methods: Patients admitted with a ST-segment elevation acute myocardial infarction and submitted to coronary angiography. We evaluated demographic and baseline clinical characteristics and treatment. Patients were divided in three groups according to the culprit artery. The study objective was the occurrence of in-hospital mortality. Logistic regression analysis was performed to identify mortality predictors.
Results: From 8.186 patients included in our national acute coronary syndromes registry, 42.2% presented with a ST-segment elevation and from these, 93.4% were submitted to coronary angiography. Patients with left main or bypass graft stenosis responsible for the infarction were excluded due to the low numbers of patients. The remaining 2.703 patients with a definite culprit artery identified were included in the study. In this population, LAD was the culprit in 49.0%, LCx in 12.5% and RCA in 38.5%. Patients with LCx culprit were younger and more often smokers, with no other differences. Heart rate and blood pressure on admission was lower in patients with RCA culprit, where it was also less frequent a Killip class >1 on admission. This group received less often beta-blockers and renin-angiotensin-aldosterone antagonists. Angioplasty was less often used in the LCx group. Symptoms-balloon time was higher for LAD group (260 minutes), followed by LCx (245 minutes) and RCA (240 minutes) (p=0.041). Hospital mortality was 4.4%, similar between groups (5.3%, 3.3% e 3.7%, p=0.103). In multivariate analysis, LCx as a culprit was not a predictor of mortality (OR 0.44, 95% CI 0.17 – 1.13, p=0.089) and RCA showed a lower risk of mortality (OR 0.46, 95% CI 0.26 – 0.85, p=0.012) compared to LAD.
Conclusions: The infarct-related artery has no impact in time-delay or treatment. LCx was associated with lower use of angioplasty and RCA with lower use of drugs associated with prognostic improvement. Compared to LAD, patients with RCA culprit have a 54% lower risk of in-hospital mortality. No difference was found for LCx.

P4574 | BEDSIDE
Myocardial infarction with ST-segment elevation and renal impairment: which equation serves best?

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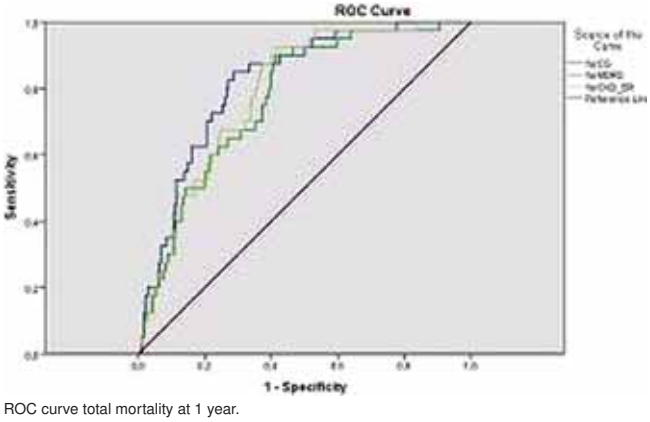
Purpose: Chronic Kidney Disease (CKD) and acute kidney lesion are a frequent morbidity in patients admitted for ST-segment elevation myocardial infarction (STEMI) and are associated with worse outcomes. Several equations to correctly identify patients with CKD through glomerular filtration rate (GFR) exist, but it is still not consensual which one is the most appropriate in the setting of STEMI. We aimed to compare which of the 3 equations - Cockcroft-Gault [CG]; Modification of Diet in Renal Disease [MDRD] and Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] – is more effective in predicting worse outcomes at 1-year follow up.
Methods: Prospective study of 327 consecutive patients [age 63.07±13.90; 73.0% men; 23.3% diabetics; 57.8% hypertensive] admitted to our, tertiary hospital, intensive care unit for STEMI between October 2009 and October 2012. GFR estimates from CG, MDRD and CKD-EPI were compared in terms of mortality risk prediction and of a composite primary endpoint (re-infarction, stroke and mortality) at 1-year follow up.
Results: Prevalence of GFR <60 ml/min/1.73m^2 was 36.3% using CG, 44.2% with MDRD and 39.8% with CKD-EPI. All analyzed equations showed good discriminatory power in predicting 1-year composite primary endpoint with CG proving to be the best formula by ROC curve analysis [AUC (CG): 0.731 vs AUC (MDRD): 0.700 vs AUC (CKD-EPI): 0.716]. All 3 equations also proved value in predicting total mortality at 1-year follow-up with CG showing the best results [AUC (CG): 0.819 vs AUC (MDRD): 0.769 vs AUC (CKD-EPI): 0.789].



ROC curve total mortality at 1 year.

Conclusions: In our population all equations were good in predicting adverse outcomes at 1-year follow up. The CG equation should be the preferred one in the setting of STEMI as it is significantly more accurate than MDRD and CKD-EPI.

P4575 | BEDSIDE

Low serum albumin as a strong predictor of adverse outcomes in ST-elevation myocardial infarction (STEMI) patients undergoing primary PCI

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Purpose: Serum Albumin is a common routine indicator of nutritional status and previous clinical studies demonstrated that hypoalbuminemia is associated with a poor prognosis in chronic cardiovascular disease, end-stage renal disease, heart failure and stroke. We aimed to investigate the prognostic value of serum albumin in patients with acute ST-segment Elevation Myocardial Infarction (STEMI) treated by a primary Percutaneous Coronary Intervention (p-PCI).
Methods: We retrospectively evaluated clinical and laboratory data of 1071 patients (male: 74%; mean age: 66.3±12.5 years) admitted to our Heart Care for STEMI. Serum albumin levels were determined in all patients at entrance. Myocardial injury was assessed by peak Troponin I (TnI) levels. Brain Natriuretic Peptide (BNP) and Left Ventricular Ejection Fraction (LVEF) were used to describe myocardial dysfunction. A 25±19 months clinical follow-up was performed, and MACEs (cardiac death, re-hospitalization for acute coronary syndrome and elective revascularization for angina) were reported.
Results: A low serum albumin (LSA) levels (serum albumin <3.5 g/dL) at admission were observed in 385 patients (34%). LSA patients were significantly in older than control group ($p<0.0001$). STEMI patients with LSA had higher baseline BNP ($p<0.0001$), peak BNP ($p<0.0001$), and had a lower Left Ventricular Ejection Fraction (p=0.001) at echocardiography imaging. No significant correlations were found between serum albumin and Troponin I levels. Regarding metabolic status, LSA patients showed lower levels of cholesterol ($p<0.0001$), LDL ($p<0.0001$) triglycerides (p=0.001), creatinine ($p<0.0001$), and T3 serum ($p<0.0001$). Moreover, low levels of haemoglobin ($p<0.0001$), and hematocrit ($p<0.0001$) and high levels of C-Reactive Protein ($p<0.0001$)and fibrinogen ($p<0.0001$)were observed in LSA group. At middle-term follow-up we observed a significant increase in all-cause mortality (Log-Rank 6.9; p=0.009) and MACEs (Log-Rank 3.9; p=0.04) in patients with hypoalbuminemia.
Conclusions: Hypoalbuminemia in acute phase of STEMI results as a strong independent predictor both for middle-term mortality and MACE in patients undergoing p-PCI. Moreover, patients with LSA are associated with greater degree of systolic myocardial dysfunction and systemic inflammation, and lower degree of metabolic and nutritional status.

P4576 | BEDSIDE

Pre- and in-hospital healthcare resource use in survivors of acute coronary syndromes in the EPICOR registry

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Purpose: To provide insight into real-world healthcare resource use during acute management of acute coronary syndromes (ACS) using data from EPICOR (NCT01171404).
Methods: EPICOR, a prospective, multinational, observational study, enrolled 10568 consecutive survivors of an ACS from 555 hospitals in 20 countries in Europe and Latin America (09/2010-03/2011). Resource use was evaluated in 4 pt groups: ST-segment elevation myocardial infarction (STEMI) vs non-ST-segment elevation (NSTE)-ACS, + or -prior history of cardiovascular disease (+CVD and -CVD).
Results: +CVD pts were older than -CVD pts (Table). More STEMI than NSTE-ACS pts underwent first ECG in the pre-hospital setting (45% vs 36%) and received pre-hospital antithrombotic medication (STEMI, 25% +CVD, 27% -CVD; NSTE-ACS, 14% +CVD, 16% -CVD). +CVD pts were less likely than -CVD pts to be catheterized. More STEMI pts had PCI and stenting, but more NSTE-ACS pts underwent CABG. Median length of hospital stay was similar in all groups. Compared with STEMI pts, NSTE-ACS pts were more likely to receive single- and less likely to receive triple-antiplatelet therapy. Use of any thrombolytic, antiplatelet or anticoagulant was slightly lower in +CVD than -CVD pts.
Conclusions: PCI was more frequent in STEMI, and CABG more frequent in NSTE-ACS pts. Unexpectedly, resource use tended to be slightly higher in –CVD than +CVD pts.

Table 1. Patient age and in-hospital resource use in EPICOR

	STEMI (n=4899)		NSTE-ACS (n=5576)	
	+CVD (n=1042)	–CVD (n=3857)	+CVD (n=2672)	–CVD (n=2904)
Age, mean (SD), years	64.6 (11.8)	58.0 (11.8)	67.3 (11.3)	60.6 (11.8)
First ECG: pre-hosp/in-hosp, %	44.7/53.0	44.5/53.6	36.4/60.6	36.4/60.9
Any cardiac catheterization, %	84.3	86.5	73.1	82.8
Any PCI/PCI + ≥1 stent, %	74.0/67.0	78.0/75.8	48.1/44.2	61.2/59.5
≥1 BMS/≥1 DES	43.8/25.4	48.5/30.5	21.8/25.0	31.0/31.1
CABG, %	1.0	1.2	3.4	3.9
Length of hospital stay, median (IQR), days	7 (5–9)	6 (5–9)	6 (5–10)	6 (4–8)
≥1 thrombolytic, %	14.5	15.8	0.3	0.6
Single/dual/triple antiplatelet therapy	7.9/68.9/22.2	4.2/70.9/24.5	14.7/77.5/6.5	8.6/80.4/10.4
≥1 anticoagulant, %	76.8	77.3	77.4	79.5

P4577 | BEDSIDE

Using landiolol before primary percutaneous coronary intervention attenuates myocardial reperfusion injury in patients with ST-segment elevation acute myocardial infarction

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Introduction: Landiolol is the beta-1 selective receptor blocker and its half-life elimination is 4 minutes. The safety and efficacy of intravenous landiolol started before coronary reperfusion in patients with ST-segment elevation acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) remains unclear. We assessed the hypothesis that early use of landiolol reduces myocardial injury without increasing adverse events for STEMI patients performed pPCI.
Methods: 161 consecutive patients with STEMI performed pPCI were recruited. Patients with heart rate<50, Killip class≧2, old myocardial infarction and 2 or 3 degree of atrio-ventricular block on admission were excluded. Thus 90 patients were enrolled. 60 patients were non-landiolol group with conventional treatment admitted from October 2010 to September 2012. 30 patients were landiolol group admitted from October 2012 to September 2013. Immediately after the admission, landiolol was started intravenously with 3 μg/kg/min and stopped within 12 hours after pPCI when oral beta-blockers were administered. ST-segment resolution (STR) was defined as more than 70% resolution of sum of ST-segment elevation at the J point between emergency room and when finished pPCI.
Result: Age, sex, coronary risk factors, medications, systoric blood pressure (154±31 vs 148±27mmHg) and heart rate on admission (84±18 vs 77±16/min), culprit lesion, SYNTAX score, reperfusion time and peak creatine kinase did not differ between landiolol group and non-landiolol group (all NS). The number of heart rate<50, shock and tachyarrhythmia within 12 hours after the admission did not differ between the two groups (all NS). Although, at the time of finishing pPCI, systric blood pressure did not differ between the two groups (115±23 vs 124±24mmHg, p=0.08), heart rate was lower (65±10 vs 77±14/min, $p<0.01$) and the rate of STR was higher (67 vs 42%, p=0.025) in landiolol group. C-reactive protein level on the second day of admission was lower (4.3±4.3 vs7.0±5.3, p=0.02) in landiolol group. Multivariate analysis showed that landiolol use was an independent predictor of STR (OR2.93, p=0.043).
Conclusion: In low risk patients with STEMI, using landiolol during pPCI may attenuate inflammatory response and myocardial reperfusion injury without increasing adverse events.

P4578 | BEDSIDE

Fragmented QRS complexes after recanalization strongly reflects impaired myocardial reperfusion in patients with first anterior STEMI

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Background and objectives: In patients with ST-segment elevation myocardial infarction (STEMI), it is still unclear whether the presence of fragmented QRS complexes (fQRS) after reperfusion therapy reflects the degree of microvascular reperfusion. The aim of this study was to evaluate the relationship between fQRS and myocardial reperfusion after recanalization in patients with anterior STEMI.
Methods and results: 90 consecutive patients with first anterior STEMI who underwent successful (TIMI-3 flow) primary percutaneous coronary intervention (PCI) within 6 hours after the onset were enrolled in this study, and divided into two groups according to the presence (group-A, n=48) or absence (group-B, n=42) of fQRS 1 hour after PCI. In group-B, ST resolution (STR) indicated by reduction of ≥50% in sum of ST segment elevation 1 hour after PCI was more often observed than in group-A (71.4% vs 33.3%). Coronary flow velocity estimated by both TIMI frame count and quantitative coronary angiogram immediately after recanalization was higher in group-B (204.6±44.1 vs 167.9±37.7mm/sec., $p<0.0001$). The positive predictive value of fQRS for impaired myocardial reperfusion (IMR) defined as myocardial blush grade of 0 or 1 after PCI was 79.2%, with a sensitivity of 84.4%, specificity of 77.8%, and negative predictive value of 83.3%. 46 patients had STR and 44 patients did not. Among the patients with STR, the negative predictive value of fQRS after PCI for IMR was 90.0%. On the other hand, among those without STR, the positive predictive value was 90.6%. Multivariate analysis showed that fQRS after PCI was a potent independent factor associated with IMR (odds ratio 12.952, p=0.0032).
Conclusions: These findings suggest that fQRS after PCI strongly reflects IMR in patients with recanalized anterior STEMI. It is possible that the predictive value of fQRS after PCI for myocardial reperfusion can be enhanced further in combination with STR.

MECHANISTIC STUDIES

P4580 | BEDSIDE
Endogenous carbon monoxide protects against cardiac injury by collateral circulation development with acute myocardial infarction

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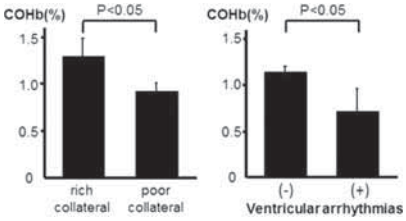
Background: Carbon monoxide (CO) is endogenously produced during the processes of heme catabolism under various pathophysiological conditions, and exerts anti-inflammatory and anti-oxidative effects. The aim of this study was to clarify the role of CO in patients with acute myocardial infarction (AMI).
Methods: To assess that, 55 patients with AMI of the first onset who received primary coronary angiography within 6 hours after the onset, 25 smokers and 30 nonsmokers, underwent blood sampling for calculation of COHb at emergency room. Rentrop grade of the collateral flow was evaluated by coronary angiography. Smokers were excluded from the subsequent analysis, since smoking affected CO levels. Rich collateral was defined as Rentrop grade 2. Poor collateral was defined as Rentrop grades 0 and 1. We compared COHb levels between nonsmoker AMI patients with and without ischemia/reperfusion-induced ventricular tachycardia (VT) or ventricular fibrillation (VF).
Results: As we expected, COHb was increased in smoker patients compared to nonsmoker patients (2.11±1.22% vs. 1.01±0.45%, $P<0.01$). Among nonsmoker AMI patients, COHb was higher in rich collateral compared to poor collateral (1.30±0.50% vs. 0.92±0.40%, $P<0.05$). Furthermore, among nonsmoker AMI patients, COHb was lower in patients with ischemia/reperfusion-induced VT and/or VF than in those without VT and/or VF (0.70±0.67% vs. 1.12±0.28%, $P<0.05$).



Comparisons of COHb.

Conclusions: These results may suggest the possibility that endogenous CO at appropriate concentrations is helpful to develop coronary collateral flow, and prevents ischemia/reperfusion-induced ventricular tachyarrhythmias.

P4581 | BEDSIDE
Association of genetic variants of the alpha-kinase 1 gene (ALPK1) with myocardial infarction in community-dwelling Japanese individuals

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Purpose: We previously showed that rs2074380 (G→A, Gly870Ser) and rs2074381 (A→G, Asn916Asp) of the alpha-kinase 1 gene (ALPK1) were significantly associated with chronic kidney disease in Japanese individuals with diabetes mellitus by a genome-wide association study. Given that chronic kidney disease is an important risk factor for coronary heart disease, we hypothesized that rs2074380 and rs2074381 of ALPK1 might contribute to the genetic susceptibility to myocardial infarction (MI) through affecting the susceptibility to chronic kidney disease. The purpose of the present study was to examine a possible association of rs2074380 and rs2074381 with MI in community-dwelling Japanese individuals.
Methods: Study subjects comprised 5771 community-dwelling individuals (41 subjects with MI, 5730 controls) who were recruited to a population-based cohort study in Inabe City, Japan. Genotypes of polymorphisms were determined by the multiplex bead-based Luminex assay, which combines the polymerase chain reaction and sequence-specific oligonucleotide probes with suspension array technology.
Results: Comparisons of allele frequencies and genotype distributions by the chi-square test revealed that the rs2074380 (allele, P=0.0051; genotype, P=0.0198) and rs2074381 (allele, P=0.0075; genotype, P=0.0275) of ALPK1 were significantly ($P<0.05$) associated with MI. Multivariable logistic regression analysis with adjustment for age, sex, body mass index, smoking status, the serum concentration of creatinine, and the prevalence of hypertension, diabetes mellitus, and dyslipidemia revealed that the rs2074380 (P=0.0354, dominant model) and rs2074381 (P=0.0438, dominant model) were significantly associated with MI, with the minor A and G alleles of rs2074380 and rs2074381, respectively, being protective against MI. A stepwise forward selection procedure revealed that hypertension, the serum concentration of creatinine, diabetes mellitus, male sex, age, and rs2074380 of ALPK1 (dominant model) were significant ($P<0.05$) and independent determinants of MI. The rs2074380 and rs2074381 were in linkage disequilibrium (r2 = 0.938, $P<0.0001$). Haplotype analysis of these polymorphisms revealed that the frequency of the major haplotype, G (rs2074380)–A (rs2074381), was significantly (permutation P=0.012) higher, whereas that of the minor haplotype A–G was significantly (P=0.020) lower, in subjects with MI than in controls.
Conclusions: ALPK1 may be a susceptibility locus for MI in Japanese individuals.

P4582 | BEDSIDE
Usefulness of Neutrophil/lymphocyte ratio as a predictor of new onset atrial fibrillation in myocardial infarction with ST elevation patients undergoing primary PCI

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Purpose: The systemic inflammatory status has been associated with New-Onset Atrial Fibrillation (NOAF) in Acute Myocardial Infarction with ST Elevation (STEMI) and its worst outcomes. The Neutrophil/Lymphocyte ratio (N/L) stands for the balance between neutrophil and lymphocyte counts in the body and can be utilized as an index for systemic inflammatory status. We evaluated the relation between admission metabolic, inflammatory, ischemic biomarkers and new-onset AF in a large STEMI population and the prognostic value of NOAF at middle term follow up.
Methods: We retrospectively examined clinical and laboratory data of 1112 consecutive STEMI patients (ranging from 21 to 99 years) admitted to our Heart Care for primary PCI from 2006 to 2011. The NOAF was defined as atrial fibrillation that occurred during the index hospitalization. A 25±18 months clinical follow-up was performed, and MACEs (cardiac death, re-hospitalization for acute coronary syndrome and elective revascularization for angina) were reported.
Results: New-onset AF was documented in 89 patients with STEMI (8.0%; mean age 73.9±9.9 years; 67% men). The NOAF group was older ($p<0.0001$) and presented higher frequency of hypertension (p=0.009), higher levels of Troponin-I (p=0.02) and BNP ($p<0.0001$). Regarding inflammatory markers, ESR (p=0.001), fibrinogen (p=0.001), CRP ($p<0.0001$) and the N/L ratio ($p<0.0001$) resulted significantly higher in the NOAF group. After adjustment of confounding factors, the independent predictors of NOAF were higher N/L ratio (OR=3.9, p=0.01) and old age (OR=3.4, p=0.02). Morever, at middle-term follow-up a significant increase in all-cause mortality (Log-Rank 19.6; $p<0.0001$), but not in MACEs (p=0.6), was observed in NOAF group.
Conclusions: Our results suggest that acute inflammatory status and in particular admission elevated N/L ratio is a strong predictor of new-onset AF in STEMI. The use of this simple routine biomarker of systemic inflammation may have potential therapeutic implication in preventing the atrial arrhytmia and improving prognosis in STEMI revascularized patients.

P4583 | BEDSIDE
The impact of a self-apposing coronary artery stent placement on the lipid core plaque burden as assessed with Near-Infrared Spectroscopy: does the lipid core burden index decrease after intervention?

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Purpose: Distal embolization is commonly caused by high pressure stent deployment in coronary artery lesions involving high risk lipid-core containing plaques (LCP). The aim of this observational study is to evaluate the impact of a self-apposing stent on the lipid core burden index (LCBI) as assessed with near-infrared spectroscopy (NIRS).
Methods: Six patients who are treated with the STENTYS self-apposing stent and where pre-stenting NIRS showed significant LCPs (LBCI>250), were enrolled in our analyses. Intravascular ultra sound (IVUS) with NIRS pullbacks were done pre-stenting, direct post stenting and after post-dilatation. Off-line quantita-

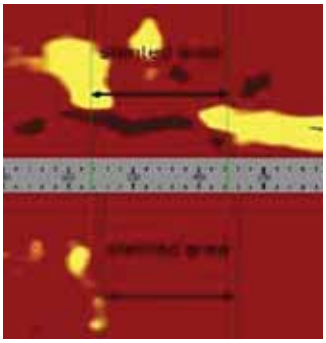
Figure 1. Pre and post stenting chemogram by NIRS.

tive coronary angiography (QCA) analyses were performed to measure minimal luminal diameter (MLD), reference vessel diameter (RVD) and % stenosis. IVUS and NIRS data were analyzed to measure minimal lumen area (MLA) and LCBI.
Results: Mean MLD was 0.8±0.4mm pre-stenting, 2.2±0.2mm post-stenting, and 3.2±0.4mm after post-dilatation (p for trend:<0.001), with a mean RVD of 3.5±0.6mm. Mean % stenosis on QCA was 77% pre-stenting, 35% post-stenting, and 16% after post-dilatation. Mean MLA was 3.1±1.0mm^2 pre-stenting, 4.9±1.0mm^2 post-stenting, and 9.0±2.2mm^2 after post-dilatation (p for trend was:<0.001). LCBI pre-stenting: 477±224; LCBI post-stenting: 145±165; LCBI after post-dilatation: 86±96 (p for trend: 0.002). The LCBI decreased with 69.6% post-stenting, and with 40.7% after post-dilatation.
Conclusions: The significant LCBI decrease post stenting and after post-dilatation suggests that a self-apposing stent does not potentially prevent LCPs from distal embolization. Both MLD and MLA increases significantly after post dilatation which shows the need for post dilatation after delivery of a self-apposing stent to avoid under-expansion.

P4584 | BEDSIDE
Plasma miRNA changes after reperfusion injury in STEMI patients following PPCI

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Purpose: MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression by interacting with multiple mRNAs. miRNAs are also released from tissue into plasma as a consequence of damage and appear to reflect both the degree of damage seen in tissues, including the heart, and also long term remodelling. The aim of this work was to measure miRNAs in the plasma of ST elevation myocardial infarction (STEMI) patients who were undergoing primary percutaneous coronary intervention (PPCI).
Methods: 50 patients admitted to hospital with STEMI and who were undergoing PPCI were recruited. Plasma extracted from blood samples that were collected from the patients prior to PPCI (baseline), 24 hours after PPCI and 3 months after PPCI was stored at -80°C. Total RNA was extracted from the plasma using miRNeasy serum/plasma kit (Qiagen). miRNAs were measured using TaqMan primers and miRNA levels were assessed using quantitative PCR. Quantification was performed using cel-miR-39-3p (000200) as the normalising miRNA. miRNAs measured were hsa-miR-133a-3p (002246), hsa-miR-194-5p (000493), hsa-miR-208b-3p (002290) and hsa-miR-214-3p (002306) (Life Technologies).
Results: Both miRNA-133a and miRNA-208b which have been shown to increase following reperfusion injury were significantly elevated at 24 hours compared to both baseline and 3 month time points. After 3 months miRNA-208b was undetectable in most patients. In contrast, miRNAs associated with heart failure (miRNA-194 and miRNA-214) did not show significant changes throughout. However, when looking at individual patients 60% of them had elevated levels of miRNA-194 and miRNA-214 after PPCI.
Conclusions: These data suggest that after reperfusion there is a release of both miRNA-133a and miRNA-208b into the bloodstream. Even before reperfusion there is an increase in these miRNAs suggesting that there is cellular damage prior to PPCI. Both miRNA-194 and miRNA-214 have implications in cardiac dysfunction and protection but it appears these are not released into the plasma as a consequence of cardiac damage. The different patient profiles of miRNA-194 and miRNA-214 with respect to long term patient outcome are currently being investigated.

P4585 | BEDSIDE
Periprocedural myocardial infarction and cardiac remote ischemic preconditioning in patients undergoing percutaneous coronary interventions: a meta-analysis of randomized clinical trials

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Aims: The cardioprotective effect of remote ischemic preconditioning (RIPC) in patients undergoing Percutaneous Coronary Intervention (PCI) remains to be established.
Methods and results: Pubmed, Cochrane and Embase were systematically searched for randomized controlled trials of RIPC in patients undergoing PCI. Peri-procedural myocardial infarction (PMI) was the primary end point (defined as troponin elevation >3 times upper reference limit) and C-reactive Protein (CRP) was a secondary end point. 5 studies with 731 patients were included. The median age of the patients was 62 (59-68) years old, 25% being female (23-33), 29% (25-33) had diabetes mellitus, and 26.5% (19-31) presenting with multivessel disease. RIPC significantly reduced incidence of PMI (odds ratio: 0.58 [0.36, 0.93]; I2 43%), with a greater benefit when performed using the lower limb (0.21 [0.07-0.66]) compared to the upper limb (0.67 [0.46-0.99]). This reduction was enhanced for patients with multivessel disease (Beta -0.05 [-0.09;-0.01], p 0.01) and with type C lesion (Beta -0.014 [-0.04;-0.010], p 0.01) and did not vary according to age, female gender, diabetes mellitus, use of beta-blockers and of angiotensin converting enzyme inhibitors. Absolute risk difference was of -0.10 [-0.19, -0.02], with a Number Needed to Treat of 10 [6-50] patients to avoid one event. CRP -0.69 [-1.69, 0.31] was not significantly reduced by RIPC.
Conclusion: RIPC reduced the incidence of PMI following PCI, especially when performed in the lower limb and for patients with multivessel disease and complex lesions.

P4586 | BENCH
PARP-1 Inhibitor PJ-34 ameliorate myocardial ischemia/reperfusion injury through Its protective effect of mitochondria

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Background: Ischemia/reperfusion injury is a major cause of myocardial cells death and heart function damage after successful reperfusion therapy. Drug post-conditioning is a valuable clinical practice to alleviate ischemia/reperfusion injury. Poly (ADP-ribose) Polymerase-1 (PARP-1) is a protein kinase which exists in the nucleus and is highly expressed in myocardial cells. The aims of our study is to find out whether PARP-1 inhibitor PJ-34 has the protection effect on isolated rat heart suffered from ischemic reperfusion injury and to investigate the potential mechanism.
Methods: We used the Langendorff perfusion apparatus to set up the experimental model of ischemic reperfusion injury of isolated rat heart. All SD rat were randomly divided into 3 groups: Control group, I/R group and I/R+PJ-34 postconditioning group. Cell death and viability were measured by LDH and MTT assay; myocardial infarct size was measured by TTC staining; the indexes of hemodynamics were measured by Medlab system; the extent of oxidative stress injury was measured by MDA assay.
Results: We found that PJ-34 postconditioning dramatically reduced the myocardial cell injury and improved cell viability compared with I/R group. Meanwhile, PJ-34 treatment efficiently decreased the myocardial infarct size and improved the indexes of heart hemodynamics compared with I/R group. Furthermore, PJ-34 postconditioning significantly reduced the intracellular MDA content and improved energy metabolism and mitochondrial function within myocardial cells compared with I/R group.
Conclusions: PJ-34 postconditioning can effectively attenuate myocardial ischemic reperfusion injury, and its cardioprotective action may be due to alleviate of oxidative stress and improve energy metabolism and mitochondrial function within myocardial cells.

P4587 | BENCH
Detection of subtle myocardial injury using dipyridamole stress contrast echocardiography deduced coronary flow reserve index on swine models

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Introduction: The extent of subtle myocardial injury is very common in clinic whereas it is difficult to be detected succinctly. Since real-time myocardial contrast echocardiography (RT-MCE) has many advantages to study different degrees of myocardial perfusion at the capillary level, we conducted an animal experiment to evaluate the variation of coronary flow reserve reduction on swine models.
Material and methods: Eighteen miniature pigs were randomized into coronary microembolization (CME) group (n=9) or as control (n=9). Sixteen swine (CME goup: 7; control goup: 9) who accomplished the experiment had no LAD stenosis after the intervention and had no anatomical variations with angiography. The anterior wall and anterior septum at basal, middle and apical levels were then defined as microembolism related segments (MRS). There were 42 (6×7) MRS in CME group whereas 54 (6×9) in control group. All the animals received dipyridamole stress RT-MCE at baseline, 6 hours and 1 week after the invasive procedure. Quantitative RT-MCE parameter, myocardial blood flow (MBF), were derived from replenishment curves. The coronary flow reserve index (CFR) was defined as segmental MBF after CME divided by the value of MBF at baseline.
Results: The results of HE staining confirmed the presence of patchy microinfarct in CME group compared with control (40.48% vs. 0%, p<0.01). Left ventricular ejection fraction had no significant differences throught the entire study (all p>0.05) in both groups. RT-MCE showed MBF on all MRS altered little in control group both under rest and stress conditions compared with those at baseline as well as in the CME group (all p>0.05). However, when the ratio of MBF were calculated, CFR at 6 hours and 1 week declined significantly compared with those at baseline (0.98±0.48 and 1.04±0.36 vs. 1.31±0.32, all p<0.05) while the parameters remained stable in the control group.
Conclusions: Slight myocardial damage can be hardly estimated by conventional echocardiographic methods. Low-dose dipyridamole stress RT-MCE provides a simple and convenient technique for the microvascular dysfunction examination, echocardiographic CRF presented good accuracy for assessing subacute microcardiovascular flow reserve reduction.

P4588 | BEDSIDE
Differences in the characteristics of in-stent neointimal hyperplasia between diabetic and non-diabetic patients: virtual histology intravascular ultrasound study

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Background: Patients with diabetes have an increased risk of in-stent restenosis after coronary stent implantation. However, differences in the characteristics of the in-stent neointimal hyperplasia between diabetic and non-diabetic patients have not been studied.
Purpose: The purpose of this study was to investigate the difference in the characteristics of the in-stent neointimal hyperplasia after stent implantation in diabetic and in non-diabetic patients with ischemic heart disease.
Methods: A total of 132 consecutive patients who underwent stent implantation for de novo lesions and indicated in-stent restenosis in the 6-month follow-up angiogram were enrolled in this study. The patients were divided into groups: with diabetes (DM group, n=76, HbA1c 6.8±1.0%) and without diabetes (non-DM group, n=56, HbA1c 5.4±0.3%). In-stent restenosis was defined as stenosis of at least 75% by visual evaluation in the stented area. Baseline characteristics, stent size, and use of a drug-eluting stent (DES) were evaluated. The % cross-sectional narrowing (neointimal plaque area divided by stent area), neointimal plaque area, and in-stent neointimal plaque histological composition ratios were determined using virtual histology intravascular ultrasound (VH-IVUS). Neointimal plaque histological composition ratios were classified as fibrous, fibro-fatty (FF), dense-calcium (DC), and necrotic core (NC). The predictors for plaque histological composition ratios were assessed using multivariate logistic regression analysis.
Results: The NC (16±12% vs. 10±7% p=0.0009) and DC (3±5% vs. 2±2%, p=0.02) ratios were significantly higher and the FF ratio (12±10% vs. 18±11%, p=0.0002) was significantly lower in the DM group compared with that in the non-DM group. However, other parameters did not differ significantly between the two groups. Only diabetes mellitus was an independent predictor for both NC≥16% [Odds ratio (OR) 3.32, 95% confidence interval (CI) 1.46-7.56, p=0.004] and DC≥3% (OR 2.51, 95% CI 1.11-5.70, p=0.03). Furthermore, only the use of a dipeptidyl peptidase (DDP) 4 inhibitor was an independent predictive factor for NC≥10% (OR 0.05, 95% CI 0.004-0.46, p=0.009) in the DM group. The higher NC and DC compositions of the in-stent neointimal hyperplasia may be associated with the higher incidence of in-stent restenosis in patients with diabetes. The DDP4 inhibitor may decrease NC component hyperplasia.
Conclusion: Differences in the characteristics of in-stent neointimal hyperplasia were observed between diabetic and non-diabetic patients with ischemic heart disease.

P4589 | BEDSIDE
Parameters of the iron homeostasis rather than anemia are better indicators of prognosis in critically ill cardiac patients

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Anemia is a common finding in critically ill patients. However, the relationship between the abnormalities in iron metabolism and the adverse outcome in a general population of patients admitted to Cardiac Intensive Care Unit (CICU) is unknown.
Aim: The predictive value of serum iron concentrations (SIC) and total iron binding capacity (TIBC) as an indirect measure of transferrin in critically ill patients was compared to the clinical risk factors, echocardiographic parameters, and laboratory findings, particularly anemia.
Methods and results: 392 critically ill patients (mean age 70 years, 43% women) admitted to CICU were prospectively analyzed. 168 patients were admitted due to acute coronary syndrome (ACS), 122 with symptoms of acute heart failure (AHF), and 102 with other acute cardiac disorders (including aortic dissection and pulmonary embolism). During 7.9 (±5.1) days of hospitalization 15 (3.8%) patients died. According to the WHO definition anemia was present in 64% patients. Mean hemoglobin (Hb) level was 11.8 g/dL (±2.2), SIC – 44.0 μg/dL (±38.9), and TIBC – 268 μg/dL (±75.1). In univariate analysis 4th NYHA class, CRP, SIC, TIBC, and left ventricle ejection fraction (LVEF) were related to mortality ($p<0.05$), while in multivariate analysis CRP, SIC, TIBC, and LVEF remained significant. The largest area under the ROC curve (AUC) was found for SIC – 0.77 (95% confidence interval [C.I.] 0.638 to 0.902), LVEF – 0.72 (95% C.I. 0.587 to 0.853), TIBC – 0.67 (95% C.I. 0.521 to 0.819), as compared to Hb – 0.535 (95% C.I. 0.407 to 0.662), figure.
Conclusions: In a heterogenous group of patients with life-threatening cardiac illnesses, among the variety of parameters being assessed at admission CRP, SIC, TIBC and LVEF, but not anemia, are independent markers of in-hospital mortality.

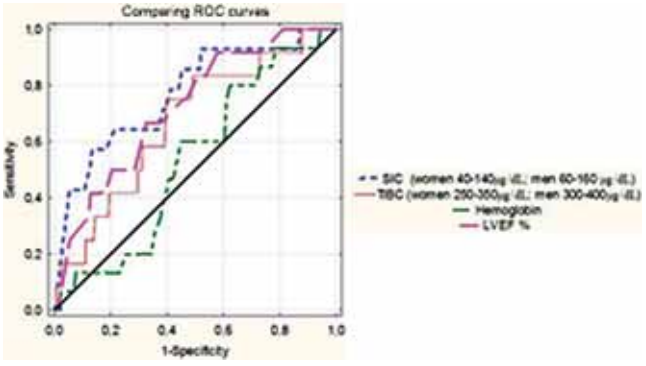

Figure 1

P4590 | BENCH
Mild hypothermia increases the inducibility of atrial fibrillation in healthy pigs

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Mild hypothermia (MH) is an established therapy to improve neurological outcome and survival after cardiac arrest. MH further reduces myocardial infarct size when initiated before reperfusion, and is tested as a therapeutic option in cardiogenic shock. However, MH also prolongs the cardiomyocyte action potential. We therefore tested the hypothesis that MH increases the inducibility of atrial fibrillation (AF).
Methods: Eight healthy, anesthetized pigs (67±7kg) were instrumented with a quadripolar stimulation catheter in the high right atrium and a decapolar catheter in the coronary sinus. Measurements were performed at hyperthermia (HT, 40.5°C, external warming), at normothermia (NT, 38.0°C) and at MH (33.0 °C, intravascular cooling device). At each temperature, the effective atrial refractory period (AERP) was measured with a S1S2 stimulation protocol. The inducibility of AF was assessed by burst protocols (cycle lengths 200/150/100/50ms, 5x10s). AF was defined as the onset of irregular atrial electrograms with an average cycle length <150ms for more than 10s.
Results: During MH, AERP (at a S1 cycle length of 400ms) was significantly longer than during NT (237±44ms vs. 177±26ms; p=0.01) and HT (157±36ms; p=0.001). The inducibility of AF (at a burst cycle length of 50ms) was significantly higher during MH (68±34%) compared to NT (25±28%; p=0.018) and HT (18±27%; p=0.007). Mean AF duration did not differ between groups (HT: 36±49s; NT: 16±5s; MH: 97±212s). Arterial potassium levels decreased with falling temperatures (HT: 4.2±0.1mmol/L; NT: 4.0±0.2mmol/L; MH: 3.5±0.1mmol/L, $p<0.05$).

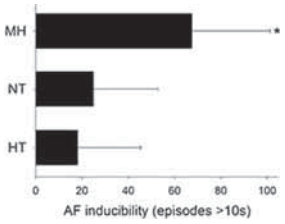

Figure 1

Conclusion: Our data imply that MH represents an arrhythmic substrate rendering the atria more susceptible to AF. Further investigations on potential electrophysiologic limits of cooling in patients are required.

STEMI

P4592 | BEDSIDE
Predictors of in-hospital ventricular arrhythmias in patients admitted with suspected non-ST-elevation acute coronary syndrome - data from the SWEDEHEART registry

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Purpose: The aim of this study was to investigate factors present on admission that are associated with in-hospital sustained ventricular tachycardia/ventricular fibrillation (VT/VF) and that can be used in the decision about the degree of cardiac monitoring.
Methods: Consecutive patients (n=333278) 18 years or older who were admitted with a suspicion of non-ST-elevation acute coronary syndrome (NSTE-ACS) and registered in the nationwide SWEDEHEART registry between 2003-2010 were included. Those with a ST-elevation myocardial infarction (STEMI) or ventricular arrhythmia/cardiac arrest prior to admission to the hospital were excluded. Baseline characteristics on admission were recorded. In-hospital sustained VT/VF was recorded as part of the registry. A logistic regression model was used to assess

the association between baseline characteristics (24 candidate variables) and VT/VF.

Results: The incidence of VT/VF was 0.6% (n=2111) in the entire cohort, whereas 1.4% (n=1330) of those with a final NSTE-ACS diagnosis (n=96,838) had VT/VF. In the entire cohort patients with VT/VF compared to those without VT/VF had a median age of 74 vs 70 years, 68,3% vs 58,8% were male, 47,2% vs 36,1% had a prior myocardial infarction, 29,6% vs 18,2% had a history of heart failure, 28,3% vs 21,8% had a history of diabetes and 52,3% vs 51,2% had a history of hypertension. Ten variables were found to be independently associated with having an in-hospital sustained VT/VF (table 1). Patients without any of these risk factors had a very low incidence (n=4 of 8039) of VT/VF.

Table 1

	OR (95% CI) for in-hopsital sustained VT/VF	P
Male sex	1.64 (1.44–1.88)	<0.001
Current smoker	1.41 (1.20–1.66)	<0.001
ST-T abnormalities	3.21 (2.69–3.82)	<0.001
Killip class >I	1.40 (1.21–1.63)	<0.001
Heart rate <60 or >100 bpm	1.72 (1.52–1.96)	<0.001
Systolic BP <100 mm Hg	3.95 (3.30–4.74)	<0.001
No history of DM and glucose ≥10 mmol/l	2.69 (2.21–3.27)	<0.001
History of DM and glucose ≥10 mmol/l	1.53 (1.29–1.82)	<0.001
eGFR <60 ml/min/1.73 m^2	1.82 (1,58–2,09)	<0.001
Age ≥65 years	1.28 (1.08–1.51)	0.004

Conclusion: We found 10 factors that are independently associated with in-hospital sustained VT/VF among patients admitted with suspected NSTE-ACS. These factors could be used to identify patients at risk requiring cardiac monitoring.

P4593 | BEDSIDE
Radiation exposure and procedure outcome of primary percutaneous coronary interventions when performed by experienced or inexperienced operators

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Background: Studies demonstrate an increase of radiation exposure by inexperienced operators and with transradial approach in learning curve, but in case of primary percutaneous coronary intervention (PCI) this phenomenon was not previously evaluated.

Purpose: The main goal of this registry was to determine the radiation exposure and 30-day mortality outcome of primary PCI of ST-elevation myocardial infarction (STEMI) performed by experienced or inexperienced operators.

Methods: We prospectively evaluated 499 STEMI patients who underwent primary PCI by experienced or inexperienced operators at a dedicated transradial (>85%) PCI center from April of 2011 to December of 2013. Diagnostic angiographies were excluded from the study. Experienced operators were defined as those that perform >250 PCIs/year in the last 5 years. The outcomes of interest were dose area product (DAP) and fluoroscopy time (FT), procedure time (PT) and the 30-day mortality rate of the patients. We have also investigated the impact of the learning curve during the interventions.

Results: 292 of the 499 consecutive STEMI patients (58.5%) were performed by experienced and 207 (41.5%) by inexperienced operators using the radial approach by 83.6% and 74.9% of the cases, respectively (p=0.017). The demographic and clinical data were not statistically different between the two subgroups. The mean age of the patients was 62.9 years, the 64.1% were male. DAP of the PCI was 8772 (4669-17197) unit versus 15048 (8830-27246) unit ($p<0.001$), FT was 541 (388-880) seconds versus 898 (593-1502) seconds ($p<0.001$) and PT was 1800 (1200-3000) seconds versus 3000 (1800-4200) seconds ($p<0.001$) when the procedure was performed by experienced versus inexperienced operators, respectively. The 30-day mortality was 10.6% versus 11.6% in the experienced versus inexperienced subgroup (p=0.731). In the total study cohort the radial artery access was associated with lower DAP ($p<0.001$), FT ($p<0.001$) and PT ($p<0.001$) as well lower mortality rate ($p<0.001$) when compared with the traditional femoral artery access.

Conclusions: In a contemporary cohort of STEMI patients undergoing primary PCI by experienced and inexperienced operators, the experience is associated with lower radiation exposure and lower procedure time, but same short-term rate of mortality. The radial access is associated with lower radiation exposure and better short-term mortality rate when compared with the femoral artery access at a dedicated transradial PCI center.

P4594 | BEDSIDE
Investigating variation in hospital acute coronary syndrome outcomes: a cohort profile of the evaluation of the methods and management of acute coronary events (EMMACE-3)

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Purpose: EMMACE-3 is a national, multi-centre, prospective, linked, longitudinal cohort study of patients admitted with an acute coronary syndrom (ACS) to National Health Service (NHS) hospitals in England. Aims were to quantify variation in health-related quality outcomes (HRQL) and to identify modifiable factors which could lead to improved quality of healthcare from an ACS.

Methods: Data were collecteted at four time points (in-hospital, 1-month, 6-month and 12-month after discharge) using HRQL indicators (EuroQol 5-dimesion, EQ-5D) and medication adherence (Morisky eight-item Medication Adherence Scale, MMAS) measures. Linkages to multiple electronic healthcare records were performed. The spectrum of ACS phenotypes includes ST-elevation myocardial infarction (STEMI), non-STEMI and troponin negative ACS (unstable angina, UA).

Results: Of the 5556 cases, across 48 NHS hospitals in England, there were 24.8% STEMI, 37.4% non-STEMI and 0.9% UA. Table 1 summarises some of the baseline characteristics. Of the survivors, the response rates exceded 95% during the in-hospital and follow-up period. Using published MMAS-8 thresholds, low drug adherence rates were 8%, 12.9% and 12,2% at 1-month, 6-month and 12-month follow-up respectively. The mean (SD) of EQ-5D scores were 0.738 (0.28) in-hospital, 0.753 (0.25) 1-month, 0.787 (0.25) 6-month and 0.790 (0.26) 12-month follow-up.

Table 1. Baseline characteristics

Baseline characteristics	N (%)	Baseline characteristics	N (%)
Mean (SD) age, years	64.4 (11.9)	Previous myocardial infarction	709 (20.4)
Men	3969 (73.8)	Cerebrovascular disease	168 (4.8)
Hypertension	1573 (45.3)	Asthma or COPD	434 (12.5)
Diabetes mellitus	537 (15.5)	Chronic renal failure	106 (3.1)
Previous angina	851 (24.5)	Chronic heart failure	68 (2.0)

Conclusions: During the one-year follow-up ACS patients showed high response rates, appeared to adhere to their prescibed medications and have consistent HRQL scores.

P4595 | BEDSIDE
The impact of slow or no-reflow phenomenon during percutaneous coronary intervention with thrombus aspiration for acute myocardial infarction

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Purpose: We aimed to evaluate the impact of slow flow and no-reflow phenomenon during percutaneous coronary intervention (PCI) with thrombus aspiration for acute myocardial infarction (AMI) on clinical outcomes.

Methods: From January 2006 to May 2013, 1723 patients underwent PCI for AMI, of whom 1074 (62.3%) underwent thrombus aspiration, and 120 (11.2%) showed slow or no-reflow. We compared clinical outcomes at discharge and 6 months after primary PCI between patients with slow flow or no-reflow and without these phenomena.

Results: In the slow or no-reflow group, the mortality and cardiac death rates at discharge (12.5% vs. 5.9%, $p<0.01$; 11.7% vs. 4.1%, $p<0.01$) and at 6 months after PCI (15.8% vs. 7.4%, $p<0.01$; 13.3% vs. 4.7%, $p<0.01$) were significantly higher. The mortality and cardiac death rates from discharge to 6 months showed no significant difference between two groups (2.9% vs. 1.7%, p=0.63; 1.9% vs 0.6%, p=0.44).

Results

	Slow or no-reflow 120 patients	Without slow and no-reflow 954 patients	p value
At discharge			
All-cause death	15 (12.5%)	56 (5.9%)	<0.01
Cardiac death	14 (11.7%)	39 (4.1%)	<0.01
TVR	0 (0%)	5 (0.5%)	0.43
TLR	0 (0%)	5 (0.5%)	0.43
6 months after PCI			
All-cause death	19 (15.8%)	71 (7.4%)	<0.01
Cardiac death	16 (13.3%)	45 (4.7%)	<0.01
TVR	12 (10.0%)	61 (6.4%)	0.14
TLR	9 (7.5%)	51 (5.3%)	0.33
From discharge to 6 months			
All-cause death	3 (2.9%)	15 (1.7%)	0.63
Cardiac death	2 (1.9%)	6 (0.6%)	0.44

TVR, target vessel revascularization; TLR, target lesion revascularization.

Conclusion: Among patients treated with primary PCI and thrombus aspiration for AMI, slow flow and no-reflow phenomenon related to poor prognosis.

P4596 | BEDSIDE

Predictors of ST-segment resolution - a multivariate analysis from the multinational MULTIPRAC registry

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Purpose: The multinational STEMI registry MULTIPRAC collected patient characteristics, treatment-related details and clinical outcomes in 2053 patients scheduled for primary percutaneous coronary intervention (PCI). We aimed to identify procedural and organizational factors, predictive of ST-segment resolution (ST-Res).
Methods: In MULTIPRAC we recorded if patients displayed ST-Res ≥50% within 1h from the PCI. In 1657 patients, of which 1490 (89.9%) had ST-Res ≥50% a univariate analysis (UVA) was performed for 28 parameters possibly related to ST-Res. A multivariate analysis (MVA) using a logistic regression model with forward selection and a significance level for entering effects of 0.10 was performed. Results are expressed as odds ratio (OR) with 95% confidence interval (CI) and p-value.
Results: In the UVA 20 parameters were associated with ST-Res. The MVA, which was based on complete datasets from 990 patients identified 8 parameters (see table below) as independent predictors of ST-Res (p≤0.05).

Predictors of ST-Res ≥50% (from MVA)

Parameter	OR	95% CI	p
Chronic dose of acetylsalicylic acid	2.56	1.04–6.34	0.042
Bivalirudin in cathlab hospital	2.04	1.07–3.90	0.031
Direct admission to cathlab	2.00	1.05–3.81	0.035
History of diabetes	0.53	0.29–0.99	0.045
Symptom onset to start of PCI >5:05h (4th quartile)	0.48	0.29–0.80	0.005
Bivalirudin before arrival to cathlab hospital	0.28	0.11–0.73	0.009
No reflow	0.13	0.04–0.48	0.002
Distal embolization	0.11	0.03–0.45	0.002
Age ≥75 years	0.52	0.27–1.03	0.06]
Killip class 3/4 on admission	0.38	0.14–1.04	0.06]

Conclusion: As expected procedural aspects known to be linked with adverse outcomes like distal embolization are inversely related to ST-Res, but importantly organizational decisions like prehospital medical management also impacted, demonstrating the possibility to optimize STEMI networks and treatments to further improve outcomes.

P4597 | BEDSIDE

Circadian dependence of myocardial infarction size from a large national multicenter registry

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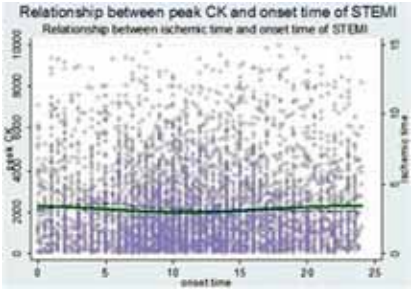
Objectives: To analyze circadian variation of myocardial infarction size and in hospital mortality in a large sample population.
Background: Different studies have shown circadian variation of ischemic burden among STEMI patients with controversial results.
Methods: 6223 patients treated with primary angioplasty for STEMI within 6 hours after symptom onset were retrieved from AMIS Plus, a large, prospective Swiss registry. Association between peak Creatine Kinase (CK), in hospital mortality and time at symptom onset was analyzed by harmonic regression method.
Results: Only the 24-hour harmonic was significantly associated with peak CK (p=0.0001), whereas the others were not. Patients with symptom onset at 23:00 had on average higher peak CK (2315 U/L) than patients with symptom onset at 11:00 (2017 U/L). The amplitude of this difference (298 U/L) was 15%, when compared to the peak CK at 11:00. When we analyzed a subset of patients with TIMI flow = 0 at the start of the procedure and no history of myocardial infarction nor known coronary artery disease and non-diabetic (n=654), a circadian cycle of 24 hour period was confirmed and the amplitude between the minimum and maximum peak CK (885 U/L) was amplified compared to the total population (34%). Same observations were found for sub-period (1999-2004, 2005-2009, 2010-2013). In-hospital mortality was 3.58%. Only the 24-hour harmonic was significantly associated with the probability of death, which was higher for patients with symptom onset at 00:00.
Conclusions: This study confirms a circadian distribution of in-hospital mortality and peak CK among STEMI patients treated with primary angioplasty. Maximal and minimal myocardial infarction size occurs at 23:00 and 11:00 respectively. In-hospital mortality is the highest at 00:00.



P4598 | BEDSIDE

Comparison of major bleeding risk prediction using CKD-EPI equations and the MDRD study equation in patients with non-ST segment elevation acute coronary syndromes

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Background: Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations estimate glomerular filtration rate (GFR) more accurately than the Modification of Diet in Renal Disease (MDRD) equation. The aim of the present study is to evaluate whether CKD-EPI equations based on serum creatinine and/or cystatin C (CysC) predict risk for major bleeding (MB) more accurately than the MDRD equation in patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS).
Methods: 350 consecutive subjects with NSTE-ACS (68±12 years, 70% male) were studied. Blood samples were obtained within 24 h of admission. GFR was estimated using the new CKD-EPI equations and the MDRD Study equation. The primary endpoint was the occurrence of MB in the follow-up, which was defined according to the Bleeding Academic Research Consortium Definition criteria as bleeding types 3–5.
Results: During a follow-up period of 697 days [IQR 393 to 1,007], 27 patients (7.7%) had MB. Patients with MB had worse kidney function parameters, regardless of the estimating equation used (p<0.001). After multivariate Cox regression adjustment, both Cys C-based CKD-EPI equations were independent predictors of major bleeding (CKD-EPI(CysC-Cr) per mL/min/1.73m^2, HR 0.98 (95% CI 0.96-0.99, p=0.01) and CKD-EPI(CysC) per mL/min/1.73m^2, HR 0.98 (95% CI 0.97-0.99, p=0.008)), while the CKD-EPI(Cr) and the MDRD Study equations did not achieve statistical significance. Moreover, both CKD-EPI(CysC-Cr) and CKD-EPI(CysC) were associated with a significant improvement in reclassification analyses (NRI 22.7% and 29.3%, respectively).
Conclusion: In this cohort of NSTE-ACS patients with a relatively preserved renal function, CysC-based CKD-EPI equations were superior to creatinine-based CKD-EPI and MDRD Study equations for predicting MB, and both improved clinical risk stratification.

P4599 | BEDSIDE

The circulating miRNA-126-3p and miRNA-423-5p are associated with structural injury and functional impairment after acute myocardial infarction

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Purpose: Recently it was shown that microRNA (miRNA), an intracellular regulator of gene expression, can be detected in the circulating blood of patients with ST-segment elevation myocardial infarction (STEMI). We sought to investigate whether the expression of selected circulating miRNAs is associated with infarct size, microvascular obstruction, left ventricular function and remodeling in patients after primary angioplasty for STEMI.
Methods: The concentrations of miRNA-126-3p, -133a, -208a and -423-5p (10^3 copies/μl) were prospectively assessed in 38 patients with first STEMI on admission and 4 months later. miRNAs were isolated using the miRNeasy Serum/Plasma Kit and quantified using standard curve method with the miScript PCR System and a median normalization procedure. The microvascular obstruction (% of gadolinium-enhanced area of infarct), area of infarct (% of left ventricle mass), left ventricular ejection fraction and end-diastolic (EDVI) and end-systolic (ESVI) volume indexes were determined by cardiovascular magnetic resonance imaging 2-4 days and 4 months after STEMI.
Results: At baseline miRNA-126-3p was significantly lower as compared to follow-up measurements (133±203 vs. 233±297, respectively, P<0.05). There was a not significant trend to higher miRNA-423-5p (P=0.11) and lower miRNA-133a (P=0.11) concentration after 4 months. miRNA-208 was not detected at baseline and after 4 months at all. At baseline miRNA-126-3p was significantly higher in patients with anterior wall infarction (275±282 vs 49±58, P<0.05) whereas miRNA-423-5p was higher in hypertensive patients (570±264 vs 236±206, P<0.01). At baseline miRNA-126-3p was inversely correlated with EDVI (R=-0.48, P<0.05), ESVI (R=-0.52, P<0.05) and infarct size (R=-0.46, P<0.05) and positively correlated with ejection fraction (R=0.57, P<0.01). Also baseline miRNA-423-5p was inversely correlated with ESVI (R=-0.47, P<0.05)

and microvascular obstruction (R=-0.50, P<0.05) and positively correlated with ejection fraction (R=0.56, P=0.013). Baseline left ventricle mass was inversely correlated with miRNA-126-3p (R=-0.46, P=0.05) and positively correlated with miRNA-133a (R=0.49, P<0.05). After 4 months an increase of left ventricular ejection fraction was associated with the increase of miRNA-423-5p (R=0.45, P=0.05), whereas changes of volume indexes were not correlated with changes of miRNAs.
Conclusions: In STEMI patients, elevated miRNA-126-5p and miRNA-423-5p as measured on admission were associated with lower myocardial and microvascular injury and better preserved left ventricular contractility.

P4600 | BEDSIDE
MicroRNA as potential biomarkers of acute myocardial damage following STEMI

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Background: Cardiovascular magnetic resonance (CMR) can identify myocardial characteristics following ST segment elevation myocardial infraction (STEMI) that are predictors of poor prognosis. These parameters include early and persistent microvascular obstruction (MVO), and infarct size (IS). Certain circulating plasma microRNAs (miRNA) have been suggested as potential biomarkers in STEMI. The aim of the study was to determine the association between CMR characteristics of poor prognosis following STEMI and miRNA 133a, 208b, 194 and 214.
Methods: 50 patients with STEMI were prospectively recruited to the study. Patients had plasma miRNA 133a, 208b, 194 and 214 measured at 24 hours following onset of pain. CMR was performed at day 2 following STEMI. 46 patients had analyzable plasma miRNA. Early MVO was measured on dynamic imaging following contrast, persistent MVO was measured at 10 minutes following contrast administration The correlation between MVO and IS, and miRNAs were assessed using Spearman Correlation. All patients provided informed written consent and the study was approved by the regional ethics committee.
Results: None of the 4 miRNA tested had a significant association with early MVO. miRNA 214 significantly correlated with persistent MVO. miRNA 133a and 208b significantly correlated with infarct size (Table 1).

Table 1. miRNA correlation with CMR parameters following STEMI.

	Early MVO	Persistent MVO	Infarct size
mRNA 133a	r=-0.17 (p=0.26)	r=0.22 (p=0.13)	r=0.32 (p=0.03)
mRNA 208b	r=-0.37 (p=0.81)	r=0.18 (p=0.23)	r=0.38 (p=0.01)
mRNA 194	r=0.10 (p=0.51)	r=-0.01 (p=0.96)	r=0.02 (p=0.87)
mRNA 214	r=-0.01 (p=0.96)	r=0.35 (p=0.02)	r=0.26 (p=0.08)

Conclusions: Circulating plasma miRNA 133a and 208b may have potential as biomarkers to predict infarct size following STEMI. Work is ongoing to establish if these miRNAs can predict prognosis.

P4601 | BEDSIDE
Myocardial displacement assessed by 2D speckle tracking echocardiography was helpful to predict microvascular obstruction in patients with ST elevation myocardial infarction after reperfusion therapy

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Microvascular obstruction (MVO) following ST elevation myocardial infarction (STEMI) is associated with larger infarct size and an increased mortality. We hypothesized that the myocardial segmental and global displacements assessed by 2D speckle tracking echocardiography (2DSTE) could predict MVO and transmural necrosis identified by cardiac magnetic resonance (CMR) after primary percutaneous coronary intervention (PCI).
Method: We enrolled 81 patients with first STEMI (Men 76, mean age was 57±8.7 years) undergoing primary PCI within 12h from symptoms onset. Culprit vessels were left anterior descending artery in 45, left circumflex artery in 10 and right coronary artery in 26 subjects. 2DSTE and CMR were performed within 72 hours after PCI. The segmental radial (SRD), longitudinal (SLD), transverse (STD), global radial (GRD), longitudinal (GLD), transverse (GTD) displacements of 18 myocardial segments were measured by Echo-PAC, GE. MVO was identified by late gadolinium enhanced CMR.
Results: There were significant differences in SRD, SLD and STD between presence and absence of >50% transmural necrosis (p<0.001). SRD ≤4.4mm associated with the highest AUC to predict transmural necrosis, with sensitivity of 70% and specificity of 80% (AUC= 0.82; p<0.001) compared to SLD (AUC= 0.62; p<0.001) and SDT (AUC= 0.79; p<0.001). Among the 425 segments with transmural necrosis, there were 277 (65%) segments with MVO. The patients with MVO associated with larger infarct size, lower LVEF, and decreased GRD, GLD and GTD (p<0.01). GRD ≤6.05mm associated with the highest AUC to predict MVO, with sensitivity of 77% and specificity of 74% (AUC= 0.77, p<0.001). GTD ≤5.59mm associated with the highest sensitivity of 88% to predict MVO (AUC= 0.74, p<0.001) compared to GRD and GLD. The sensitivity and specificity of STD ≤3.15mm to predict segmental MVO were 67% and 74% (AUC= 0.77; p<0.001), respectively.
Conclusion: Myocardial displacement assessed by 2DSTE was helpful to predict transmural necrosis and MVO in acute phase of patients with STEMI after reperfusion therapy. SRD is the best to predict transmural necrosis and GRD is the best to predict MVO.

P4602 | BEDSIDE
Can apical ballooning cardiomyopathy and anterior STEMI be differentiated based on b1 and b2-Adrenergic receptors polymorphisms

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Aim: Catecholamine excess along with an exaggerated sympathetic nervous system stimulation appears to play a major role in the pathophysiologic mechanism of Tako-tsubo cardiomyopathy (TTC) which mimic acute ST elevation myocardial infarction (STEMI). The aim of the present study was to verify differences in the distribution of allelic variants of β1 and β2 adrenergic receptor genes between patients with TTC and patients with anterior STEMI compared to a group of normal subjects.
Methods and results: β1 and/or β2 adrenergic receptor polymorphisms in 94 patients with TTC (92 females, 98%; mean age 67.1±11.5 years; range 35 to 87 years) were compared with 109 controls (103 female, 94%; mean age 62.0±10.2 years; range 44 to 92 years) and 59 female patients with anterior STEMI (55 females, 93%; mean age 71.7±12.3 years; range 32 to 96 years). Differences in genotypic frequencies between groups were assessed by means of the Pearson $\chi 2$ test. β1adrenoreceptor (Gly389Arg), β2 adrenoreceptor (Arg16Gly) and β2 adrenoreceptor (Gln27Glu) genotype frequencies were significantly different among the three groups but in the post-hoc analysis, the differences among TTC and anterior STEMI were not anymore significant. The cardiovascular risk factor profile was worse in anterior STEMI who had more commonly a history of diabetes and coronary artery disease.
Conclusion: In a large TTC group of patients compared with anterior STEMI, we found a common relationship between β adrenoreceptor polymorphisms and both pathologies but they were different in terms of cardiovascular risk factors.

P4603 | BENCH
Acute myocardial infarction results in a monocyte genomic response that is conserved between humans and mice

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Purpose: Acute myocardial infarction results in the activation of the innate immune response. Monocytes are critical in this response with roles in myocardial inflammation and repair. In experimental models, the selective targeting of inflammatory monocytes reduces infarct size and adverse left ventricular remodelling. The relevance and applicability of these observations to human disease remains unclear with no immune-modulating therapeutic having yet been translated in this setting to routine clinical practice. We used gene-expression profiling of isolated peripheral blood monocytes in both mice and humans to test the hypothesis that the monocyte response following AMI was conserved between species.
Methods: Female C57BL/6J mice underwent AMI by surgical coronary artery ligation or sham procedure. At 48 hours, CD11b+CD115+Ly6G- monocytes were isolated from blood following terminal anaesthesia by fluorescent activated cell sorting (n=6/group). Peripheral monocytes were isolated by negative selection from 30 patients acutely at the time of presenting with ST elevation myocardial infarction and after 48 hours, and from 24 patients with confirmed stable coronary atherosclerosis as controls. RNA from isolated monocytes was hybridised to Illumina beadchips.
Results: Gene-expression analysis of peripheral circulating monocytes 48 hours following AMI revealed 233 genes were significantly differentially expressed in mice and 122 genes in humans (all P<0.01, FDR<0.25, fold change >1.5). 14 genes including IL1R2 and LCN2 were significantly differentially expressed (P<0.01, FDR<0.25, fold change >1.5) in both species. Gene set enrichment analysis (GSEA) identified a number of biological processes that were significantly enriched in both species e.g. cell adhesion pathways (P<0.01) and MAP kinase signalling (P<0.01). Ingenuity pathway analysis identified a number of upstream regulators conserved between both species e.g. IL6, IL1β, TNF-α (P<0.01) in addition to downstream functions including cell phagocytosis and cell-to-cell signalling (all P<0.001). Furthermore GSEA of both monocyte gene profiles confirmed significant enrichment between datasets (P<0.01, FDR<0.25).

Conclusions: We conclude that the monocyte genomic response 48 hours following AMI is conserved between species, validating the experimental model for (1) investigation of pathogenesis of AMI (2) evaluating new immune-modulating therapeutics and (3) identifying potential therapeutic targets.

CARDIOPULMONARY RESUSCITATION

P4605 | BEDSIDE
Can pH and lactate predict favourable functional status and long-term survival after an out of hospital cardiac arrest? A substudy of the Harefield Cardiac Arrest Study (HCAS)

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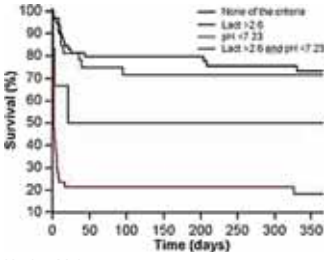
Purpose: An out of hospital cardiac arrest (OOHCA) results in systemic hypoperfusion which is associated with acidaemia and lactaemia. We tested whether pH and lactate values in the post-arrest period would predict favourable functional status and survival.
Methods: The HCAS study analysed 182 patients with OOHCA brought to a Heart Attack Centre. The pH and lactate measurements were available for 144 patients. We anlaysed 1-year mortality and functional status at discharge using a modified Rankins score (mRS: 0-6), where mRS0-3 indicates favourable functional outcome. We determined the optimal criterion values for pH and lactate in predicting these outcomes using receiver operating curve (ROC) analysis and tested these criteria using multivariate models.
Results: ROC analysis identified a cut off for pH<7.3 (AUC=0.84) and lactate>2.6mEq/L (AUC=0.74) for predicting poor functional outcomes and a cut off for pH<7.23 (AUC=0.81) and lactate >2.6mEq/L (AUC=0.83) for predicting 1-year mortality. The positive predictive value of a combined criteria of pH<7.23 and lactate>2.6 for poor functional status was 87%; and 1-year mortality was 81%. Multivariate analyses identified pH<7.23 as a predictor of mRS0-3 (OR=0.21,95%CI: 0.07-0.66, p=0.006) and 1-year mortality (HR=4.41, 95%CI: 2.49-7.81, p<0.001); and lactate>2.6 as a predictor of mRS0-3 (OR=0.32, 95%CI: 0.12-0.85, p=0.022) and 1-year mortality (HR=1.91,95% CI: 1.04-3.52, p=0.039). A combined criteria pH<7.23 and lactate>2.6 was a strong predictor of mRS0-3 (OR=0.22, 95%CI: 0.07-0.71, p=0.011) and 1-year mortality (HR=4.39, 95%CI: 2.50-7.73, p<0.001).



Kaplan-Meier curves.

Conclusions: These data demonstrate that a combined criteria of pH <7.23 and lactate >2.6 in the post-arrest period predicts functional status at discharge and survival at 1 year.

P4606 | BEDSIDE
Accuracy of continuous thermodilution cardiac output by pulmonary artery catheter during therapeutic hypothermia in post-cardiac arrest patients

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Introduction: The accuracy of continuous thermodilution cardiac output measurements (TDCCO) by pulmonary artery catheter (PAC) may be questioned during therapeutic hypothermia in post-cardiac arrest patients. The Fick calculated cardiac output based on pulmonary artery blood gas mixed venous oxygen saturation (FCO-BG-SVO2) may be considered as the golden standard. Continuous SVO2 by PAC (PAC-SVO2) is also not validated during hypothermia.
Methods: We analyzed 102 paired TDCCO/FCO-BG-SVO2 and 88 paired BG-SVO2/PAC-SVO2 measurements in 32 post-cardiac arrest patients during induction and maintenance of therapeutic hypothermia. Two different techniques for cardiac output assessment may be considered interchangeably if (1) the Pearson correlation coefficient (R^2) is >0.60, (2) the bias and limits of agreement are clinically acceptable, (3) the percentage error (=2 times the standard deviation of the bias divided by the mean FCO-BG-SVO2) is <30% and (4) the level of concordance is >90%.
Results: TDCCO was poorly correlated with FCO-BG-SVO2 (R2 0.21) with a large bias (bias -0.15±1.76 l/min), broad limits of agreement ([-3.61; 3.45] l/min) and an unacceptable high percentage error (105%). None of the criteria for clinical interchangeability were met. TDCCO had limited trending ability (R2 0.03). FCO based on PAC-SVO2 was highly correlated with FCO-BG-SVO2 (R2 0.72) with a small bias (-0.08±0.72 l/min) and slightly too high percentage error (44%).
Conclusion: Our results show an extreme inaccuracy of TDCCO by PAC in post-cardiac arrest patients during therapeutic hypothermia. The decision to start or uptitrate inotropics should be based on clinical signs and SVO2 instead of TDCCO.

P4607 | BEDSIDE
The impact of ventricular arrhythmias during acute coronary syndromes: timing matters

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Introduction: Despite improvements in management strategies, ventricular arrhythmias (VA) remain a serious complication of acute coronary syndromes (ACS).
Objective: To assess the predictors and prognosis of VA during ACS, with special attention to arrhythmia timing.
Methods and results: We performed a retrospective observational cohort study including 1373 consecutive patients (P; mean age 64 years, 77.3% male) admitted in a Coronary Unit for the period of 3 years, with a 6 month follow-up. Severe VA were identified in 4.9% P, from whom 88.1% presented ventricular fibrillation and the remaining 11.9% sustained ventricular tachycardia. Considering timing, 91.0% occurred during the first 24 hours (early VA) and 9.0% after that period (late VA). In multivariate analysis, the independent predictors of VA were male sex (p=0.010), systolic blood pressure at admission (p<0.001), ST elevation ACS (p=0.044), renal failure (0.026), heart failure (0.024) and acute stent thrombosis (0.003). P with VA had higher mortality during hospital stay in multivariate analysis (p=0.021). Considering arrhythmia timing, late VA were more frequent in older P (p=0.006) and were associated with markers of disease severity during hospitalization, as heart (p=0.021) and renal failure (p<0.001), left ventricular dysfunction (p=0.010) and higher Grace risk score (p=0.037). Mortality during hospital stay was higher in late VA when compared to early VA (50.0% vs. 13.1%, p=0.020). During follow-up, early VA were not associated with an unfavorable prognosis, but late VA were (Fig. 1).

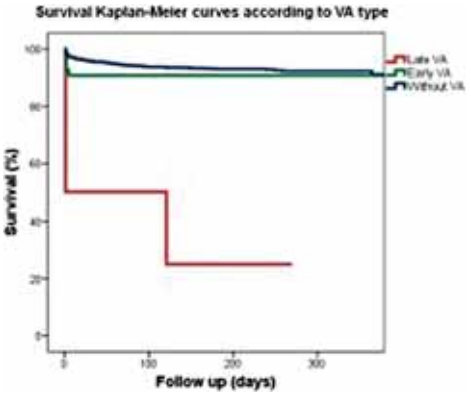

Figure 1

Conclusion: VA timing during ACS may influence prognosis, perhaps because the substract for arrhythmia development at early or late stage is different.

P4608 | BEDSIDE
Impact of time to cooling initiation and time to target temperature in patients treated with hypothermia after cardiac arrest

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Introduction: In patients resuscitated from cardiac arrest (CA) treated with hypothermia (TH), little is known about the role of time to initiation of TH (TIH) and time to target temperature (TTT) in the prognosis of these patients.
Methods: A retrospective analysis was performed on 145 CA survivors who underwent TH between 1/2003 and 1/2013. The objective was to evaluate the independent prognostic impact of TIH and TTT on survival freedom from important neurological sequelae 6 months after CA. Patients were retrospectively divided into 2 groups: Alive and Cerebral Performance Categories Scale [CPC] ≤2 and dead or CPC >2.
Results: At 6 months, 61 patients were still alive (42.1%), 58 them with a good neurological outcome (95.8%). Among these, TH was initiated earlier (TIH: 87±17 min vs. 111±14 min; p=0.042), and the target temperature was achieved more quickly (TTT: 316±30 min vs. 365±27 min; p=0.017). Multivariate analysis selected longer duration of CA (OR 1.06 per min), a non-shockable initial rhythm

Abstract P4608 – Table 1. Characteristics of patients

	Alive and CPC≤2 (n=59)	Death or CPC>2 (n= 86)	Univariante analysis p value	Multivariate analysis		
				OR	95% CI (OR)	p value
Age	57.9 (54.0–61.8)	65.1 (62.3–68.0)	0.003	1.04	1.005–1.076	0.024
Shock on admission	15 (25.4%)	51 (59.3%)	<0.001			
Arterial blood pH	7.26 (7.22–7.29)	7.14 (7.11–7.17)	<0.001	0.009	0.001–0.382	0.014
Initial rhythm (VF/VT)	56 (94.9%)	45 (52.3%)	<0.001	13.775	3.384–56.065	<0.001
T-nonCPR (min)	3.4 (2.2–4.6)	5.6 (4.2–7.0)	0.022			
Time Bystander-CPR (min)	4.9 (3.4–6.5)	5.4 (4.0–6.8)	0.656			
T-ALS (min)	10.8 (8.9–12.7)	16.9 (14.9–18.9)	<0.001			
T-ROSC (min)	19.4 (16.9–22.0)	28.2 (25.6–30.9)	<0.001	1.063	1.013–1.116	0.013
TIH (min)	87 (70–104)	111 (96–125)	0.042			
TTT (min)	316 (286–346)	365 (338–392)	0.017	1.005	1.002–1.009	0.006

(OR 13.8), severe acidosis (OR 0.009 per .01 unit), older age (OR 1.04 per year) and longer TTT (OR 1.04 per min) as associated with a poor prognosis.
Conclusion: The most important prognostic factors for death or lack of neurological recovery in patients with CA treated with TH are initial rhythm, time from CA to ROSC and arterial pH at admission. Although the speed of cooling initiation and the time to reach target temperature may play a role, its influence on prognosis seems to be less important.

P4609 | SPOTLIGHT
Does length of use of CPR feedback devices affect CPR quality?

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Purpose: CPR feedback devices are useful to improve CPR quality in BLSD training, even if it is not known the amount of time they need to be used. In this study we compared the results of using CPR feedback devices for 2-mins and 20-mins.
Methods: We evaluated 1-min compression-only CPR quality using a wireless skill evaluator manikin at the end of two different 5-hour lay-rescuers BLS-D courses (performed according to ILCOR 2010 Guidelines). Course A consisted of 20-minutes training per person with real-time visual feedback by a skill evaluator software, whilst Course B consisted of 2-minutes per person only. The parameters we considered were Total CPR Score (a comprehensive scoring algorithm developed with the collaboration of AHA ECC Subcommittees), number of compressions per minute, percentage of correctly released compressions, compression mean depth and percentage of compressions with correct hand position.
Results: Course A consisted of 111 people (66.7% males; mean age 37.8±11.7 years), whilst Course B consisted of 223 people (53.4% females; mean age 33.9±14.1 years). Sex, weight, height and BMI were not significantly related to Total CPR Score. There was no statistically significant difference (calculated with Mann-Whitney test) between Course A and Course B in Total CPR Score (95% (95%CI, 93.7-97) vs 95% (95%CI, 93-95), p=0.17), number of compressions per minute (118 (95%CI, 116-119) vs 119 (95%CI, 118-120), p=0.25), percentage of correctly released compressions (97% (95%CI, 95.7-99 vs 97% (95%CI, 96-98.6), p=0.70), compression mean depth (53 mm (95%CI, 52.7-54) vs 54 mm (95%CI, 53-55), p=0.56) and percentage of compressions with correct hand position (100% (95%CI, 100-100) vs 100% (95%CI, 100-100), p=0.61).
Conclusions: There was no significant difference between 20-minutes and 2-minutes visual feedback to improve CPR quality. It seems that the use of the feedback device itself, not how long it is used for, has a key role for CPR quality improvement.

P4610 | SPOTLIGHT
Do school children remember BLS one year after 1-hour course?

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Purpose: It has already been demonstrated that school children are able to learn and perform CPR, but their retention of BLS knowledge after 1 year is not known. We want to assess children's knowledge of the BLS sequence one year after the BLS course and compare it to that of an adult group.
Methods: We gave an anonymous questionnaire to a group of school children a year after completing a 1-hour BLS course. The questionnaire consisted of three multiple-choice questions on the first two rings of the Chain of Survival. The first question was about recognizing a person in cardiac arrest, the second was about the importance of the early activation of the emergency system and the third was about the correct compression:ventilation ratio. We gave the same questionnaire to a group of lay adults a year after completing a 5-hour BLS-D course.
Results: The school children group consisted of 84 subjects (52.4% females), mean age 13±0.5 years. The adult group consisted of 49 subjects (57.1% males), mean age 38.8±12.3 years. In the school children group, the first question was answered correctly by 88.1%, the second by 44% and the third by 95.2%. Comparing these results to those of the adults, there was no significant difference (calculated with chi-square test) in the first question (88.1% vs 85.7%, p=0.90) or the second (44% vs 59.2%, p=0.13), but there was a statistically significant difference in the third question answers (95.2% vs 67.3%, p<0.0001).
Conclusions: Children's retention of BLS knowledge after one year is good, but it is necessary to stress more the importance of the early activation of the emergency system. Moreover, the children remember better the correct compression:ventilation ratio than adults, despite the shorter duration of the course.

P4611 | BEDSIDE
Cardiac tamponade is the major cause of death in stanford type A acute aortic dissection: Insight from unenhanced post-mortem computed tomography

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Background: The incidence and cause of death in type A acute aortic dissection (AAD) are little known because of the feature of sudden death and the difficulty in diagnosis. Nowadays, autopsy images, such as unenhanced postmortem computed tomography (uPMCT), is gradually accepted and expected to detect the actual state of sudden death in emergency department (ED).
Purpose: The purpose of this study is to reveal the incidence and cause of death in patients with type A AAD who were transferred to ED due to ardiopulmonary arrest (CPA) and dead in ED.
Methods and results: From April 2009 to March 2012, consecutive 529 patients who were transferred to ED due to CPA were retrospectively reviewed. After trauma and suicide cases were excluded, total 283 patients underwent uPMCT in ED. Among them, 28 patients (9.9%) were diagnosed type A AAD by uPMCT (non-survivors). Visible intimal flap was detected in 13 patients (46.4%), intramural hematoma was in 18/27 (66.7%), and bloody pericardial effusion was in 26 (93%). Bloody pericardial effusion alone was in just 4 patients (14.3%). To evaluate risk factors associated with death in ED, 23 patients survived type A AAD in ED during the same period (survivors) were also analyzed. Bloody pericardial effusion was observed more frequently in non-survivors than survivors (90.3% vs. 36.8%; P<0.001). Logistic regression analysis revealed that bloody pericardial effusion was an independent risk factor for death in ED (Odds ratio =9.57; 95% CI, 1.43-63.8; P=0.020)

Prognostic risk factors in type A AAD

Methods	Univariate analysis				Multivariate analysis			
	OR	Lower 95% CI	Upper 95% CI	P value	OR	Lower 95% CI	Upper 95% CI	P value
Age	1.05	1.00	1.09	0.044	1.05	0.97	1.14	0.253
Gender	2.86	0.88	9.25	0.080	7.06	0.94	52.9	0.057
Diameter of AA	0.94	0.89	1.00	0.066	0.92	0.84	1.01	0.075
IMH of AA	3.74	1.11	12.7	0.034	3.90	0.67	22.8	0.130
Bloody pericardial effusion	16.0	3.53	72.6	<0.001	9.57	1.43	63.8	0.020

AAD indicates acute aortic dissection; OR, odds ratio; CI, confident interval; AA, ascending aorta; IMH, intramural hematoma.

Conclusion: In patients with CPA, around 10% of the patients had Type A AAD and its major cause of death was cardiac tamponade. The evaluation of cardiac tamponade in patients with CPA is crucial in emergency department.

P4612 | BEDSIDE
Difference between comatose patients resuscitated from out-of-hospital cardiac arrest associated with acute coronary syndrome and those with subarachnoid haemorrhage in the emergency department

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Introduction: Comatose patients resuscitated from out-of-hospital cardiac arrest (OHCA) associated with subarachnoid haemorrhage (SAH) often mimic those associated with acute coronary syndrome (ACS) upon clinical and electrocardiographic (ECG) evaluation in the emergency department (ED). The aim of this study was to clarify the difference between resuscitated comatose patients with ACS and those with SAH during initial evaluation in the ED.
Methods and results: Among consecutive 141 patients resuscitated from OHCA, 23 comatose patients resuscitated from OHCA associated with ACS (ACS-OHCA group) and 20 comatose patients resuscitated from OHCA associated with SAH (SAH-OHCA group) were included. The clinical and ECG data obtained during initial evaluation in the ED were compared between the groups. Female gender, asystole or pulse less electrical activity (PEA) as initial cardiac

rhythm, and preserved left ventricular ejection fraction (≥50%) on the echocardiogram were significantly more common in patients of the SAH-OHCA group (P<0.05 in each factor). Although ST-T abnormalities suggesting myocardial damage (ST elevation and/or ST depression) in the 12-lead ECG were found in most of the patients in both groups, absence of ST elevation in any leads without aVR and absence of reciprocal ST depression were significantly more common in patients of the SAH-OHCA group (P<0.05 in each factor).
Conclusions: Despite the difficulty of history taking, gender, initial cardiac rhythm, and the assessment of echocardiogram and 12-lead ECG were important to differentiate between comatose ACS-OHCA patients and comatose SAH-OHCA patients before further diagnostic work up such as coronary angiography and head computed tomography.

P4613 | BEDSIDE
Hemostasis alterations in cardiac arrest patients submitted to coronary interventions and treated with mild hypothermia initiated by cold fluids. A word of caution

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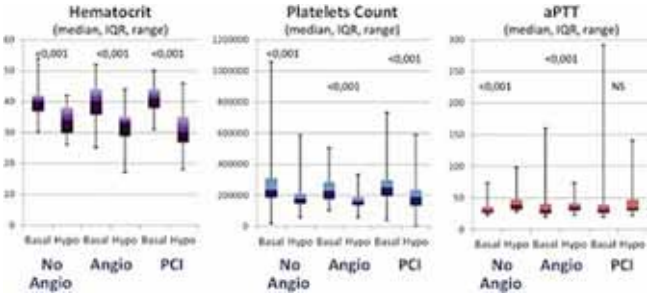
Purpose: Mild (32–33°C) therapeutic hypothermia (TH) affects hemostasis of patients (pts) with out-of-hospital cardiac arrest (OHCA) and crystalloid hemodilution may induce a hypercoagulable state. Both effects could impair the effectiveness of antithrombotics and coronary interventions (PCI). The study aims to elucidate in which way the induction of mild TH by cold crystalloids infusion affects hemostasis and interfere with PCI.
Methods: Observational, prospective analysis of all comatose resuscitated pts. admitted to a tertiary center from March 27, 2004 to December 31, 2012 treated with TH and undergoing early Angio, PCI, or conservatively managed. Mild TH was initiated by a bolus infusion of cold 0.9% saline fluid (4°C; 30 ml/kg/30 min) and maintained for 24 h. At baseline and during TH blood counts and coagulative parameters were assessed.
Results: 141 pts. were enrolled (median: 64.5 (IQR: 55-73) yrs., males: 67%, first shockable rhythm: 70%, interval OHCA-resuscitation ≤20 min: 81%). 97 pts. (69%) underwent early Angio, and 45 (32%) of them PCI. During TH, hematocrit (-21%; p<0,0001) and platelet count (-29%; p<0,0001) declined, whereas APTT increased (+16%; p<0,001) in the overall population as well as in the different groups (see figure below). Bleeding requiring transfusion occurred in 5% of pts., but the risk was higher in PCI treated pts (11%, P=0,0759). No stent thrombosis occurred.



Hematologic changes in different groups.

Conclusion: Mild TH initiated by cold crystalloid fluids infusion is associated with a reduction of hematocrit and platelet count while it prolongs clotting time. These changes should be considered when OHCA patients are submitted to emergency PCI because they could increase the bleeding risk and interfere with interventions.

CORONARY DISEASE

P4615 | BEDSIDE
Effect of cilostazol on carotid intima-media thickness and vascular events in patients undergoing coronary stent implantation

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Purpose: Although patients with coronary artery disease are at increased risk for further ischemic events, changes in intima-media thickness as a surrogate measure of systemic atherosclerosis have not been examined in patients undergoing percutaneous coronary intervention. We assessed the impact of cilostazol on carotid intima-media thickness and vascular events after completion of dual antiplatelet therapy in patients with coronary stent implantation.
Methods: A total of 347 patients with coronary stent implantation who had no indication for further revascularization at angiographic follow-up were randomly assigned to receive aspirin and cilostazol (cilostazol group, n=172) or aspirin monotherapy (aspirin group, n=175) after discontinuation of a thienopyridine. The primary outcome was the change in the mean of the maximal common carotid artery intima-media thickness on both the left and right sides at 2 years after randomization.
Results: The patients had a mean age of 67 years, and 44% of patients had common carotid plaque, defined as intima-media thickness of more than 1.5 mm. At 2 years, the increase in the mean of the maximal common carotid intima-media thickness was smaller in the cilostazol group than in the aspirin group (0.053±0.309 mm versus 0.135±0.259 mm, P=0.02). A composite of death, myocardial infarction, cerebral infarction occurred in 9.4% in patients with carotid plaque and 2.7% in patients without carotid plaque (hazard ratio [HR], 3.71; 95% confidence interval [CI], 1.34 to 10.3; P=0.01). Furthermore, the rate of the vascular events including coronary or cerebrovascular revascularization was 21.5% in patients with carotid plaque and 12.1% in patients without carotid plaque (HR, 1.88; 95% CI, 1.10 to 3.22; P=0.02). The vascular event rate was significantly lower in the cilostazol group than in the aspirin group (12.0% versus 20.3%; HR, 0.56; 95% CI, 0.33 to 0.98; P=0.04). The beneficial effect of cilostazol on clinical outcomes was similar in patients with and without carotid plaque.
Conclusions: Among patients undergoing coronary stenting, the addition of cilostazol to aspirin slowed progression of carotid intima-media thickness after completion of dual antiplatelet therapy, leading to a reduction in vascular events at 2 years.

P4616 | BEDSIDE
Generation differences in long-term clinical outcomes after percutaneous coronary intervention across POBA-era, BMS-era and DES-era

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Background: Since the introduction of balloon coronary angioplasty in 1979, percutaneous coronary intervention (PCI) has evolved with technological advance of devices, improvement of operators' techniques and establishment of medical therapy for secondary prevention. However, little is known regarding improvement of clinical outcomes in patients with PCI in general practice. We examined a temporal trend of the long-term clinical outcomes across the different generations (the POBA era, the BMS era and the DES era).
Methods: We analyzed long-term clinical outcomes in patients with PCI in Juntendo University from January 1984 to February 2010. The patients were divided into three groups according to the procedure data (POBA-era; January 1984 – December 1997, BMS-era; January 1998 – July 2004 and DES-era; August 2004 – February 2010). Primary endpoint was a composite of major adverse cardiovascular events including all-cause mortality, non-fatal myocardial infarction, non-fatal stroke and revascularization.
Results: A total of 3831 patients were examined (the POBA-era; n=1147, the BMS-era; n=1180 and the DES-era; n=1504). The data of baseline characteristics showed that the mean age was higher in the DES-era patients, body mass index was higher in the DES- and BMS-era patients and a higher prevalence of diabetes and hypertension was observed in the DES- and BMS-era. The success rate of PCI was lower among the patients in the POBA-era (POBA; 88.1%, BMS; 95.9% and DES; 95.3%). Unadjusted Cumulative event-free survival rate for 3-year MACE was significantly different among the eras (Figure 1). Multivariable Cox regression analysis showed that the DES-era was a predictor for long-term occurrence of MACE (DES- vs BMS era; hazard ratio (HR) 0.67, 95% confidence interval (CI) 0.49–0.91, P=0.01, DES- vs POBA-era; HR 0.7, 95% CI 0.46–1.08, P=0.1, BMS- vs POBA-era; HR 1.04, 95% CI 0.74–1.50, P=0.8). Body mass index, acute coronary syndrome, statin use and a hemoglobin value were also predictors.
Conclusions: Long-term clinical outcomes in patients who underwent PCI in our general clinical practice were more favorable in the DES-era compared with the BMS- and the POBA-eras, despite the higher risk profiles of the patients in the DES-group.

P4617 | BEDSIDE
Clinical implications of the new adult treatment panel IV (ATP IV) guidelines for secondary prevention in patients undergoing percutaneous coronary intervention

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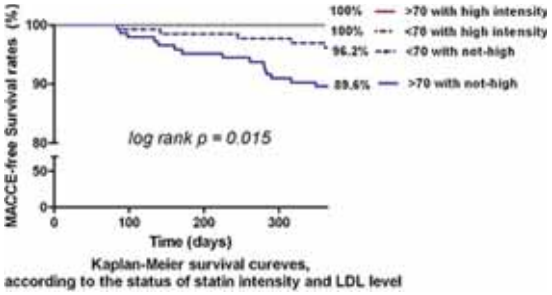
Background: The new ATP guideline recommends high-intensity statin therapy, lowers low-density lipoprotein cholesterol (LDL-C) by ≥50%, with specific statins and doses in patients with atherosclerotic cardiovascular disease. But the effectiveness of high-intensity statin therapy in real-world clinical practice is not known.
Methods: We included 304 statin naïve patients undergoing percutaneous coronary intervention (PCI), and compared incidence of 1 year-MACCEs including death, acute MI, ischemic stroke and revascularization between high-intensity (atorvastatin 40 or 80 mg, rosuvastatin 20 or 40 mg) Vs. low to moderate-intensity statin therapy (other statins or dose), ≥50% Vs. <50% reduction of LDL-C level and <70 mg/dL Vs. ≥70 mg/dL of LDL-C level.

Results: The incidence rates of 1-year MACCEs were significantly lower in patients with ≥50% reduction in LDL-C level, <70 mg/dL of LDL-C level (1.4% vs 8.2%; p=0.042, 3.5% vs. 9.4%; p=0.015). Patients treated with high-intensity stain therapy tend to have a lower rates of 1-year MACCEs although it is not statistically significant (0% vs. 7.3%; p=0.126). 1-year MACCEs free survival rates according to the combined status of statin intensity and LDL-C level were significantly different between four groups (<70 mg/dL with high-intensity Vs. ≥70 mg/dL with high-intensity Vs. <70 mg/dL with low to moderate-intensity Vs. ≥70 mg/dL with low to moderate-intensity; 100% Vs. 100% Vs. 96.2% Vs. 89.6%; log rank P=0.015). (figure)



Kaplan-Meier survival cureves, according to the status of statin intensity and LDL level

Conclusions: Among patients undergoing PCI and need secondary prevention, lowering LDL-C level below 70mg/dL and above 50% reduction of LDL-C show the better clinical outcomes. Additionally, patients treated with high-intensity statin therapy was associated with improved clinical outcomes regardless of LDL-C level.

P4618 | SPOTLIGHT

No temporal improvements in survival after out-of-hospital cardiac arrest in patients with a history of chronic obstructive pulmonary disease

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Purpose: Survival after out-of-hospital cardiac arrest (OHCA) has tripled during the past decade following national initiatives to improve cardiac arrest management in Denmark. However, it remains unknown whether changes were consistent in patients with a history of chronic obstructive pulmonary disease (COPD).
Methods: Patients >18 years old with OHCA of a presumed cardiac cause, and in whom resuscitation was attempted, were identified through the Danish Cardiac Arrest Registry 2001–2011.
Results: A total of 3,399 patients with a history of COPD up to ten years prior to OHCA were included. The median age was 75 years (interquartile range 68-81) and 61.2% were men. OHCA in private-home location constituted 81.3%; 48.7% of the arrests were witnessed; the median time from recognition of arrest to rhythm analysis by ambulance-crew was 12 minutes (interquartile range 7-19); and 15.4% of the patients had a shockable rhythm as a first recorded heart rhythm. Bystander cardiopulmonary resuscitation (CPR) increased significantly during the study period, from 17.2% in 2001 to 49.4% in 2011, p<0.0001. Survival upon hospital arrival increased over time from 8.9% in 2001 to 20.8% in 2011, p<0.001 (Fig. 1), whereas no significant changes were observed in 30-day survival: 4.4% in 2001 to 4.1% in 2011, p=0.06; or in 1-year survival: 3.8% in 2001 to 3.0% in 2011, p=0.13.

Conclusions: In patients with COPD survival upon hospital arrival increased significantly over time while 30-day and 1-year survival did not. These findings indicate that improvements made in pre-hospital settings had an impact, but improvements in in-hospital cardiac arrest management had no impact on long-term survival for patients with a history of COPD.

P4619 | BEDSIDE

Superiority of wall motion score index over left ventricle ejection fraction in predicting cardiovascular events after a non-anterior acute myocardial infarction

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Purpose: There are few data on the prognostic significance of the wall motion score index (WMSI) compared with left ventricle ejection fraction (LVEF) after an acute myocardial infarction (AMI). Previous studies suggest the superiority of WMSI in patients with less myocardial damage. They calculate these echocardiographic variables during the hyperacute postinfarction period, when the regional compensatory hyperkinesis of healthy segments is maximal and it could pose a limitation in their comparison. Our objective was to compare WMSI and LVEF after the hyperacute phase of non-anterior AMI.
Methods: We analyzed the echocardiograms of 165 consecutive patients (76% male; mean age: 63.7±13.5 years) admitted for non-anterior AMI. They were performed after the first 48 hours of admission and before hospital discharge. We evaluated the correlation between WMSI and LVEF and their ability to predict the combined endpoint (all-cause mortality and rehospitalization for heart failure) as a primary objective and the independent events of the combined endpoint as a secundary objetive.
Results: There was a strong negative linear correlation between WMSI and LVEF (r=0,72; p<0.0001). During a median follow up of 30.45 months (24.23-49.47), 41 patients (14.7%) presented the combined endpoint, 30 (10.9%) died and 17 (6.1%) were hospitalized for HF. By univariate analysis, both LVEF and WMSI were predictors of the combined endpoint and all-cause mortality (p<0.0001), although only WMSI was a predictor of readmission for HF (p=0.008). By multivariate analysis, WMSI proved to be a more powerful predictor of events. When WMSI was included in the model, LVEF did not provide additional prognostic information (predictive model of clinical variables: R2=0.34; predictive model of clinical variables and WMSI: R2=0.42; predictive model of clinical variables and LVEF: R2=0.36)
Conclusions: Both LVEF and WMSI provide important prognostic information after a non-anterior myocardial infarction. Beyond the hyperacute phase, WMSI is a more powerful prognostic predictor.

P4620 | BEDSIDE

Hyperglycemia at admission in acute myocardial infarction: can it predict the long-term prognosis?

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Purpose: The predictive value of elevated plasma glucose during an episode of acute myocardial infarction (MI) has been evaluated mainly in the setting of short-term prognosis. We aimed to evaluate the impact of admission glycaemia in diabetic and non-diabetic patients, admitted for acute MI, in long-term increase risk.
Methods: We evaluated 2462 patients, admitted to an intensive care unit for acute MI, from May 2004 to August 2013. The patients were divided in four groups according to the quartiles of glycaemia at admission: group 1 (≤100 mg/dL – n=606, 24.6%), group 2 (101-122 mg/dL – n=616, 25.0%), group 3 (123-162 mg/dL – n=620, 25.2%) and group 4 (≥163 mg/dL – n=620, 25.2%). Clinical and laboratorial characteristics, management and follow-up were analyzed.
Results: This sample included 722 (29.3%) previous diabetic and 1740 (70.7%) non-diabetic patients. Hyperglycaemia at admission was associated to worse global cardiovascular risk profile, more ST elevation, higher levels of necrosis and inflammation biomarkers, lower left ventricle ejection fraction, higher oral glucose tolerance test and glycated haemoglobin (HbA1c). Group 4 patients had significantly higher in-hospital mortality, compared with other groups. However, in a multivariate regression analysis, hyperglycaemia at admission was not significantly associated with higher in-hospital mortality. The 1 and 2-year mortality was higher in group 4 and a glycaemia at admission ≥163 mg/dL was an independent predictor of long-term mortality.

Glycaemia at admission and mortality

Glycaemia at admission (mg/dL)	In-hospital mortality (%)	1-year mortality (%)	2-year mortality (%)
≤ 100	2.8	3.9	6.0
101–122	3.1	4.8	5.4
123–162	5.0	4.1	5.0
≥ 163	13.4	9.2	12.3

Conclusions: The role of hyperglycemia at admission in acute MI, more than being a stress-induced marker, appears to be associated to undetected disorders of glucose metabolism or diabetes, representing an independent predictor of long-term prognosis but not of in-hospital mortality.

P4621 | BEDSIDE
Prehospital STEMI diagnosis - Is electronic ECG transmission superior to paramedic cardiac catheterization lab activation?

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Introduction: Prehospital STEMI diagnosis with direct cardiac catheterisation lab transfer, with an emergency department bypass strategy, significantly reduces door to balloon (DTB) time in primary percutaneous intervention (pPCI). Prehospital diagnosis may be made by paramedics in the field or by a physician via electronic ECG transmission to a hospital-based computer or smart phone. At present, despite a national acute coronary syndrome programme, electronic ECG transmission is possible in only some ambulances in the west of Ireland, and national implementation of such a system would be costly. This allowed a direct comparison between both modes of prehospital STEMI diagnosis in the same region, within the same ambulance service over a given time period.
Purpose: The aims of this study were twofold. First, to investigate whether electronic ECG transmission, reduced the rate of inappropriate cardiac catheterisation lab activation in the west of Ireland, and second, to determine whether prior ECG transmission improved DTB time in these patients.
Methods: All patients transferred by ambulance directly to the cath lab as a 'Code STEMI' over a fifteen month period were included. Transmitted ECGs were matched with corresponding patients.
Results: In total, 76 patients were transferred directly from ambulance to cath lab with a prehospital diagnosis of STEMI. 46 (60.5%) had prior ECGs transmission. Of these, there were 6 (13.0%) inappropriate referrals versus 7 (23.3%) in the 30 patients without ECG transmission (p=0.09). The mean door to balloon time for those with transmitted ECGs was 42.9 minutes versus 41.0 for those without (p=0.76).
Conclusion: ECG transmission did not significantly reduce the rate of inappropriate cath lab activation. Moreover, ECG transmission did not impact on DTB time in patients transferred directly to the cath lab. ECG transmission did not confer any significant advantage in this small patient cohort. This should be reassessed in time with a larger sample size.

P4622 | BEDSIDE
Impact of emergency medical service use on ischemic time intervals in ST-elevation myocardial infarction patients

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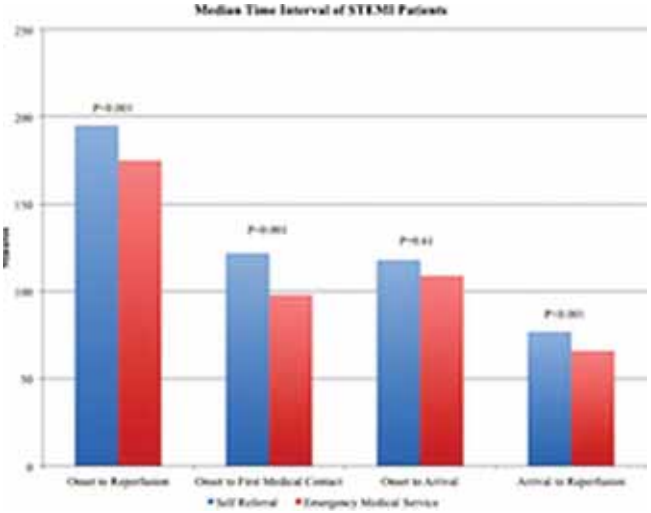
Background: Ischemic time is an important prognostic factor in STEMI patients. Emergency medical service (EMS) utilization can reduce different components of ischemic time by appropriate triage of STEMI patients.
Methods: Data from the Acute Coronary Survey in Israel registry (ACSIS) 2000-2010 were analyzed to evaluate factors associated with EMS use, and its impact on different components of ischemic time.
Results: The study population comprised of 3031 STEMI patients treated with primary reperfusion therapy (64% primary PCI and 36% thrombolysis) among whom only 1566 patients (52%) used EMS. Predictors of EMS use were family history of ischemic heart disease (OR=1.25, p=0.02), syncope (OR=1.37, p=0.04) and dyspnea (OR=2.02, p=0.006), while hypertension and smoking were predictors of self referral (OR=1.22, p=0.02 and OR=1.27, p=0.005, respectively). EMS use reduced onset-to-reperfusion time (175 IQR [120-260] vs. 195 IQR [130-330] min. p<0.001), mainly by reducing time to first medical contact (98 IQR [53-175] vs. 122 IQR [66-270] min, p<0.001), arrival-to-reperfusion time (66 IQR [48-74] vs. 77 IQR [69-75] min. p<0.001), without an impact on onset to hospital arrival time (109 IQR [72-186] vs. 118 IQR [62-231], p=0.61). On a multi-variate analysis, reduction in arrival-to-reperfusion time was associated with reduced cardiovascular events at 30 days (OR=0.51, p=0.02).
Conclusion: EMS use is more prevalent among high-risk STEMI patients, with a presentation of heart failure and syncope, reduces ischemic time, which is associated with reduced cardiovascular events at 30 days.



P4623 | BEDSIDE
Stable coronary artery disease, quality of life, and atrial fibrillation. AVANCE study. A national survey

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Purpose: To assess whether atrial fibrillation (AF) was associated with quality of life (QOL) in a national-wide survey of patients with stable coronary artery disease (SCAD).
Results: See Table. Patients with AF were significantly older, had higher heart rate, had more comorbidities and had a lower estimated glomerular filtration rate. ARB, ACEI, statins were similar among groups. There was a trend to a higher use of beta blockers among AF patients (p=0.08). AF patients also had significantly more anginal episodes per week, and had a higher rate of prior CABG. QOL was significantly worse in AF patients than SR in all SAQ domains. After adjustment with covariates significant at bivariate analysis, AF was no longer significantly associated with worse QOL.
Methods: Two thousand and thirty-nine patients with SCAD were consecutively recruited in an observational, multicentric, transversal registry. There were 62 patients with no information on rhythm; other 36 were on pacemaker rhythm. There were 116 patients with AF (6.0%) and 1825 in sinus rhythm (SR). Seattle angina questionnaire (SAQ) was filled by the patients.

Table 1

	Sinus rhythm (n=1825)	AF (n=116)	P
Age, years	67.2±10.4	75.1±7.0	<0.005
Male, %	73%	73%	NS
Heart rate, bpm	66.1±10.6	73.8±14.2	<0.005
Antiaggregation, %	95.2	76.7	<0.005
Anticoagulation, %	4.5	87.9	<0.005
Renal disease, MDRD<60, %	9.9	19.8	0.002
SAQ domains (healthy person = 100)			
Physical limitation	55.8±20.5	44.2±23.0	<0.005
Stability of angina	67.3±30.4	59.4±31.0	0.009
Frequency of angina	83.8±20.4	78.7±21.5	0.012
Satisfaction with treatment	75.8±15.2	70.1±18.8	0.002
Perception of disease	59.9±22.9	54.4±24.0	0.16

Conclusions: AF patients had a statistically significant worse QOL than patients with SR. However, after adjustment this difference was not statistically significant, suggesting that AF in SCAD patients is rather a marker of comorbidities and older age rather than a marker of QOL.

P4624 | BEDSIDE
Impact of cardiac computer tomography on the frequency and disease severity of patients with suspected angina who are referred for invasive coronary angiography

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Purpose: In 2008 coronary computer tomographic angiography (CCTA) was introduced as a routine imaging modality at our hospital. We wanted to assess the impact of CCTA on 1) the frequency of patients with suspected angina referred for invasive coronary angiography (ICA), and 2) the proportion of significant stenosis detected on ICA after the introduction of CCTA.
Methods: From 2007 to 2012 all patients with suspected stable angina undergoing elective ICA were considered and the number of patients with significant stenosis (≥50% diameter stenosis) were noted. In 2012, in order to define the pattern of diagnostic methods and downstream testing, all patients with suspected angina and referred for exercise-test, CCTA, single-photon emission computed tomography (SPECT) or ICA were registered.
Results: From 2007 to 2012 a total of 1551 patients suspected of stable angina were referred for ICA. No significant differences in the absolute number of patients undergoing ICA per year was seen (figure; p=0.85).The relative number of patients with significant stenosis on ICA did not significantly change over time: 37%, 38%, 37%, 44%, 43% and 32% (figure; p=0.75). Amongst 1069 patients which were examined for suspected stable angina in 2012 the pattern of diagnostic methods was: exercise-test (n=37), CCTA (n=450), SPECT (n=310) and ICA (n=272). CCTA triggered 44 ICA, of which 19 (43%) had significant stenosis. SPECT triggered 52 ICA, of which 12 (23%) were positive.
Conclusion: The introduction of CCTA for routine clinical use did not affect the frequency of patients with suspected stable angina referred for ICA. Surprisingly, neither the proportion of patients with significant coronary stenosis on ICA

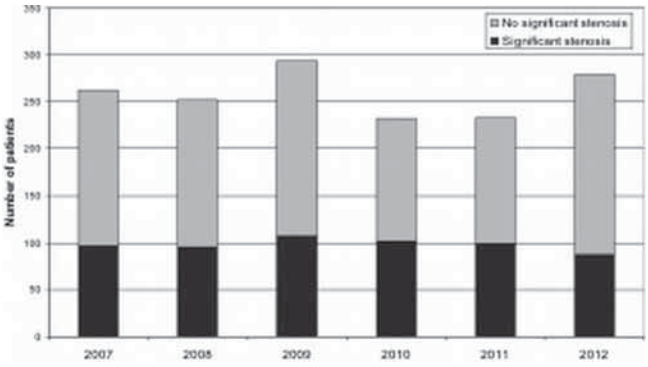

Figure 1. Frequency of ICA.

changed significantly over time. Finally, CTCA did not result in excessive invasive downstream testing.

ACUTE CORONARY SYNDROMES: ONGOING CHALLENGES

P4626 | BEDSIDE
Three decades of acute coronary syndrome: are we there yet?

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Purpose: Despite therapeutic advances in recent decades, ischemic heart disease remains the leading cause of death worldwide. We intended to evaluate changes in the profile and management of patients with acute coronary syndrome (ACS) over the past 3 decades.
Methods: Prospective study of 1999 patients admitted for ACS, in different periods of the last 3 decades, to our tertiary hospital intensive care unit. We divided the patients into 3 groups: patients admitted between October (Oct) 1989 - Oct 1992 [group A: n=516, 25.8%; 64.3% male; 30.2% unstable angina (UA)]; patients admitted between Oct 1999 - Oct 2002 (group B: n=663, 33.2%; 64.4% male; 20.2% UA) and patients admitted between Oct 2009 - Oct 2012 (group C: n=820, 41%; 68.9% male; 12.9% UA). We compare them with respect to baseline characteristics, treatments performed and outcomes during hospitalization and at 1 year follow-up.
Results: Group C had lower in-hospital mortality (A=14.1% vs B=11.8% vs C=6.7%, $p<0.01$), and at one year follow-up (A=24.8% vs B=21.9% vs C=13.0%, $p<0.01$). Baseline characteristics showed no differences between groups in terms of gender, age and previous history of diabetes, but group C had more previous history of myocardial infarction (A=6.6% vs B=4.2% vs C=20.7%, $p<0.01$) and hypertension (A= 53.7% vs B=48.9% vs C=67.6%, $p<0.01$), while group A had more history of smoking (A=38.8% vs B=31.2% vs C=31.2%, $p<0.01$) and angina (A= 51.2% vs B=19.3% vs C=24.9%, $p<0.01$). In respect to risk stratification group B was more frequently submitted to thrombolysis (A=5.6% vs. B=9.5% vs. C=0.6%, $p<0.01$) while group C was more often treated by percutaneous coronary intervention (A=13.2% vs B=31.5% vs C=81.0%, $p<0.01$). In terms of medical treatment group C was more often treated with aspirin (A=90.1% vs B=87.5% vs C=97.1%, $p<0.01$), beta-blocker (A=25.2% vs B=46.6% vs C=50.7%, $p<0.01$) and angiotensin-converting enzyme inhibitors (A=19.6% vs B=29.6% vs C=60.2%, $p<0.01$). As for complications, group A had more ischemic arrhythmias (A=19.4% vs B=21.7% vs C=12.9%, $p<0.01$), need for temporary pacemaker (A=5.2% vs B=2.6% vs C=1.7%, $p<0.01$), prevalence of post- infarction angina (A=47.6% vs B=38.1% vs C=14.3%, $p<0.01$) and evolved more frequently in Killip class>1 (A=37.5% vs B=28.7% vs C=25.9%, $p<0.01$).
Conclusion: The advent of new therapies, particularly percutaneous coronary intervention, has improved the prognosis of patients admitted with ACS, with these now presenting less and less in-hospital complications as well as lower mortality both during in-hospital stay and at 1 year follow-up.

P4627 | BEDSIDE
Appropriateness of helicopter transfer for primary percutaneous intervention in a national acute coronary syndrome programme

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Introduction: The National Acute Coronary Syndromes Programme in Ireland advocates transfer of STEMI patients from the field or from outside hospitals directly to the cardiac catheterisation lab of primary PCI centres, bypassing the emergency department, if feasible within 90 minutes of diagnosis, with a target diagnosis to reperfusion time of less than 120 minutes, and an acceptable rate of inappropriate cath lab activation of 15%. We are currently experiencing a surge in helicopter transfer of such patients.
Aims: The aim of this study was to determine the appropriateness of helicopter transfer of STEMI patients for primary PCI, in terms of success rates both in prehospital diagnosis and in achieving target times.
Methods: Paramedic documentation and electrocardiograms of all patients transferred directly to the catheterisation lab for primary PCI by helicopter over a 7 month period were reviewed.
Results: There were 50 helicopter transfers to the catheterization lab over the 7 month period, 38 (76%) from the field and 12 (24%) from outside hospitals. From the field, 31 (81.6%) STEMI diagnoses were correct. Of these, 30 patients (96.7%) underwent primary PCI. 17 (56.7%) achieved diagnosis to door times of less than 90 minutes (median 83, range 47-161 minutes) and 13 (43%) were reperfused within 120 minutes of diagnosis (median 137, range 52-214 minutes). There were 5 helicopter transfers from outside hospitals for primary PCI. 1 (20%) achieved the target door and reperfusion times of 90 and 120 minutes respectively. Median diagnosis to door and reperfusion times were 130 minutes (range 68-239), and 141 (range 120-287) minutes respectively. For the remaining 4 cases (80%), awaiting helicopter transfer delayed reperfusion therapy as no patient had a contraindication to thrombolysis at an outside hospital.
Conclusion: Among field transfers, rate of inappropriate activations was in line with international standards. For transfers from the field, times achieved were suboptimal. For transfers from outside hospitals, rates in achieving target times were poor, with helicopter transfer sometimes causing unnecessary treatment delays. Helicopter transfer for primary PCI in Ireland should be utilised only if anticipated ECG to primary PCI centre door time is less than 90 minutes. Otherwise, immediate thrombolysis should be considered prior to transfer.

P4628 | BEDSIDE
Comparative effects of "nitrate centered" and "diuretic centered" treatment of acute decompensated heart failure on clinical congestion, NT-proBNP and renal function markers

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Background: Our purpose was to compare effects of prolonged optimal-dosed nitrate infusion plus low doses of i.v. diuretics ("nitrate centered strategy" - NC) and moderate doses of i.v. diuretics plus short intermittent nitrate infusion ("diuretic-centered strategy" - DC) on congestion symptoms and signs, NT-pro-BNP and renal function markers (eGRF and Cystatin C) in pts with acute decompensated heart failure (ADHF).
Methods: In single-blind parallel-group randomized study we assigned pts with "wet-warm" ADHF to receive either optimal-dosed GNT infusion ≥72 hrs plus low doses of i.v. diuretic (≤80 mg pd for furosemide), NC group, n=19 per protocol, age 59,4±1,1 yrs or moderate doses of i.v. diuretic (41-120 mg pd for furosemide) plus short intermittent (<10hrs pd, ≤3 days) GNT (DC group, n=48 per protocol, age 62,1±1,7 yrs). Primary endpoints were dyspnoe assessed by Borg scale and eGRF (MDRD) at days 4-6 (D4-6) and discharge (Dsc), as well as serum Cystatin C and NT-pro-BNP (ELISA) at D4-6 and D25.
Results: Total 1st week furosemide dose in NC group was 192±20,9mg, in DC group – 396±15,3mg, duration of GNT infusion – 3,2±0,3 vs 0,76±0,07 days ($p<0,001$). Symptomatic hypotension occurred in 3 (23%) and 2 (3,4%) pts, correspondingly, and transfer to p.o. diuretics in 7,3±1,3 and 8,5±1,7 days ($p<0,05$). While dyspnoe intensity at D1 in NC group was 7,8±0,4 and DC - 7,1±0,36 ($p>0,05$), its on-treatment decrease ($p<0,01$ from D1 in both) was more pronounced in NC group (at D4-6 - 4,1±0,2 vs 5,2±0,3, $p<0,05$, at Dsc - 2,2±0,13 vs 2,8±0,17, $p>0,01$). The same was true for CVP lowering from D1 (correspondingly, 194±14,7 and 186±12,9 mm H20, $p>0,05$) to D4-6 (78±5,2 vs 97±5,8mm H20, $p<0,05$ between groups). NT-pro-BNP, eGRF and Cystatin C data see in table.
Conclusion: In ADHF patients "nitrate centered" strategy compared to "diuretic centered" one is associated with more pronounced and more early clinical decongestion and NT-pro-BNP lowering, as well as better preservation of renal function assessed by eGRF and Cystatin C.

Abstract P4628 – Table 1

Groups	NT-pro-BNP, M ± m pg/ml			eGFR, M ± m ml/min per 1.73 m^2			Cystatin C, M ± m ng/ml		
	D1	D4–6	D25	D1	D4–6	Dsc	D1	D4–6	D25
NC	1238±342	871±244**#	747±128**#	65±3,9	54±3,2*	85±5,77**#	3271±517	3528±624**#	2714±478**#
DC	1172±304	1061±271	871±249**	61,5±3,78	48±2,95**	67±4,84	3314±578	3895±683**	3071±614**

*p<0,05, **p<0,01 compared to D1; #p<0,05 compared to Group DC.

P4629 | BEDSIDE
Survival of patients presenting as sudden cardiac arrest with STEMI on post-resuscitation ECG is dependent on the initial arrest rhythm

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Purpose: Patients presenting with cardiac arrest, suspected of having acute coronary syndrome (ACS) have high mortality. Post-resuscitation ECG showing ST elevation myocardial infarction (STEMI) is used to identify patients who may benefit from emergent revascularization. Our aim was to determine if the initial cardiac arrest rhythm predicts survival.
Methods: At our large, academic medical center, all patients who had cardiac arrest prior to emergent coronary angiography between Jan 1, 2001 and Dec 31, 2010 were studied. The post-resuscitation (pre-cath) ECG's were reviewed by 3 cardiologists who were blinded to the outcome, to confirm the diagnosis of STEMI. Survival of the patients during the index hospitalization was correlated with whether the rhythm was shockable (ventricular tachycardia/fibrillation) or non-shockable (Pulseless Electrical Activity/Asystole).
Results: Of 188 patients who had cardiac arrest prior to emergent angiography, 166 had a post-resuscitation (pre-cath) ECG available for review. Of those, 89 patients with a confirmed STEMI compatible ECG were further analyzed (see Table1). Chi-square test and Fisher's exact test were used to compute statistical significance. The age range was 22-92 years (mean 62.5 yrs ±13.6), 76% were male.

Patients with STEMI on post-resuscitation ECG (n=89/166 [53.6%]).

	Shockable rhythm n=76/89 (85.4%)	Non-shockable rhythm n=13/89 (14.6%)	p-value
Survival	47/76 (61.8%)	0/13 (0.0%)	<0.0001
Full Neurologic Recovery	42/47 (89.3%)	N/A	N/A

Conclusions: Survival of patients presenting with sudden cardiac arrest, who had STEMI on post-resuscitation ECG and subsequent emergent angiography with successful revascularization, is dependent on whether the initial arrest rhythm was shockable or not. Those patients who survived had good neurologic recovery. In contrast, those with an initial non-shockable rhythm uniformly had poor survival.

P4630 | BEDSIDE
Cardiac arrest in a 10-year primary percutaneous coronary intervention registry: incidence, features and outcome

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Purpose: Three-quarters of deaths consequent to acute coronary syndrome occur in pre-hospital phase, probably caused by cardiac arrest (CA). There are limited data about survival of patients (pts) with STEMI and out-of-hospital cardiac arrest (OHCA) treated with primary PCI (PPCI), because of their exclusion from interventional trials and registries due to their extremly poor survival. Further, ESC STEMI Guidelines just in 2012 recommended the treatment with PPCI of those patients.
Methods: We retrospectively analyzed the data of 1289 consecutive pts with STEMI admitted for PPCI in our tertiary center from December 1st, 2003 till December 31, 2012. Pts were divided in two groups: STEMI and STEMI-OHCA. Afterwards, we grouped STEMI-OHCA patients as following: STEMI-OHCA comatose or not and STEMI-OHCA with CA before (strictly out-of-hospital, OH) or after (intra-hospital, IH) Emergency Medical System (EMS) call.
Results: In our population there were 82 (6.4%) pts with STEMI-OHCA, 54 comatose (65.8%) and 52 (63.4%) with CA strictly OH. CA was due to shockable rhythm in 95% of pts. In comparison to STEMI group pts from STEMI-OHCA were younger (62 vs 66 yr, p 0.014), haemodinamically more frequently instable (higher TIMI index, Killip class, percentage of shock; all $p<0.05$), with more frequent LAD lesions (66 vs 47%, p 0.002) and LM (4 vs 0.7%, p 0.02). Again the in-hospital, 30-day and overall mortality of pts from STEMI-OHCA group was higher (20 vs 6%, 20.7 vs 6.6%, 31.7 vs 10.5%; $p<0.001$), but peculiarly more events were observed among those comatose (30 vs 0%, 32 vs 0%, 37 vs 28%; $p<0.001$) and with OH (28.8 vs 3.3%, p 0.05; 28.8 vs 6.7%, p 0.017; 38.5 vs 20%, p 0.08). The presence of shock was associated with very bad outcome (HR 3.775, $p<0.001$), either in STEMI and STEMI-OHCA pts.
Conclusions: Pts with STEMI-OHCA treated with PPCI have higher short, mid e long-term mortality than pts with STEMI without CA. However, pts with STEMI-OHCA non-comatose and with CA after EMS call have short and mid-term similar to pts with other STEMI.

P4631 | BEDSIDE
Clopidogrel vs. prasugrel and ticagrelor in patients with acute myocardial infarction complicated by cardiogenic shock: An IABP-SHOCK II sub-analysis

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Purpose: All randomized controlled trials comparing clopidogrel with prasugrel or ticagrelor excluded patients with acute myocardial infarction (AMI) and cardiogenic shock. Therefore, prospective data is lacking comparing different ADP-receptor antagonsits in this setting. The aim of this sub-analysis of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial was to compare the clinical outcome of patients treated with clopidogrel vs. the more potent ADP-receptor antagonists prasugrel or ticagrelor in cardiogenic shock.
Methods: In the primary study 600 patients with cardiogenic shock complicating an AMI were included and randomized to the IABP or no-IABP group between June 2009 and March 2012. The primary endpoint of the sub-analysis was 30-day and 1-year all-cause mortality with respect to different ADP-receptor antagonists. Secondary safety endpoints were GUSTO bleedings during the 1-year study period.
Results: After exclusion of patients not receiving an ADP-receptor antagonist as acute medical therapy (86 patients) or those receiving different ADP-receptor antagonists as acute medical therapy (14 patients), 498 patients were analysed. 387 patients (77.7%) received clopidogrel and 111 patients (22.3%) either prasugrel or ticagrelor as acute antiplatelet therapy. Baseline patient characteristics differed significantly between patients receiving clopidogrel or the potent drugs prasugrel/ticagrelor. Unadjusted all-cause 30-day and 1-year mortality was lower in prasugrel/ticagrelor vs. clopidogrel treated patients (30-day: 29.7% vs. 41.9%, $p<0.05$, 1-year: 38.0% vs. 54.4%, $p<0.01$). In a multiple logistic regression analysis, the adjusted rate of mortality did not differ for both time points between both groups (OR: 1.24, 95% CI 0.72-2.12, p=0.44). Unadjusted bleeding complications were lower in prasugrel/ticagrelor vs. clopidogrel treated patients (30-day: combined GUSTO bleedings: 18.0% vs. 29.3%, $p<0.05$, 1-year: combined GUSTO bleedings: 21.5% vs. 35.5%, $p<0.05$). Adjusted bleeding complications will be presented at the congress.
Conclusion: The comparable outcome with respect to the adjusted rate of mortality suggests that the use of potent receptor antagonists like prasugrel or ticagrelor in AMI patients complicated by cardiogenic shock might not be associated with an improved survival, however, we did not detect an increase in bleeding complications in prasugrel/ticagrelor treated patients indicating that the use of prasugrel or ticagrelor might not be harmful in selected patients.

P4632 | BEDSIDE
Prevalence and significance of troponin elevations in patients without acute coronary disease

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Purpose: The frequency and prognostic importance of elevated troponin concentrations in patients with acute coronary syndrome (ACS) have been thoroughly described in previous publications. Only few studies have examined troponin concentrations in the general hospitalized population without suspicion of ACS. The purpose of this study is to describe and compare the prevalence of elevated troponin T (cTnT) and troponin I (cTnI) concentrations measured with recently developed high-sensitive assays in an unselected, consecutive population of patients, admitted to an emergency department.
Method: Patients aged >18 years admitted to an emergency department in a district hospital were included in the study. Blood samples were drawn at admission. CTnT was analysed with a high-sensitive cTnT assay with a limit of detection (LoD) of 5ng/L and a 99th percentile of 14ng/L. CTnI was measured using a new high-sensitive research cTnI assay with a LoD of 0,8ng/L and a 99th percentile of 48ng/L.
Results: Between the 10th and 24th of May 2013, 1097 patients were admitted to the emergency department. 99.5% of the patients agreed to participate and serum was available in 1029 (92.3%) of patients. ACS was suspected in 128 (12.4%) of the patients. The remaining patients were admitted with a broad spec-

Elevated hscTnI and hscTnT

	Median (IQR)(ng/L)	n >99th percentile (%)
All patients (n=1029)		
hscTnI	3.2 (1.0–9.9)	82 (8.0%)
hscTnT	10.2 (4.4–23.3)	406 (39.5%)
All patients admitted with other diagnoses than ACS (n=901)		
hscTnI	3.3 (1.1–10.3)	68 (6.6%)
hscTnT	10.5 (4.4–23.3)	368 (35.8%)

trum of medical and surgical conditions. HscTnI was detectable in 84.9% of the patients and HscTnT in 84.0% ($p<0.05$). For HscTnI and HscTnt concentrations, see table. Elevation of troponin (>99th percentile) was significantly more frequent for HscTnT than for HscTnI (39.5% vs. 8.0%, $p<0.001$). Both HscTnI and HscTnT were significantly correlated with age and glomerular filtration rate, the correlation for HscTnI was however significantly weaker than for HscTnT.
Conclusion: Of patients admitted to the hospital with diagnoses other than ACS, hscTnT was elevated above the 99th percentile in more than 1/3 of the patients and hscTnI in less than 1/10. These results demand questions asked on the specificity of troponin elevations for ACS especially for troponin T. Furthermore, the results emphasize the need of further studies on the release mechanisms of the cardiac troponins.

P4633 | BEDSIDE
Left main coronary artery disease in elderly: clinical situation and long-term prognosis in percutaneously revascularized patients

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Purpose: Is to evaluate the clinical characteristics and prognostic impact of left main coronary artery disease (LMCA) angioplasty (PCI) in elderly population.
Methods: Data on all patients with LMCA consecutively treated with PCI in a high volume tertiary hospital between June 1997 and October 2011 were prospectively collected. The last follow-up information was obtained between January and May 2013 with a mean follow-up of 4,5±2,8 years.
Results: Total of 570 patients were included in the registry, being 33,6% of them ≥76 years old (elderly group) with a mean age of 80,5±3,4 years as compared with 62,8±9,4 years of the younger group (<76 years). Main statistically significant differences between both groups were: higher proportion of women (31,6% vs 18,7%), lower prevalence of smoking habit (24,1% vs 51,4%), worse clinical situation at presentation (NYHA class III/IV in 14,4% vs 10,2%), lower left ventricle ejection fraction at admission (49,9% vs 53,8%) and higher prevalence of comorbidities such as renal insufficiency (42,0% vs 20,4%) or anemia (48,9% vs 26,6%) among elderly population as compared with younger patients. While the indication for PCI in elderly were mostly acute coronary events (with ST elevation 15,2% vs 12,9% or without ST 51,9% vs 39,2%), in younger patients that was stable ischemic heart disease (46,6% vs 31,6%); p=0,022. Angiographically older patients presented significantly more extensive coronary disease, with LMCA and multivessel lesions in 26,0% versus 13,9% in the younger group. From a technical point of view, intravascular ultrasound was used less frequently (31,5% vs 42,7%; p=0,016) and bare metal stents more frequently (20,5% vs 10,4%; p=0,003) in patients ≥76 years. Events rates at the end of follow-up were as follows: higher all-cause death (46,2 vs 18,9%; p<0,001), similar non-fatal myocardial infarction (12,7% vs 16,6%; p=0,255) and non-fatal cerebrovascular events (3,4% vs 3,4%; p=1,0), lower target lesion revascularization (5,3% vs 12,3%; p=0,007), similar hospitalizations for cardiovascular (37,4% vs 31,5%; p=0,175) and higher rate for non-cardiovascular reasons (46,9% vs 32,4%; p=0,002). In the multivariable analysis age was not associated with worse prognosis (HR 1,071, 95%CI 0,574-1,996).
Conclusions: Elderly patients have doubled long-term mortality compared with younger patients. However, our results indicate that this worse prognosis seems to be related with non-cardiovascular reasons, thus the PCI of the LMCA in octogenarians, even in worse circumstances, could be considered as an option for myocardial revascularization.

P4634 | BEDSIDE
Determinants of prehospital use of opioids in AMI patients and association with early outcomes. Results from the FAST-MI 2010 registry

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Aim and methods: We assessed correlates of prehospital opioid use and associations with in-hospital complications in FAST-MI 2010, a nationwide French registry including 4,169 patients with AMI at the end of 2010 in 213 centres (76% of active centres in France). Of those, 1,860 were initially transported by physician-staffed ambulances (SAMU), of whom 408 (22%) received opioids in the ambulance.
Results: Prehospital opioids were less often used in patients ≥75 years (11% vs 26.5%, P<0.001), in women (15% vs 24%, P<0.001), but more in patients with STEMI (31% vs 7%, P<0.001), and with a pain score ≥7 (47% vs 21.5%, P<0.001). By multiple logistic regression analysis, use of opioids was independently correlated with age <60 (OR 2.82, 1.78-4.46), STEMI (OR 4.66, 3.32-6.53), pain score ≥7 (OR 2.88, 2.00-4.14), typical chest pain (OR 2.17, 1.37-3.45) and time from onset to first call <60 minutes (OR 1.40, 1.08-1.81); the association between female sex and less use of opioids was of borderline significance (OR 0.74, 0.54-1.02, P=0.06).
Prehospital use of opioids was associated with a decrease in heart rate (-1.9±19.1 vs +4.3±20.0 bpm, P<0.001) but a larger increase in systolic blood pressure (+14±28 vs +11±29 mm Hg, P=0.03), while change in Killip class was similar in patients with or without opioids (P=0.94). None of the in-hospital complications significantly differed between patients receiving prehospital opioids or not, after adjustment for age, GRACE score and type of MI: in-hospital death (OR 0.81, 0.30-2.17), VF (OR 2.08, 0.93-4.63), AF (OR 0.90, 0.51-1.60), A-V block (OR 1.59, 0.83-3.06), recurrent MI (OR 1.98, 0.83-4.76), cardiogenic shock (OR 1.75, 0.71-4.33), TIMI major bleed (OR 0.42, 0.15-1.24), transfusion (OR 0.32, 0.10-1.05).
Conclusion: In ambulance-transported AMI patients, opioids were used in a minority of patients, despite a strong level of recommendation. Even in patients with high pain scores, less than one out of two patients received opioids. Use of opioids in the prehospital setting was associated with a decrease in heart rate, and appeared neutral as regards in-hospital complications.

P4635 | BEDSIDE
Allergic inflammatory cells and coronary instability: evidence from a cytofluorimetric study

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Purpose: Inflammation may play a role in the pathogenesis of coronary plaque instability with lymphocytes, macrophages and neutrophils activation widely studied in the past years. However, the role of allergic inflammatory cells, such as eosinophils and basophils, in coronary instability has been, until now, poorly explored. The aim of this study was to compare eosinophils and basophils activation in patients with coronary artery disease (CAD) and either stable or unstable clinical presentation.
Methods: 51 patients undergoing coronary angiography were enrolled; 31 of them presented with non ST-segment elevation myocardial infarction (n-STEMI) (61%) and 20 with stable CAD (39%). Patients with in-stent restenosis or stent implantation in the last 12 months, as well as those having inflammatory conditions were excluded. Clinical characteristics, therapy on admission, routine laboratory data, angiographic data were available for the overall population. Eosinophils ad basophils activation were assessed with Flow Cytometry Analysis in all patients, respectively by CD66b, CD69 and CD203c expression measured as Median Fluorescence Intensity (MFI) on admission peripheral blood.
Results: The two study groups were similar for all clinical, routine laboratory or angiographic data, except for CRP serum levels, which were higher in n-STEMI patients as compared with stable angina patients (p=0,003). Among flow cytometry data, the two study groups had similar eosinophils activation (CD66b) [6.6 (4.9-7.7) vs 6.62 (5.27-8.73), p=0.63], but eosinophils degranulation (CD69) and basophils activation (CD203c) were higher in n-STEMI patients as compared with stable angina 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].
Conclusions: Our study shows that allergic inflammatory cells activation may play a role in coronary instability. Future studies should assess if these cells may become new therapeutic targets in a subset of n-STEMI patients.

SUPPORTIVE AND PALLIATIVE CARE

P4637 | BEDSIDE
Palliative care in cardiological patients, a forgotten problem

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Purpose: Traditionally palliative care has been related with oncology, but there are other specialities, as cardiology, with this kind of patients. The purpose of this study was to investigate the characteristics and magnitude of the problem in a clinical cardiology unit.
Methods: We included consecutively 205 patients admitted in the clinical cardiology unit. The NECPAL CCOMS-ICO© instrument was filled for every patient to identify cases in need of palliative care. It has 4 items and covers the need of palliative care and, general and specific clinical indicators of severity and progression of the illness. It includes a limiting question about the expectative of patient death next 12 months. A patient was considered palliative if the answer to the limiting question was negative, and another question of the other three items was positive in accordance of the established criteria. Quantitative data is presented as mean±SD and proportions as percentages. T-Student was performed to analyze differences between continuous variables, and Pearson $\chi 2$ test was used with proportions. All statistical tests are two-sided and considered significant at $p<0.05$.
Results: Median age was 72,17±13,92 years and 47,8% were women. Overall mortality at six months was 7,3%. 20% of the patients had palliative criteria who were older (82,05 vs. 69,7 years; p<0,001), with lower Barthel index (56,39 vs. 80,72; p<0,001), and higher Charlson index (5,46 vs, 3.38; p<0,001). They used more acute opioid drugs (9,8 vs. 1,2%; p=0,04), but there were no differences in

the use of chronic opioid drugs. Family care was the most important type of social support for this patients (56,1%), only 24,4% had asked about palliative care, and only 73,2% of them were identified as palliative by their physician. Palliative markers distribution for this patients were: nutritional 17,1%, functional 45,8%, fragility 7,3%, emotional distress 48,8%, use of sanitary resources 73,2%, and 2 or more pathologies 41,5%. All this markers were more prevalent between palliative care patients ($p<0,05$). Mortality was higher between palliative care patients (34,6 vs. 0,6%; $p<0,001$).
Conclusions: There is a great amount of patients in a clinical cardiology unit who could take benefit of palliative care, and they have a high mortality. Poor general clinical indicators of severity and progression of their illness were noted. Cardiologists have moderate sensitivity concerning palliative care, and patients do not usually ask for this type of care.

P4638 | BEDSIDE
Palliative care in heart failure: a multicenter prevalence analysis

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Background: The concept of palliative care is currently broadened to chronic patients with limited prognosis with the aim of covering patients' and carers' needs for a better quality of life. Heart failure (HF) is a chronic and prevalent syndrome which entails frequent hospital admissions and poor prognosis.
Objective: to assess the actual prevalence of needs of palliative care in HF.
Methods: During a 3-month period all patients attended in three specialized HF units from university hospitals in our Metro area were assessed by a simple validated questionnaire, the NECPAL CCOMS-ICO©. It consists of 4 blocks: 1) a "surprise question" to clinicians/nurses: "Would you be surprised if this patient died within 12 months?"; 2) needs according to health professionals or patient-family demand of palliative care treatments; 3) generic clinical markers of health status; and 4) disease-specific clinical markers of severity. Questionnaires were filled by nurses and/or physicians in charge for each consecutive patient. A patient was considered NECPAL+ when the "surprise question" was a No and one or more of the other blocks was positive.
Results: A total of 996 questionnaires were answered. Mean age was 68 ± 12 years-old and 70% were men. When clinicians/nurses were asked, in 35.7% of cases they would not be surprised if their patient died in the next 12 months. 32.6% of patients were NECPAL+. Only 6.1% of patients had a positive answer in block 2 (clinicians considered a need of palliative care in only 4.6% of patients). By contrast, 71.2% of patients had at least 1 positive answer in block 3 (the most frequent having $\geq$2 concomitant diseases). Regarding block 4 (cardiac disease specific items), 34.5% of patients had $\geq$1 positive answer and 15% had $\geq$2 among the 6 evaluated items. 18.9% had left ventricular ejection fraction $<$30% or pulmonary hypertension (PA pressure $>$60 mmHg), and 15.3% were in NYHA functional classes III/IV.
Conclusions: The prevalence of HF patients with needs of palliative care is high. Specific-HF items contributed less than expected to the positivity of the NECPAL questionnaire. Based on our data, palliative care interventions should be implemented in multidisciplinary HF units to improve patients' and carers' quality of life.

P4639 | BENCH
Advanced heart failure support: a new teaching methodology

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Background: Worldwide, Acute Heart Failure (AHF) is a highly prevalent condition at the emergency room. The correct systematization of both AHF diagnosis and treatment by physicians, could reduce the length of stay, the rate of 30-day re-hospitalizations and improve long-term survival.
Objective: To systematize the management of AHF patients. In each of the 3 (three) training stations 3 (three) cases of AHF are simulated, using a ABCDE-FGH system (A- A Clinical Hemodynamic Profile Evaluation; B- Breath; C- Circulation; D-Diuretics; E-Electrocardiogram; F- Frequency of the Heart (Heart rate); G-Guarantee of non suspension of active drugs and H-Heparin) and algorithms based in the clinical-hemodynamic class (CHC) of the patients (A, B, C, L), to guide the best decisions for each case.
Methodology: The Advanced Heart Failure Support course (AHFS) employs an interactive methodology of teaching. It consists of a 6 hours course, with previous reading of the course manual given 30 days in advance, active teaching methodology using algorithms, tutorial sessions, medical simulation with advanced mannequins and three practical stations named "initial", "intermediate" and "final" of diagnosis and treatment of patients with AHF at in-hospital scenarios.
Results: From 2008 to 2009, 12 AHFS courses were performed, training 432 physicians (36 candidates in each), including internal medicine, critical care physicians, cardiologists and residents from 6 cities, the majority male (57.8%). At the initial test performed at the beginning of the course, the mean evaluation score was 76.6 and at the end of the course 86.4 ($p<0.0001$), with a relative incremental of 12.8% on the grades. A 100% score was obtained by 73 (17.9%) physicians in the first test and by 156 (36.2%) physicians in the final test, with an increment of 2.1 times. At the first test female physicians had a better performance than male ($p=0.0233$). In the continuous psychomotor and practical evaluation, all the students showed improvement in the diagnosis and treatment skills of the clinical hemodynamic class.
Conclusion: This new teaching methodology named "AHFS course" showed to be effective in training physicians in the diagnosis and treatment of AHF. The broad diffusion and application of this methodology may improve treatment of AHF patients. In 2014 AHFS courses are being implemented and may become an useful training tool around the world.

P4640 | BEDSIDE
Change in readmissions and follow-up visits due to introduction of heart failure clinic and heart failure computer program in a general hospital between year 2007 and 2012

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Purpose: Heart failure is a leading cause of acute hospitalizations which are associated with unacceptably high post-discharge mortality, re-hospitalization rates and health-care costs. From year 2000 to 2006 we recorded a constant increase in the number of total admissions to Department of Internal Medicine (DIM), including admissions due to Heart Failure (HF). Reducing hospital readmission rates is a national priority and for this reason we introduced a once weekly HF clinic. At the same time we developed a computer registry, containing a supporting program for better disease management and optimization of guidelines recommended therapy.
Methods: We made the retrograde data analysis of the treatment of HF patients on DIM in our hospital according to the number of admissions, in hospital stay, mortality, quality of pharmacological treatment and the effect of ambulatory work on hospital care in years before and after the introduction of a HF clinic. We also made a financial evaluation of this manner of HF patient treatment.
Results: In 2006 we introduced HF clinic with simultaneous development of registry database to monitor and closely follow-up HF patients. Between year 2007 and 2012 three cardiologists and one nurse specially trained for working with HF patients yearly performed up to 550 examinations with 320 patients. The share of patients receiving basic treatment improved from year 2005 to 2012 for ACEi (from 79% to 97% respectively), beta blockers (from 42% to 90%) and aldosterone antagonists (from 29% to 64%). Between year 2006 and 2012 the number of admissions due to HF decreased from 461 yearly admissions to 228 yearly admissions (from 10,6% to 5,1% of total admissions) and mortality due to HF decreased form 20,6% to 16,2% (in 2001 it was as high as 31%). In the same period the share of costs due to HF (hospital care, treatment, diagnostics according to DRG system) decreased from 4,9% to 2,6% of all cost for HF our country (HF treatment costs in our country in the year 2012 amounted to 168 M €). Currently there are 650 patients in registry database; 53% men, 47% women; average age is 76.0 years; the average NYHA class is 2.57 and mortality rate 7.7%.
Conclusions: Since introduction of HF clinic and computer registry in our hospital the number of admissions due to HF decreased significantly, as well as mortality due to HF. In the HF clinic we have achieved high share of guidelines recommended basic treatment. We also managed to reduce the total cost for treating HF patients.

P4641 | BEDSIDE
Prevalence of depression, frequency of antidepressant pharmacotherapy and survival in systolic heart failure patients

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Background: Compared with the general population, depression is more prevalent in heart failure (HF) and associated with increased mortality. Little is known on the frequency of administration and effects of antidepressants in HF. This study aimed to assess in a large, well characterized cohort of subjects hospitalized for decompensated systolic HF the prevalence and survival of patients with depressed mood (with and without antidepressants) versus that of patients without depressed mood (with and without antidepressants).
Methods: In 864 participants of the Extended Interdisciplinary Network Heart Failure (E-INH) Study (67 ± 12.5 years; 72% male; left ventricular ejection fraction 30.4 ± 8.2%; NYHA class III-IV 42%) the self-administered 9-item patient health questionnaire (PHQ-9) was used for depression screening at baseline. Patients scoring $\geq$11/$<$11 were classified as patients with/without depressed mood. Baseline assessment included also history of depression and use of antidepressants. Median follow up for vital status was 18 months (100% complete).

Results: Of 864 patients 29% (n=253) had a PHQ-9 score≥11. In this subpopulation with depressed mood only 70 of 253 patients (28%) had a history of depression: 35 (13.8%) on antidepressants and 35 (13.8%) not. Of the total cohort 71% (n=611) had a PHQ-9 score<11. However, 54 of them (8.8%) had a history of depression: 27 (4.4%) treated with antidepressants and 27 (4.4%) not.
After 18 months, 68 of 253 (26.9%) patients with depressed mood at baseline had died: 40 (15.8%) without history of depression, 11 (4.3%) with history of depression not on antidepressants and 17 (6.7%) on antidepressants. In this group antidepressant therapy was a predictor of death in univariate analysis (log rank, P=0.002). Of patients without depressed mood 83 of 611 (13.6%) had died: 67 (10.9%) without history of depression, 8 (1.3%) with history of depression not on antidepressants and 8 (1.3%) on antidepressants.
Conclusion: Depression is frequent in HF patients, unknown and rarely treated in the majority of cases. Our data confirm that patients with depressed mood have a worse prognosis than patients without depressed mood. Moreover, irrespective of current PHQ-9 score, patients with history of depression seem to have a worse prognosis than patients without history of depression possibly indicating a different pathophysiology. The highest proportion died of those patients who had a history of depression and took any antidepressant agent. Although this subgroup was small, this finding warrants careful further observation.

P4642 | BEDSIDE
Feasibility and accuracy of nurse performed pocket-size ultrasound imaging of the pleura and vena cava inferior to assess volume state in patients with heart failure in an outpatient clinic

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Purpose: Pleural effusion in heart failure (HF) patients correlate well with decompensation and assessment of the dimension and collapsibility of the inferior vena cava (IVC) may help to identify both decompensation as well as dehydration. Follow-up in multidisciplinary HF clinics are shown to improve patient treatment. As this may improve treatment of HF we aimed to study the feasibility and accuracy of routinely nurse performed pocket-size ultrasound imaging of the pleura and vena cava inferior after specific training.
Methods: Patients in an outpatient HF clinic at a non-university hospital were included. Before the study start two specialized nurses underwent a specific training period, with cardiologists as supervisors, with respect to assessment of the pleural cavities and dimension and collapsibility of the IVC. They used a PSID with B-mode and colour flow imaging, and measured dimensions on the PSID. The dimension of the IVC was measured in supine position both end-expiratory and after sniff in sagittal axis. The amount of PLE was measured in sitting position as the dimension of the echo-free space between the diaphragm and basal lung. Reference echocardiography was performed by one of four cardiologists in all patients by high-end echocardiography, including assessment of both pleural cavities.
Results: Mean (SD) age in 62 (48% women) patients was 74 (12) years, ejection fraction 34 (13) %, NYHA 2.4 (0.6), and N-terminal pro brain natriuretic peptide (proBNP) 3761 (3072) ng/l. Time consumption for PSID examination performed by nurses was median 5 minutes, and reference examination was performed immediatetely. By PSID examination IVC was assessed in all patients, and some amount of pleural effusion was detected in 36 pleural cavities in 23 patients (reference; 39 and 26, respectively). Correlation (95% CI) for the measurements of pleural effusion, end-expiratory and end-inspiratory IVC was 0.97 (0.91-1.00), 0.89 (0.81-0.95) and 0.79 (0.57-0.93), respectively. Coefficient of variation for end-expiratory IVC was 10% and 95% limit of agreement was -6 to 7 mm, respectively. The very few undetected cases (by nurses) with pleural effusions by PSID were in patients were the amount was classified as minor and located only in the costodiaphragmal recess.
Conclusions: Specialized nurses were after dedicated training able to reliably classify volume state by assessing both the pleural cavities and the dimension and collapsibility of the inferior vena cava with an excellent agreement with high-end ultrasound examinations done by cardiologists. This may improve follow-up of heart failure patients.

P4643 | SPOTLIGHT
Good management of patients with heart failure: what matters?

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Purpose: Heart failure (HF) is a complex clinical syndrome highly prevalent among the elderly. Evidence-based (EB) treatment with ACEIs/ARBs or β-blockers is the mainstay of secondary prevention after HF. The aim of this study is to examine the influence of patients' characteristics and organisational determinants on hospital readmission and on initiation/adherence to EB medications.
Methods: The study population comprised patients resident in a Local Health Authority discharged from any Italian hospital between 1/1/2008 and 31/12/2010 with a primary diagnosis of HF, identified through the hospital discharge records database. The outcomes of interests were the rate of hospital readmissions for HF at 1 year after discharge, the proportion of patients with at least 1 prescription of ACEIs/ARBs or β-blockers within 90 days of discharge (drug initiators) and the proportion of patients with at least 2/4 prescriptions of ACEIs/ARBs or β-blockers within 180/365 days of discharge (adherent patients). Differences in adherence were examined in relation to patients', general practitioners (GPs) and primary care units (PCUs) characteristics using a multilevel modified Poisson regression model.
Results: The study sample includes 7716 patients, 56% female, with a mean age of 81±10 years. The readmission rate for HF was 27%. Older patients had a higher risk of readmission, while those treated by GPs practicing in rural area (RR=0.88; 95% CI=0.79–0.97) and those referred to PCUs with HF clinical pathway (RR=0.84; 95% CI=0.77–0.93) had a lower readmission rate. The proportion of patients with ≥1 prescription of ACEIs/ARBs was 65% at 90 days and 53% at 1 year from discharge. Lowland GPs' patients were more likely to initiate ACEIs/ARBs. Lower initiation and adherence were found in women (RR=0.95; 95% CI=0.92–0.99) and older patients (RR=0.70; 95% CI=0.65–0.77). Moreover the proportion of patients treated with β-blockers was 54% at 90 days and 43% at 1 year from discharge. Older patients were less likely to initiate treatment and to be adherent. Patients of GPs practicing in mountain area and patients referred to PCUs with implemented HF clinical pathways were significantly more likely to receive a prescription of β-blockers.
Conclusions: Our results suggest that older patients are less prone to initiate and to be adherent to secondary prevention medications after HF. Physicians should be encouraged to implement strategies aimed to increase patients' initiation and adherence to EB drug treatments.

P4644 | BENCH
Advanced heart failure support: a new teaching methodology

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Background: Worldwide, Acute Heart Failure (AHF) is a highly prevalent condition at the emergency room. The correct systematization of both AHF diagnosis and treatment by physicians, could reduce the length of stay, the rate of 30-day re-hospitalizations and improve long-term survival.
Objective: To systematize the management of AHF patients. In each of the 3 (three) training stations 3 (three) cases of AHF are simulated, using a ABCDEFGH system (A- A Clinical Hemodynamic Profile Evaluation; B- Breath; C- Circulation; D-Diuretics; E-Electrocardiogram; F- Frequency of the Heart (Heart rate); G-Guarantee of non suspension of active drugs and H-Heparin) and algorithms based in the clinical-hemodynamic class (CHC) of the patients (A, B, C, L), to guide the best decisions for each case.
Methodology: The Advanced Heart Failure Support course (AHFS) employs an interactive methodology of teaching. It consists of a 6 hours course, with previous reading of the course manual given 30 days in advance, active teaching methodology using algorithms, tutorial sessions, medical simulation with advanced mannequins and three practical stations named "initial", "intermediate" and "final" of diagnosis and treatment of patients with AHF at in-hospital scenarios.
Results: From 2008 to 2009, 12 AHFS courses were performed, training 432 physicians (36 candidates in each), including internal medicine, critical care physicians, cardiologists and residents from 6 cities, the majority male (57.8%). At the initial test performed at the beginning of the course, the mean evaluation score was 76.6 and at the end of the course 86.4 ($p<0.0001$), with a relative incremental of 12.8% on the grades. A 100% score was obtained by 73 (17.9%) physicians in the first test and by 156 (36.2%) physicians in the final test, with an increment of 2.1 times. At the first test female physicians had a better performance than male (p=0.0233). In the continuous psychomotor and practical evaluation, all the students showed improvement in the diagnosis and treatment skills of the clinical hemodynamic class.
Conclusion: This new teaching methodology named "AHFS course" showed to be effective in training physicians in the diagnosis and treatment of AHF. The broad diffusion and application of this methodology may improve treatment of AHF patients. In 2014 AHFS courses are being implemented also in Portugal and may become an useful training tool around the world.

P4645 | BEDSIDE
Treatment of patients with heart failure by following international guidelines: first results from the RUssian hoSpital Heart Failure Registry (RUS-HFR)

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Purpose: The main purpose of the RUS-HFR was to evaluate how recommendations according evidence-based therapy regarding pharmacological and non-

pharmacological aspects (including high-tech methods) for chronic systolic HF are adopted in Russian clinical practice.
Methods and results: The RUS-HFR is a prospective, multicentre, observational study conducted in 3 Cardiology Centers (St. Petersburg - the central coordinator of the project, Samara, Orenburg). Data collection started in Oct 2012 and continues today. Inclusion criteria were HF NYHA I-IV, LVEF≤40%, age 18-75 years. Up to Jun 2013, 251 patients had been enrolled in three participating clinics. The mean age of the patients was 59.0±11.5 years and 81.9% were men. Main etiologies were ischemic in 58.3-76.2%, hypertensive in 68.3-93.7%, and due to dilated cardiomyopathy in 3.0-4.2%. More than half of the patients (58.8%) were in NYHA class II-III. Mean LVEF was 28.8%. The left bundle branch block (duration of QRS >150 msec) was observed in 15,9% and 20,8% patients in St. Petersburg and Samara, respectively. RAS blockers, β-AB, and mineralocorticoid antagonists (MRAs) were used after hospital discharge in 82.2%, 80.6, and 74.3.0% of patients, respectively. The rate of prescription of these drugs prior admission and after discharge of hospitalized patients with HF did not differ significantly. Diuretics prior to hospitalization were not prescribed in 30%, 35%, 11% of patient with NYHA II, III and IV, respectively. Overall, 66.7-83.3% of patients were on oral diuretics and 5.5-45.8% of patients were treated with digitalis at hospital discharge. Inotropes were administered in 1.6-12.5% of the patients. CRT and ICD have been previously implanted with 4.3% and 5.5% of patients from St. Petersburg clinic, respectively. Indications for implantation of ICD and CRT were determined at 25% and 8% of HF patients in St. Petersburg and Samara, respectively. Indications for heart transplantation were identified only a single patient from St. Petersburg (center with heart transplant program).
Conclusions: The first data from RUS-HFR showed that the percentage of patients with HF receiving RAS blockers, β-AB, MRAs compares with results of European Registers. The most commonly prescribed were RAS blockers and beta-blockers, MRAs were used more rarely. Oral diuretics were not indicated for the clinically manifested HF at 11-35% of cases prior to admission and at discharge of hospitalized patients, which is unacceptable. High-tech methods of treatment in HF patients (NYHA II-IV) in hospitals participating in RUS-HFR were not properly recommended.

P4646 | BEDSIDE
Advance care planning for patients hospitalised for heart failure in a multiethnic south east asian cohort

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Purpose: There is limited data on the feasibility of Advance Care Planning (ACP) in the multi-ethnic South East Asian (SEA) society where different cultures have disparate beliefs about death. A pilot study conducted in our institution showed that it is feasible to implement ACP in SEA patients with heart failure in the outpatient setting. As a result, the ACP programme was implemented in our institution. We plan to report our experience after implementation of the ACP programme.
Methods: Patients hospitalised for acute decompensated heart failure were recruited over a 7 month period from 1st June to 31st December 2013.
Results: 48 (7.2%) patients agreed to participate in ACP programme out of 718 screened patients. Mean age was 68.5 years with predominance of male (75%). Ethnic distribution followed the national demographic (66.7% Chinese, 16.7% Indian, 12.5% Malay, 4.1% other races). 85.4% of participants had more than one ACP session with a mean duration of 60 minutes per session, and 31% had completed the ACP documentation. Majority of participants (89.4%) had not heard of the ACP programme before enrolment. All except 1 participant had no documentation on preferred mode of care or had nominated a substitute decision maker prior to enrolment. Most patients (77.3%) were satisfied with the ACP discussion sessions in the post discussion survey. There were 4 deaths during the recruitment period with 100% honouring of the preferred delivery of care as stated in the ACP forms. For the 670 patients who declined to participate, 8.4% not ready to discuss ACP, 11% do not see a need to discuss ACP, 1.8% topic too sensitive, 36% need to consult family first, 42.8% due to other reasons (language barrier, patient too ill to discuss, confused patients).
Conclusion: There is a low acceptance of ACP among SEA patients hospitalised for heart failure. This result is in contrast to the high participation rate in our pilot study involving patients attending heart failure clinic. Significant challenges faced were low awareness of ACP among patients, caregivers and healthcare workers. Future strategies to increase public awareness and acceptance of ACP are warranted.

P4647 | BEDSIDE
Patient-centered home-based management of heart failure, findings from a randomized clinical trial evaluating effects on knowledge, self -care and quality of life

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Purpose: To keep heart failure patients updated in signs and symptoms in case of worsening heart failure is essential for health related quality of life (HRQoL). We wanted to evaluate if a new home-based tool for heart failure (HF) could improve self-care behavior and HRQoL, increase knowledge in HF, prolong time to worsening of HF and reduce hospital days.
Methods: We performed a prospective, multi-center, randomized controlled trial. 72 patients hospitalized for HF, were at discharge randomized to either an intervention group (IG) equipped with a tablet and scale plus standard care or a control group (CG), subject to standard care. The mean age was 75±8, 68% were male, 74% were NYHA class III, the rest NYHA class II.
Results: Self-care after 3 months evaluated with EHFScB-9 improved in both groups but more pronounced in the intervention group (p=<0.02). The HRQoL increased more in the intervention group (p=<0.05). More patients achieved maximum score in knowledge in IG compared to CG but there was no significant difference in mean knowledge after 90 days. There was a significant reduction in hospital days due to HF between the groups (RR: 0.38, 95% CI: 0.31-0.46, p<0.05), a statistically significant reduction in hospital days by 62%.
Conclusion: A patient-centered home-based tool with tablet and scale resulted in increased knowledge of heart failure, adherence to therapy, improved HRQoL, reduced time to readmission and days spent in hospital. An easy navigated tablet together with a patient-scale and useful information has the potential to be a valuable tool in the self-care of HF patients.

BIOMARKERS UPDATE – I

P4649 | BEDSIDE
Myocardial gremlin-1 expression serves as an additional biomarker in the risk assessment of patients with progressive systemic sclerosis and cardiac involvement

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Background: Cardiac involvement in patients with progressive systemic sclerosis (Ssc) is associated with a poor clinical outcome. Gremlin-1 (Grem1) is involved in fibrotic tissue formation in various organs. We investigated the prognostic value of Grem1 in patients with SSc and suspected cardiac involvement.
Methods and results: 25 consecutive patients underwent clinical work-up including laboratory testing, echocardiography, right heart catheterization, cardiac MRI, holter recordings, and endomyocardial biopsy to detect the degree of cardiac inflammation and fibrosis. Standard histopathology, Grem1 expression and the degree of myocardial fibrosis were assessed. Primary endpoint was defined as a combined endpoint of death of all causes, adequate ICD-shock or rehospitalization due to heart failure.
Endomyocardial biopsies detected fibrosis in all patients: Mild fibrosis in 7.7%, moderate fibrosis in 61.5%, and severe fibrosis in 26.9%. The degree of cardiac inflammation was distributed as the following: No inflammation in 3.8%, isolated inflammatory cells in 38.5%, some inflammatory cells in 30.8%, several focused inflammatory cells in 15.4%, and massive inflammation in 7.7%.
In patients with SSc, the expression of Grem1 correlated with the amount of fibrosis and the inflammatory degree for trend. Patients with mild fibrosis were Grem1 negative, while 50% of patients with moderate fibrosis were Grem1 positive and 85.7% of patients with severe fibrosis were Grem1 positive. All Patients with massive inflammation in their myocardium showed Grem1 positive staining.
During a mean follow up-time of 22.5 months, 9 patients reached the primary endpoint: 6 patients died, 3 patients where documented with adequate ICD-shocks due to ventricular tachycardia. Patients with an event during follow up showed a higher degree of fibrosis and inflammation in their histopathological findings. Patients suffering from an event during follow up also presented more often with positive Grem1 expression in their myocardium than patients without any event.
Conclusions: Grem1 may serve as an additional biomarker in the risk assessment of patients with Ssc as the rate of cardiovascular events correlated with the Grem1 expression along with the fibrotic and inflammatory degree of the myocardium. Patients with cardiac involvement have a poor prognosis with an event rate of 36% within 22.5 months of follow up and therefore may benefit from an intensified risk stratification and early ICD implantation.

P4650 | BENCH
Eplerenone prevents pressure overload-induced dilatative cardiomyopathy in mice with abolished cardiac ANP signaling

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Background: Cardiac atrial natriuretic peptide (ANP) exerts endocrine hypotensive effects and local actions moderating hypertensive remodelling. The relevance of these paracrine actions is emphasized by the phenotype of mice with car-

diomyocyte (CM)-restricted inactivation (KO) of the ANP receptor (GC-A) or of the downstream kinase (cGKI), which develop dilatative cardiomyopathy in response to left ventricular (LV) pressure overload. The mechanisms mediating the cardiac ANP effects are uncertain. Endocrine ANP reduces mineralocorticoid receptor (MR) signaling, including suppression of adrenal aldosterone production and of MR-induced renal sodium retention. We hypothesized that paracrine ANP inhibits the adverse heart effects of MR activation. And, therefrom, that the cardiac alterations observed in CM GC-A KO and CM cGKI KO mice are due to enhanced MR signaling.
Methods: CM GC-A KO, CM cGKI KO and control mice fed with the MR blocker eplerenone (~100 mg/kg/day) or vehicle were subjected to transverse aortic constriction (TAC) or sham operation. After 3 weeks, LV functional, cellular and molecular changes were evaluated by echocardiography, histology, western blotting (SERCA2a) and RT-PCR (CTGF). These studies were complemented with experiments in HEK 293 cells coexpressing GC-A, cGKI and MR.
Results: Eplerenone had no effect on the mild, compensated LV hypertrophy of control mice subjected to TAC. However, MR blockade attenuated the TAC-induced enhanced LV enlargement and myocyte hypertrophy in CM GC-A KO and CM cGKI KO mice and completely prevented LV dilation, systolic dysfunction and interstitial collagen deposition. Adverse hypertensive LV remodelling in these mice was accompanied by a marked induction of CTGF and inhibition of SERCA2a expression. These molecular changes were fully prevented by eplerenone. In HEK 293 cells, ANP, via GC-A/cGKI activation, attenuated the aldosterone-induced nuclear translocation of MRs. Moreover, coimmunoprecipitation and FRET studies revealed that a portion of MRs forms a dynamic, ANP-modulatable protein complex with GC-A at the cells membrane.
Conclusions: This study demonstrates that MR blockade prevents dilatative cardiomyopathy in mice with ablated cardiac ANP signaling. Together with our observations in HEK 293 cells this suggests that ANP inhibits the genomic effects of the aldosterone-MR pathway in cardiomyocytes. A cardiac imbalance between ANP and aldosterone activities can contribute to adverse remodelling in chronic pressure overload.

P4651 | BEDSIDE
Brain derived neurotrophic factor levels after acute aerobic exercise in Chagas heart disease patients

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Purpose: Chagas heart disease (CHD), the most important clinical manifestation of Chagas disease, causes heart failure, complex arrhythmias, thromboembolism and sudden death. A diffuse damage in the autonomic nervous system is a pathological feature commonly present in variable degrees in patients with CHD. The neurotrophin Brain Derived Neurotrophic Factor (BDNF) plays important functions in the nervous system and an important role in metabolic events, being susceptible to regulation by physical activity. However, the acute effect of aerobic exercise on the BDNF levels in CHD remains unknown, as well as its relationship to exercise intensity.
Methods: Thirty CHD patients (47.85±8.71 years, 20 male) were selected for this study. All patients underwent clinical evaluation, echocardiography, the Cardiopulmonary Exercise Testing (CPET) and blood sampling for measurement of serum BDNF. The CPET was performed on a treadmill ramp protocol and the intensity of exercise was determined as the percentage of maximum heart rate (HRmax = 220 minus the patient age) during the test. For moderate exercise the percentage was set at 60-79% and for high intensity above 80% of the HRmax. Patients were classified into two groups according to exercise intensity. Blood samples were taken at rest and immediately after the CPET. Serum BDNF levels were determined by ELISA. Parametric paired t-test and Pearson correlation test and Nonparametric Mann–Whitney and Spearman Rank correlation test were performed for data analysis.
Results: In the overall study population, there was a significant decrease in serum BDNF levels after acute exercise ($p=0.006$). Concerning the intensity of physical exercise, patients who underwent CPET at moderate intensity (n=11) exhibited no changes in serum BDNF levels ($p=0.477$). However, patients who underwent CPET at high intensity (n=19) had a significant decrease in BDNF levels ($p<0.001$).
Conclusion: The acute aerobic exercise was associated with a reduction in serum BDNF levels in patients with CHD, which was related to exercise intensity. High intensity aerobic exercise may negatively affect BDNF levels and, consequently, hippocampal plasticity in patients with CHD.

P4652 | BEDSIDE
Cystatin-C serum levels and vascular function in heart failure

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Purpose: Heart failure (HF) is a complex clinical syndrome accompanied by hemodynamic disorders, endothelial dysfunction, atherosclerosis, inflammation and activation of neurohormone and the sympathetic nervous system, subsequently accelerating the disease progression. Recently, new biomarkers might have an additional contribution to reveal an early decline in renal function and to improve the prognostic assessment in patients with HF. In this study we aimed to examine the association between cystatin-C and vascular function in patients with chronic HF.
Methods: We enrolled 79 consecutive patients with HF and 79 healthy subjects, adjusted for age and sex. Serum levels of cystatin-C were measured by commercially available ELISA kits. Creatinine clearance was estimated using Cockcroft-Gault formula (eCcl). Augmentation index (AIx) of the central (aortic) pressure waveform and aortic pressures were calculated, as a composite index of wave reflections and arterial stiffness, using a validated, commercially available system.
Results: Patients with HF, compared with control subjects, had significant higher AIx (23.56±9.54% vs. 20.38±6.89%, $p=0.04$). Moreover, patients with HF, compared to control subjects, had significantly increased levels of logCystatine-C (3.38±0.21ng/ml vs. 3.27±0.25ng/ml, $p=0.005$). Interestingly, in HF patients AIx was correlated with logCystatine-C levels ($r=0.26$, $p=0.03$). Finally, levels of logCyctatin-C were inversely associated with creatinine clearance ($r=-0.21$, $p=0.04$).
Conclusions: The present study demonstrated that HF patients had significantly impaired vascular function. Moreover, patients with HF, had significantly increased levels of logCystatine-C. Interestingly, in HF patients arterial stiffness was correlated with cystatine-C levels. These findings suggest a possible common pathophysiologic link of arterial stiffness and novel biomarkers of renal function.

P4653 | BEDSIDE
Association between the C825T polymorphism in the G protein beta 3 subunit (GNB3) gene and chronic heart failure

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Background and aim: The single nucleotide polymorphism (SNP) C825T in the G protein beta 3 subunit (GNB3) gene is associated with a high risk of arterial hypertension (AH), arrhythmias, obesity, metabolic syndrome, atherosclerosis, diabetes mellitus. The aim of this study was to examine C825T SNP in relation to clinical, cardiac, renal and bone status in chronic heart failure (CHF) patients.
Methods: The C825T polymorphism was detected by polymerase chain reaction followed by restriction-enzyme digestion in the blood isolated from 66 Russian CHF pts with I-IV NYHA functional class (FC) without primary renal, autoimmune, endocrine and oncological diseases. We performed echocardiography (left ventricular ejection fraction (LVEF) by Simpson's method, transmitral flow and mitral annulus tissue Doppler), dual-energy X-ray absorptiometry, 24 hour (h) ECG and blood pressure (BP) monitoring, 6-minute walking test, glomerular filtration rate (e-GFR: MDRD and CKD-EPI equations), 24h urinary albumin excretion (UAE), history/clinical data analysis. All pts were stable on medical therapy in accordance with current guidelines. The median (interquartile range) of the age was 63.0 (57.0-69.0) years; LVEF - 34.0 (26.7-39.0)%. 91% were men, 85.5% had coronary artery disease (CAD), 9.1% - AH, 5.4% - dilated cardiomyopathy.
Results: The distribution of the genotypes (CC, CT, and TT) was 71.2%, 19.7% and 9.1%, respectively. 1st group includes the pts with CC, 2nd group - CT and TT genotypes. No difference was detected between the groups in the age, body weight, BP, NYHA FC, CAD and AH history ($p>0.05$). The carriers of the CC genotype had longer duration of CHF [4.5 (1.5-11) vs 2 (1-4) years, $p=0.036$] and lower LVEF in comparison with others [32.4 (25.4-38.3) vs 37.3 (32.4-43.1)%, $p=0.03$]. UAE [12.8 (8.1-23.0) vs 6.0 (5.7-6.2) mg/24h, $p=0.036$] and bone mineral density [BMD: 0.9 (0.8-1.1) vs 0.8 (0.7-0.9) g/cm^2, $p=0.041$] were higher in the 1st in comparison with the 2nd group. Maximal 24h RR interval was longer in the CC group in comparison with others [1824 (1736-2288) vs 1632 (1492-1956) mc, $p=0.041$]. No association was found between C825T SNP and E/A ratio, E/Em ratio, LV hypertrophy, e-GFR, BP monitoring and 6-minute test results.
Conclusion: Homozygous 825C allele carriers show an increased risk for low systolic function, long max 24h RR interval, microalbuminuria and high BMD. Further studies are necessary to determine the clinical applicability of genetic polymorphism of the GNB3 C825T as predictors for severe cardiac dysfunction, chronic kidney disease and osteoporosis in CHF.

P4654 | BENCH
Human placenta derived multipotent cells modulate cardiac injury–from bench to small and large animal ischemic heart failure study

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Objectives: The aims of this study were to evaluate the feasibility of human placenta-derived multipotent cells (hPDMCs) in cardiac repair and to define the underlying mechanisms.
Background: Recent studies have shown that hPDMCs are capable of multilineage differentiation. In addition, the lack of ethical concerns in procurement of these multilineage progenitors and their immunomodulatory properties make

them good candidates for cell therapy of damaged organs. However, the feasibility of hPDMCs in cardiac repair is unclear.
Methods: Cardiomyogenic gene expression of hPDMCs and other human somatic cells was analyzed by RT-qPCR. In vitro cardiomyogenic differentiation potential was tested using co-culture method with mouse neonatal cardiomyocytes. In vitro proangiogenesis was tested by tube-formation assays using human endothelial cells. Myocardial infarction was induced in severe combined immunodeficiency mice and minipigs (Lanyu breed) by permanent left anterior descending artery ligation, followed by hPDMCs or vehicle implantation with follow-up for up to 8 weeks. The animals underwent serial echocardiography study. The heart sections were analyzed for cardiac regeneration, neovasculogenesis, and TUNNEL stain.
Results: hPDMCs expressed much higher level of cardiomyogenesis genes at baseline than human bone marrow mesenchymal stem cells or fibroblasts. Upon co-culture with mouse neonatal cardiomyocytes, hPDMCs were able to differentiate into striated cardiomyocyte. The proangiogenic effects of hPDMCs were confirmed in vitro by tube-formation assays. These proangiogenic effects were mediated by hPDMCs secretion of HGF, GRO-α, and IL-8. Transplantation of hPDMCs into the hearts of severe combined immunodeficiency mice after LAD artery ligation improved left ventricular function, with significantly enhanced vascularity in the cell-treated group. The minipigs undergoing hPDMCs treatment after myocardial infarction showed significant improvement of contractility than the control group (p=0.016) at 8 weeks post injury. Tissue analysis confirmed the increased vascularity of hPDMCs treatment, cardiomyogenesis differentiation, and anti-apoptotic effect on cardiomyocytes of hPDMCs.
Conclusion: Our findings offer evidence that hPDMCs can modulate cardiac injury in both small and large animal model, possibly through cardiomyogenesis, proangiogenesis, and suppression of cardiomyocyte apoptosis. This study offers mechanistic insights and preclinical evidence on using hPDMCs as a therapeutic strategy to treat severe cardiovascular diseases.

P4655 | BENCH
Prolonged physical exercise increases functional capacity and reduces myostatin expression in soleus muscle of spontaneously hypertensive rat with heart failure

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Chronic heart failure (HF) is associated with skeletal muscle atrophy. The myostatin/follistatin pathway modulates skeletal muscle mass with myostatin levels being negatively correlated with muscle mass. Physical exercise has an important role in heart failure treatment. However, mechanisms involved in exercise-induced physical capacity improvement are not completely understood. The aim of this study is to determine whether aerobic physical training attenuates muscle atrophy and/or modulates myostatin/follistatin expression in soleus muscle.
Methods: Male sixteen-month-old spontaneously hypertensive rats (SHR) were assigned to sedentary (SHR-Sed) and exercise (SHR-Ex) groups (n=8). SHR-Ex were subjected to a treadmill exercise protocol, five days a week, 12 m/min, 30 min, for four months. Transthoracic echocardiogram was performed before and after the training period. During euthanasia, we evaluated features of heart failure such as pleuropericardial effusion, ascites, left atrial thrombi, right ventricular hypertrophy, and lung congestion. Morfometry was analyzed in histological sections. Protein expression was evaluated by Western blot. Statistical analyses: Student's t test and Goodman test; p level was set at 5%.
Results: Functional capacity was better in SHR-Ex (walking distance: SHR-Sed 242$\pm$34; SHR-Ex 394$\pm$65 m; $p<0.05$; test duration: SHR-Sed 21.7$\pm$1.87; SHR-Ex 28.4$\pm$2.40 min; $p<0.05$). SHR-Ex presented a lower frequency of heart failure features than SHR-Sed. Echocardiographic parameters did not differ between groups before or after training. Soleus fiber cross sectional area did not differ between groups (SHR-Sed 2,422$\pm$123; SHR-Ex 2,364$\pm$252 μm^2). Myostatin levels were lower in SHR-Ex (SHR-Sed 0.79$\pm$0.17; SHR-Ex 0.46$\pm$0.15 arbitrary units; p=0.002) and follistatin did not differ between groups (SHR-Sed 0.54$\pm$0.36; SHR-Ex 0.69$\pm$0.64 arbitrary units; p=0.59).
Conclusions: Low intensity aerobic physical training improves functional capacity and reduces frequency of heart failure features. Training reduces myostatin protein expression in soleus muscle.

P4656 | BEDSIDE
Serum angiopoietin-related protein 2 levels are independently associated with heart failure

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Background: Metabolic derangement in heart failure (HF) has been obtained much attention recently. Several adipokines are known to be upregulated in patients with HF. Angiopoietin-related protein 2 (ANGPTL2) is primarily secreted by adipose tissue and closely associated with adiposity, insulin resistance, and inflammation. Here we investigated the association of circulating ANGPTL2 levels with HF in subjects of our country.
Methods and results: A total of 310 patients were enrolled from the cardiovascular clinic, and 170 of which were diagnosed as HF with New York Heart Association functional class II-IV. Serum ANGPTL2 levels, echocardiography, and Tl-201 single-photon emission computed tomography (SPECT) were analyzed. ANGPTL2 levels were significantly higher in patients with HF than those without HF (5.08$\pm$2.35 vs. 3.50$\pm$1.25 ng/ml, $P<0.0001$), irrespective of gender, diabetes and coronary artery disease (CAD). In correlation analysis, ANGPTL2 was positively correlated to age, creatinine, fasting glucose, hsCRP, NT-proBNP, adiponectin, and negatively correlated with waist circumference, high-density lipoprotein cholesterol, and left ventricular ejection fraction. However, ANGPTL2 was not associated with summed stress score, an indicator of CAD severity derived from SPECT study, in both HF and non-HF group patients. In multivariate model, levels of creatinine, NT-proBNP, and adiponectin levels were independent determinants for ANGPTL2. Multivariate logistic regression analysis demonstrated that ANGPTL2 concentration was an independent risk factor for HF (odds ratio 1.76, 95% confidence interval 1.39 – 2.22; $P<0.001$).
Conclusions: Upregulation of circulating ANGPTL2 levels in patients with HF implies that ANGPTL2 might be an important pathophysiological mediator of HF.

P4657 | BEDSIDE
Left ventricular assessment by novel echocardiographic markers in patients with heart failure: relationship with matrix metalloproteinase 9

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Purpose: Global longitudinal peak systolic strain (GLPS) and torsion are new echochardiographic indices which have been proposed to evaluate overall left ventricular function in heart failure (HF). Adverse left ventricle remodeling is associated with worse outcome and impaired hemodynamics in HF. We investigated the associations of novel echocardiographic indices with circulating biomarkers of remodeling and left ventricle tension such as matrix metalloproteinase 9 (MMP9).
Methods: The study population consisted of 40 consecutive patients (mean age 60$\pm$14 years) with systolic HF of non ischemic etiology. All subjects were at New York Heart Association (NYHA) stage II and III. Left ventricle ejection fraction (EF) was estimated by biplane Simpson's formula. The GLPS was evaluated by Automatic Function Index (AFI) software and torsion was calculated as the difference between the apical and basal rotation, measured by 2D speckle tracking echocardiography at the end of the systole. The ratio of E/Eprime was calculated as the ratio of mitral peak early diastolic velocity divided by the early diastolic velocity of the longitudinal motion of the mitral annulus as an index of left ventricle filling pressures. MMP9 levels were measured by enzyme-linked immunosorbent assay (ELISA) as an index of remodeling and BNP was measured to evaluate left ventricle tension.
Results: GLPS was inversely associated with EF (r=-0.76, $p<0.001$), and positively correlated with MPP9 levels (r=0.53, p=0.03) and BNP levels (r=0.79, p=0.002) and E/Eprime (r=0.48, p=0.02). Torsion was significantly associated with BNP levels (r=-0.67, p=0.03). EF was also inversely correlated with MMP9 levels (r=-0.62, p=0.03) and BNP levels (r=-0.86, p=0.003). Interestingly, E/Eprime was not associated with MMP9 levels (p=0.75). To further elucidate which echocardiographic or clinical parameter (GLPS, EF, E/Eprime, age and NYHA) is better associated with circulating biomarkers of left ventricle remodeling we applied a stepwise regression model which revealed that only GLPS was significantly associated with MMP9 levels [b=0.14, 95%CI (0.06, 0.23), p=0.004].
Conclusions: These findings indicate that novel echocardiographic indices and especially systolic strain are well associated not only with EF but also with left ventricle loading conditions and remodeling process. These findings supply that these markers may be used to further understand the pathophysiology of HF and to monitor the progression of the disease.

P4658 | BEDSIDE
MicroRNA-21 and microRNA-133 levels in peripheral blood mononuclear cells are associated with functional capacity in patients with heart failure with preserved ejection fraction

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Purpose: MicroRNAs (miRNAs) are essential regulators of gene expression implicated in cardiovascular function and disease. MiRNA-21 and miRNA-133 have been shown to play a role in ventricular and vascular remodeling. However, there are limited data regarding their role in heart failure with preserved ejection fraction (HFPEF). The aim of this study is to investigate the association between miRNA-21 and miRNA-133 levels in peripheral blood mononuclear cells (PBMCs) and exercise capacity in patients with HFPEF
Methods: We included patients with symptoms and signs of heart failure who had an LVEF $>$50% and evidence of HFPEF. All subjects underwent a complete echocardiographic study and a cardiopulmonary exercise test.

PBMCs were isolated and miRNA levels were determined by quantitative real time reverse transcription PCR.
Results: Twenty patients (9 males, aged 58±16 years) were analyzed (NYHA II in 75%, III in 25%). The mean miRNA-21 levels were 3.9±0.61, mean miRNA-133 levels were 11.7±3.4 and mean peak VO2 were 16±5 ml/kg/min. Multivariable regression analysis sustained positive association between miRNA-21 levels and peak VO2 (p=0.004, r=0.51) and a negative association between miRNA-133 levels and peak VO2 (p=0.002, r=0.53).
Conclusions: MiRNA-21 and miRNA-133 may be an important marker or modulator of functional capacity in patients with HFPEF. Further studies are needed to assess their role as therapeutic targets in those patients.

P4659 | BEDSIDE
Lower plasma omega-6 polyunsaturated fatty acid level as a novel determinant for short-term adverse events after acute decompensated heart failure

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Purpose: Plasma omega-6 (n-6) polyunsaturated fatty acid (PUFA) level was reported to be associated with cardiovascular events especially in atherosclerotic disease. However, its prognostic significance in patients with acute decompensated heart failure (ADHF) remains unknown.
Methods: We examined 280 consecutive ADHF patients who admitted to our institution between January 2013 and December 2013 from prospective registry. Patients who had acute coronary syndrome and/or failed to be followed-up over 60 days were excluded. Finally, 207 patients were divided into two groups according to lower plasma n-6 PUFA (dihomo-gamma-linolenic acid plus arachidonic acid) (below 161 μg/ml, the median) or higher plasma n-6 PUFA (above 161 μg/ml) level at admission. Adverse events were defined as relapse of HF and death within 60 days after admission.
Results: Adverse events were occurred in 21 patients (10%). Lower plasma n-6 PUFA group had significantly higher incidence of adverse events compared with higher plasma n-6 PUFA group (16.0% vs 3.1%, P=0.003). Patients with lower plasma n-6 PUFA level had lower blood pressure, hemoglobin, serum albumin, plasma omega-3 PUFA levels and higher serum creatinine level on admission than those without. There were no significant differences between the two groups in terms of age, gender, body mass index, etiology of ADHF, cardiovascular medications, left ventricular ejection fraction, serum troponin-T, C-reactive protein (CRP) and plasma brain natriuretic peptide (BNP) levels on admission, and initial treatments for HF. Multivariate logistic regression analyses showed that lower plasma n-6 PUFA level (odds ratio 4.9, 95% CI 1.5-22.3, P=0.009), lower hemoglobin (odds ratio 3.9, 95% CI 1.4-11.5, P=0.01), and higher plasma BNP levels (odds ratio 4.1, 95% CI 1.4-14.0, P=0.01) were independent determinants for adverse events within 60 days after admission, among variables including age, gender, body mass index, blood pressure, plasma omega-3 PUFA, serum albumin, CRP and creatinine levels on admission.
Conclusions: Lower plasma n-6 PUFA level was a strong independent determinant for adverse events within 60 days after admission, suggesting plasma n-6 PUFA could be a potential surrogate marker for short-term adverse events in patients with ADHF.

P4660 | BEDSIDE
Discovering a novel biomarker candidate panel for predicting treatment response in heart failure

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Purpose: The main aim of this study was to discover novel biomarkers in plasma that could predict treatment response in patients with heart failure using plasma proteomics.
Methods: 100 patients with heart failure were recruited and their treatment with ACE-inhibitors and β–blockers was optimised over 6 months. Major adverse events (death or heart failure hospitalisation) were recorded over the next 24 months. Plasma proteins in heart failure responders (n=50, male/female 50%/50%, age 76.64±8.14 years) who responded to standard treatment were compared to 50 heart failure non-responders (n=50, male/female 50%/50%, age 76.64±8.14 years) who were dead (n=18) or re-hospitalised (n=32). Plasma samples were pooled, depleted of 14 high abundance proteins and then trypsinised to peptides. Peptides were analysed on 2-dimensional liquid chromatography coupled to electrospray high-definition ion mobility tandem mass spectrometry. PLGS 2.5 sotware was employed to identify and quantify proteins.
Results: 165 proteins identified were similar between heart failure responders and non-responders, as defined by fold-change<2 and p>0.05. 39 proteins identified were up-regulated and 16 proteins were down-regulated significantly in the heart failure non-responder group (fold-change>2 and p<0.05). Several of these proteins have the potential to become novel biomarker candidates for predicting treatment response in patients with heart failure which are classified according to 5 pathobiological processes (Table 1).

Table 1. Up-regulated proteins in non-responders

No	Pathobiological process	Description	Fold change
1	Cardio-renal system	Cystatin C	7.10
2	Vascular system	Intercellular adhesion molecule 2	2.97
3	Inflammation	Mannose binding protein C	2.36
4	Neurohormones	Hepatocyte growth factor like protein	2.16
5	Matrix and cellular remodelling	Retinol binding protein 4	2.03

Conclusions: The discovery of new biomarkers for predicting treatment response in this study will lead to the development of a more personalised treatment by giving guidance to medical therapy. As a result, the unnecessary prescription of therapy to heart failure non-responders may be avoided. In addition, novel therapeutic targets could be identified for design of new therapy strategies to improve poor outcomes in patients with heart failure.

SLEEP APNEA AND CENTRAL NERVOUS SYSTEM

P4662 | BENCH
Intermittent hypoxia relevant to sleep apnea increases oxidative stress and accelerates systolic dysfunction in heart failure

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Purpose: Prevalence of sleep apnea syndrome (SAS) is much higher in patients with heart failure (HF) and complication of SAS may aggravate their poor prognosis. The aim of this study was to investigate the effect of repetitive hypoxic stress on left ventricular (LV) myocardium in normal and failing heart.
Methods: Male Syrian (normal, n=18) and Bio14.6 cardiomyopathic (CM, n=27) hamsters at 20 to 24 weeks of age were exposed to intermittent hypoxia (IH: 1.5 minutes of 5% oxygen, followed by 5 min of 21% oxygen for 8 h/day during daytime) or normoxia for 14 days. In CM hamsters, hydrogen gas (3.05 vol/100 vol) was given at the time of during hypoxia. After evaluation of cardiac function by echocardiography, heart was examined by light and electron microscopy, immunohistochemistry, and RT-PCR.
Results: In Syrian hamsters, IH tended to increase E/e', but had no effect on LV ejection fraction (EF) (Table). In CM hamsters, however, IH accelerated systolic dysfunction as well as the development of diastolic dysfunction. Histologically, in contrast to normal hamsters, IH increased cardiomyocyte diameter (19.9 vs. 17.4 μm), interstitial fibrosis (29.9 vs. 9.6%), and Z-band streaming with contraction band necrosis in CM hamsters. Furthermore, IH increased oxidative stress such as 4-hydroxy-2-nonenal proteins, superoxide production and c-fos mRNA expression in CM hamsters. Hydrogen gas inhalation scavenged free radicals and decreased oxidative stress, consequently preserving cardiac function in CM hamsters.

Data of echocardiography

	Dd (mm)	Ds (mm)	E/A	E/e'	LVEF (%)
Syrian normoxia	4.65±0.26	3.19±0.20	1.43±0.13	17.6±2.74	61.0±0.47
Syrian hypoxia	5.13±0.04	3.64±0.09	1.45±0.11	26.6±5.27	60.7±1.22
CM normoxia	6.52±0.56§	4.92±0.64	1.77±0.05§	25.2±2.38	42.5±2.30§
CM hypoxia	6.81±0.33§	5.68±0.44§	1.37±0.04‡	28.1±1.32	34.2±4.68§†
CM hypoxia+hydrogen gas	6.21±0.63	4.79±0.89	1.47±0.03	23.0±3.84	49.5±9.86

Data are shown as mean ± SE (n=3–5). §P<0.05, compared with syrian normoxia; †P<0.05, compared with syrian hypoxia; ‡P<0.01, compared with CM normoxia.

Conclusion: IH accelerated degeneration of cardiomyocytes and systolic dysfunction at least partly through increased oxidative stress in CM hamster, which might account for the poor prognosis of HF patients with sleep apnea. Short-term inhalation of hydrogen gas might be effective in reducing oxidative stress and in preventing hypoxia-induced cardiac remodeling.

P4663 | BEDSIDE
Polysomnographic features of patients with congestive heart failure

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The research leading to these results has received funding from the European Union Seventh Framework Programme [FP7/2007-2013] under grant agreement n° 241558 (SICA-HF). The research leading to these results has received funding from the Russian Ministry of Science and Education within the FTP "R&D in priority fields of the S&T complex of Russia 2007-2012" under state contract №02.527.11.0007.
Purpose: To study the functional characteristics of sleep and structure of sleep breathing disoders in patients with congestive heart failure (HF) III-IV functional class, NYHA classification.
Design and methods: Fifty-nine subjects were enrolled (53 males and 6 females,57.1±9.5 years). HF resulted from CAD in 57 cases, and from cardiomy-

opathy – in 2. All patients underwent ECHO (GE Vivid 7, Norway) using standard protocol and full polysomnography (Embla N7000 (MedCare Flaga, Iceland).
Results: All patients had decreased systolic function (Simpson EF – 27.8±17.1%). According to polysomnography data total sleep time (TST) was 380 (310; 435) min. Sleep efficiency was 74.3% (63.4; 82.0). Sleep latency was increased up to 20.1 (10.3; 46.0) min. Sleep architecture was abnormal: the amount of stage 1 was increased to 8.9 (6.8; 13.1) %TST, but the most prevalent was stage 2 – 52.0 (45.5; 57.8) %TST. Surprisingly, the amount of stages 3 and REM were relatively normal and constituted 18.2 (14.7; 25.1) and 19.5 (16.4; 22.8) %TST, respectively. Also the latency to REM sleep was rather shortened: 61.0 (48.8; 97.8) min. Wake after sleep onset index was increased: 25.7 (18.0; 36.6) %TST. Regarding sleep breathing disorders 3 patients had no sleep-breathing disorders (apnea-hypopnea index, AHI, less than 5 episodes per hour/sleep), while 19 subjects had mild sleep apnea, 16 – moderate, and 20 – severe sleep apnea ($\chi 2$= 8.08; p=0.044). 20 patients (35.1%) demonstrated obstructive sleep apnea with AHI 13.5 (95% CI 9.8-27.1) episodes per h/sleep; 4 patients had central apnea with AHI 36.3 (95% CI 10.2-54.3) episodes per h/sleep, and mixed apnea was the predominant type (52.6%), and was detected in 30 subjects, AHI – 22.6 (95% CI 19.6-33.2) (Kruskall-Wallis test, $\chi 2$= 5.13; p=0.07).
Conclusion: Heart failure III-IV NYHA patients are characterized by abnormal sleep architecture (rather poor sleep efficiency, excess of stage 2 and prolonged wakefulness after sleep onset). Sleep-related breathing disorders are also common with mixed apnea as the predominant type.

P4664 | BEDSIDE
Cyclic variation of heart rate score by Holter ECG for screening sleep disordered breathing in heart failure patients

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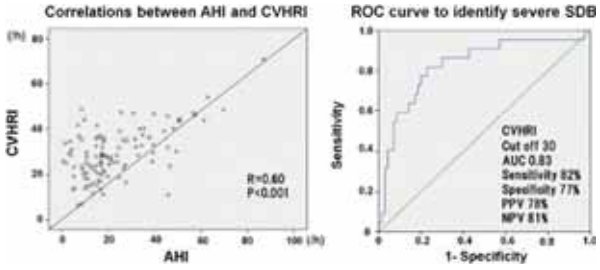
Purpose: Sleep disordered breathing (SDB) has a critical association with cardiovascular mortality and morbidity, especially in patients with heart failure (HF). However, because of the complexity to refer the polysomnography, the majority of SDB patients remain undiagnosed. On the other hand, the abnormality of heart rate variability has been reported in patients with SDB. To explore an efficient ECG-based screening tool for SDB, we examined the usefulness of cyclic variation of heart rate score (CVHRS) by Holter ECG in HF patients.
Methods: In this study, 112 patients with HF (mean age 58.6 years, body mass index 23.6, left ventricular ejection fraction 45.5%) were enrolled. The exclusion criteria were the presence of atrial fibrillation (n=8) and receiving implantable pacemaker device therapy (n=2), and 102 patients were analyzed. We simultaneously performed Holter ECG and polysomnography in night time, and measured apnea-hypopnea index (AHI) and CVHRS. We determined the temporal position of the individual dips comprising the CVHRS, using time-domain methods. CVHRS was measured as cyclic and auto correlated dips in smoothed interbeat interval time series.
Results: There were 77 patients with mild to moderate SDB (5≦AHI<30/h) and 25 patients with severe SDB (AHI≧30/h). There was a significant positive correlation between CVHRS and AHI (R=0.60, P<0.001). From the ROC analysis, CVHRS (a cut off value of 30) identified severe SDB with sensitivity 82%, specificity 77%, positive predictive value 78%, negative predictive value 81% and area under the curve 0.83.



Conclusions: CVHRS determined by Holter ECG is a useful screening index for severe SDB in HF patients.

P4665 | BENCH
Parametric electrical impedance tomography: a novel noninvasive method that accurately identifies pulmonary congestion

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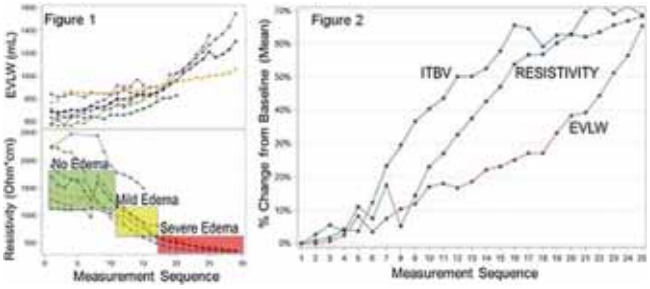
Introduction: In heart failure, accurate identification of lung fluid accumulation prior to occurrence of symptoms may prevent hospitalizations. However, currently approved parameters from implanted devices do not seem to impact clinical outcomes. Parametric Electrical Impedance Tomography (pEIT) is a novel proprietary algorithm that analyses Resistivity (Ohm*cm) of intrathoracic electrical impulses independent of other organs in the thorax.
Aim: This study tested the hypothesis that pEIT accurately and precisely reflects intravascular and extravascular lung fluid volumes in a sheep model of progressive pulmonary edema.
Methods: Pulmonary edema was induced in 6 anesthetized sheep by IV volume infusion. Pulmonary & systemic arterial hemodynamics, and volumetric intrathoracic blood volume (ITBV) and extravascular lung water (EVLW) measured by Transpulmonary Thermodilution were correlated with Resistivity pEIT measurements.
Results: Pulmonary edema was induced in all 6 sheep (EVLW ≥30% change from baseline). Changes in pEIT significantly correlated with changes in Left Ventricular End Diastolic Pressure (R=-0.88±0.06, p<0.0001), ITBV (R= -0.88±0.10, p<0.0001) and EVLW (R= -0.93±0.07, p<.0001) (Fig 1 shows simultaneous EVLW and Resistivity measurements). Changes in Resistivity followed changes in ITBV but preceded EVLW changes (Fig 2). Mean Resistivity across repeated measurements was 1,378±22 Ohm*cm (CI: 18-29 Ohm*cm, coefficient of variation (CV) 1.6%) at baseline and 761±20 Ohm*cm (CI: 18-22 Ohm*cm, CV 2.6%) during pulmonary edema.



Resistivity vs Volumetric measurements.

Conclusions: The novel pEIT method was highly reproducible, detected early the pulmonary congestion, prior to accumulation of extravascular lung water and showed very good correlation with the level of pulmonary congestion.

P4666 | BEDSIDE
Adaptive servo-ventilation beneficially effects on cardiac remodeling in patients with severe dilated cardiomyopathy

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Background: Adaptive servo-ventilation (ASV), a novel positive airway pressure therapy, was reported to have a beneficial effect on chronic heart failure (CHF). However, the effect on reverse remodeling in CHF with idiopathic dilated cardiomyopathy (DCM) has not yet been explored.
Methods and results: A total of 103 patients (59±15 years, male 73%, NYHA ≥II, left ventricular ejection fraction (LVEF) ≤40%), who were receiving optimal medical and cardiac devices therapy, were studied. ASV therapy was initiated using the AutoSet CS device with full face masks during the night. Before and 6 months after the introduction of ASV, blood tests and 2D echocardiography were performed. Those patients were divided into 2 groups according to left ventricular end-diastolic dimension (LVEDD); group A, severely dilated left ventricle with LVEDD ≥70mm (n=46); group B, LVEDD <70mm (n=57). Patients in group A were associated with younger age (56±14 vs. 62±15 years, p=0.02), male sex (85% vs. 65%, p=0.03), implanted CRT device (57% vs. 33%, p=0.02) and lower LVEF (17±6 vs. 25±7%, p<0.01). Plasma BNP level, blood hemoglobin and creatinine levels, apnoea hypopnea index, and medications including ACE inhibitor/ARB and β-blockers were not different in both groups. In each group, patients were divided into 2 categories; patients who were able to continue the ASV for 6 months (ASV treated) and could not use the ASV because of discomfort (non-ASV treated). In group A, ASV treated patients showed significant increase in LVEF (4±6 vs. -2±4, p=0.016) compared to non-ASV treated patients. ASV therapy tended to improve parameters such as LVEDD and plasma BNP level (-2±6 vs. 1±5 mm, p=0.07; -383±1246 vs. 369±537 pg/mL, p=0.08, respectively). However, in group B, there was no difference in change of cardiac function between ASV treated and non-ASV treated patients. Estimated end systolic wall stress (ESWS) was calculated by the Wilson formula; 0.98*0.334*SBP*LVESD/PWTs*(1+PWTs/LVESD)-2 (10^3 dyne/cm^2). ESWS was correlated strongly with LVEDD (p<0.001, R=0.75), suggesting improvement of cardiac function with ASV in patients with severe DCM might be resulting from favorable haemodynamic effect on increased wall stress in those patients.
Conclusions: ASV treatment improved cardiac function in patients with severe DCM, possibly through favorable haemodynamic effect.

P4667 | BEDSIDE

Association of sleep apnea and atrial fibrillation in patients with systolic left venricular dysfunnction

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Background: Both sleep apnea and atrial fibrillation (AF) are commonly known as determinants for poor prognosis in patients with systolic left ventricular dysfunction. There is only few evidence about the association of sleep apnea syndroms and atrial fibrillation in these patients.
Methods: We studied a total of 274 consecutive patients with congestive heart failure (CHF) (LVEF <40%, 75% male, Age 71±11,2, BMI 27±5,4, 77% NYHA III/IV, LVEF 28±9,3%, sinus rhythm 55,9%, AF 30,6%). Sleep apnea was detected both by a commercial sleep screening device (Apnea Link) and a novel Holter-ECG-based algoritm.
Results: There was a high prevalence of sleep apnea (AHI Apnea Link 21,3/h, AHI Holter ECG 18,1/h). Both methods exhibited a significant association (r=0,86). There was a statistical significant higher prevalence of sleep apnea syndroms in patients with atrial fibrillation than in sinus rhythm (*p<0,05, ***P<0,001). The incidence of atrial fibrillation was associated with the severity of sleep disordered breathing (Fig. 1).

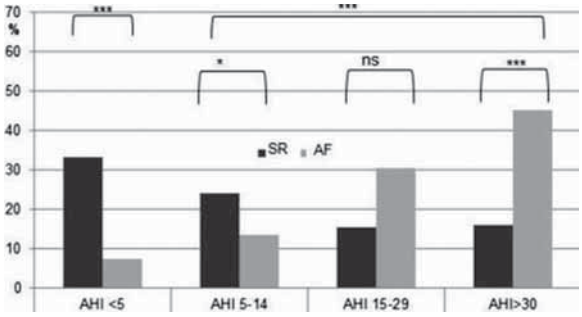

Figure 1

Conclusion: Severity of sleep apnea in patients with CHF is significantly associated with the incidence of atrial fibrillation. Furthermore, CHF-patients with AF appear to have a higher risk for sleep breathing disorders, especially patients with persistent and permanent AF.

P4668 | BEDSIDE

Baroreflex activation therapy improves status of resistant hypertension patients with heart failure

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Purpose: Treatment guidelines call for control of blood pressure (BP) as a preventative measure in patients with preserved-ejection fraction heart failure (HFpEF). Signs and symptoms of HFpEF are not uncommon among patients with resistant hypertension (rHTN). Baroreflex activation therapy (BAT) provides long-term BP reductions in rHTN. It is therefore of interest to understand if BAT affords the same benefits in patients with both rHTN and HFpEF.
Methods: Patients enrolled in the Rheos Pivotal Trial of BAT in rHTN were followed twice annually after completing the 12-month endpoint. Patients with HFpEF were retrospectively identified by a panel of physicians with relevant expertise.
Results: Presence of HFpEF was adjudicated in 82 patients with complete data through 12 months: 24 from medical history, 42 with BNP >100 pg/mL and 16 based on chart review. Baseline ejection fraction was 65±9%. BAT reduced BP, including a ~20 mmHg reduction in pulse pressure, and the effects were maintained over 5 years. Quality of life improved during year 1 while left ventricular mass and BNP trended downward.
Conclusions: BAT provided sustained clinical benefit to rHTN patients with early-stage HFpEF, which included BP control, improved quality of life and regression of ventricular hypertrophy. Prospective trials are in order to assess benefits of BAT in advanced HFpEF.

Chronic effects of baroreflex activation

	Baseline	1 year	2 years	3 years	4 years	5 years
Completed follow-up (N)	82	82	61	67	53	9
	Baseline	Δ1 year	Δ2 years	Δ3 years	Δ4 years	Δ5 years
Systolic BP (mmHg)	178.9±24.6	−36.1±2.9§	−30.7±4.4§	−37.3±4.2§	−36.8±4.6§	−30.3±5.4§
Diastolic BP (mmHg)	99.7±17.0	−16.3±1.7§	−14.2±1.9§	−18.3±2.3§	−17.7±2.4§	−13.3±3.8†
	Baseline (N)		Δ6 months (N)		Δ12 months (N)	
Left ventricular mass index (g/m²)	127.6±41.1 (14)		−6.7±3.7 (14)		−13.5±6.6° (14)	
SF-12 physical score	44.9±8.2 (64)		+2.1±0.9* (64)		+2.3±0.9† (64)	
B-type natriuretic peptide (pg/mL)	167.2±133.0 (38)		+0.2±26.8 (38)		−11.8±27.9 (38)	

Baseline: mean±SD; changes: mean±SE. Significance: °p=0.06, *p<0.05, †p≤0.01, §p<0.001.

P4669 | BEDSIDE

Cardiac function and sleep quality in patients with chronic heart failure and sleep disordered breathing were improved by leg thermal therapy

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Purpose: Improvement of Quality of Life (QOL) in patients with chronic heart failure (CHF) is a goal together with improvement of prognosis. CHF patients often have insomnia that makes their QOL poor, and has adverse effects on cardiac function because of increased nocturnal sympathetic nerve activity. If we could help CHF patients have better sleep, it should let them have better QOL and improve cardiac function. Eventually, it may contribute to better prognosis. Thermal therapies are known to increase deep sleep. However, they could sometimes cause adverse events, such as hypotension and ischemic attacks, in CHF patients. We previously introduced a safer topical method, leg thermal therapy (LTT). In this study, we examined the effects of LTT on cardiac function and sleep quality in CHF patients.
Methods: Thirty inpatients with stable CHF (age 58±12 y.o., male 21, NYHA II-IV) received LTT (heating at 45℃ for 15 minutes followed by 30 minutes insulation) for 3 consecutive nights. We measured flow mediated vasodilation responses (%FMD), plasma brain natriuretic peptide level (BNP) and sleep structure by polysomnography, before and after intervention. We examined a parameter, circulatory lag time (LT), which has been reported useful, by automatic calculation that calculates time differences between starting points of nasal airflow after sleep apnea and rise in fingertip oxygen saturation. LT reflects arrival time of oxygenated blood by hyperventilation after sleep apnea from lung to fingertip. We have confirmed that the LT correlates well with ventricular ejection fraction and cardiac index, and to represent significantly impaired cardiac function if is over 35 seconds.
Results: All of the patients had sleep apnea, which eventually enabled us to calculate LT. LTT significantly improved %FMD (4.8±2.7 to 7.6±4.2%, p<0.001) and decreased BNP (433±349 to 333±275 pg/mL, p<0.05). Structured sleep analysis showed that LTT decreased sleep stage 1 (21±12 to 17±10%, p<0.05) and increased stage 2 (60±12 to 64±8%, p=0.08), which indicated improvement of sleep structure. In patients with longer LT (>35 sec), LTT significantly decreased LT (44±7 to 38±4 sec, p<0.05). Decrease in sleep stage 1 and 2 correlated with improvement of LT (r=0.48 p=0.05, r=-0.51 p<0.05; respectively).
Conclusions: LTT ameliorated impaired sleep quality and CHF status in our CHF patients. LTT might improve cardiac and arterial function as well as sleep quality in CHF patients. LTT may have potency as a safe home complementary therapy to improve QOL and hemodynamic status, and hopefully eventual improvement of prognosis of CHF patients.

P4670 | BEDSIDE

Hyponatremia, related to cardiac sympathetic nerve activity, has the prognostic significance of chronic kidney injury in patients with chronic heart failure

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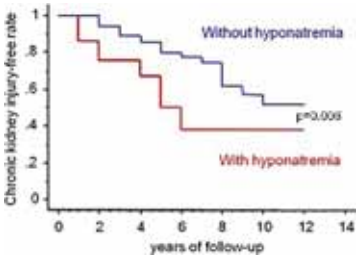
Background: Hyponatremia is associated with poor outcome in patients with chronic heart failure (CHF). However, the pathophysiological basis of hyponatremia remains to be fully clarified from the viewpoint of cardiac sympathetic activity, and there is little information on the prognostic value of hyponatremia in cardiorenal syndrome in CHF patients.
Methods: We studied 112 CHF outpatients with left ventricular ejection fraction (LVEF) less than 40%. At the entry, cardiac MIBG imaging was performed in all patients, and MIBG washout rate (WR) was calculated as an index of cardiac sympathetic nerve activity. The measurement of serum creatinine level (sCr) was also measured at entry, and repeated every at least 6 month after the entry, and chronic kidney injury (CKI) was defined as an increase of more than 0.3mg/dl in baseline sCr value.
Results: Thirty-one patients had hyponatremia (≤135mg/dl). The patients with hyponatremia significantly lower LVEF and 6-minute walk distance, higher WR and serum uric acid, blood urea nitrogen, plasma norepinephrine levels, and more use of diuretics than those without hyponatremia. Multivariate logistic regression analysis revealed that WR (p=0.038) and serum uric acid level (p=0.048) were independently associated with hyponatremia. During a mean follow-up of 5.3±3.1

years, 37 patients had CKI. Patients with hyponatremia had a significantly higher risk of CKI than those without hyponatremia (53% vs 37%, p=0.006, adjusted hazard ratio 1.97 (95%CI: 1.02-3.81)).



Conclusion: Hyponatremia is related to cardiac sympathetic nerve activity and has the prognostic significance of chronic kidney injury in CHF patients.

P4671 | BEDSIDE
Time course of adaptive servo-ventilation effects on central sleep apnea in patients with chronic heart failure

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Background: Central sleep apnea (CSA) is prevalent in patients with heart failure (HF). Although adaptive servo-ventilation (ASV) suppresses CSA, it remains unknown whether long-term ASV leads to alleviation of CSA.
Methods: Cardiorespiratory polygraphy and echocardiography were performed at baseline and 3.5±0.8 months (mean ± SD) of follow-up in 28 patients with HF (NYHA II and III; left ventricular ejection fraction (LVEF) <45%) and CSA (apnea-hypopnea index (AHI) ≥15/h). Of these, 17 patients consented and 11 patients declined to undergo ASV treatment. Effect of ASV on AHI was confirmed with polygraphy and device integral counters.
Result: One-night ASV reduced AHI from 27±15/h to 3±3/h ($p<0.0001$). AHI on ASV using device counters were similar with AHI measured by polygraphy. Long-term ASV alleviated AHI from 27±15/h to 11±7/h ($p<0.001$). Difference between AHI at baseline and AHI on ASV was closely correlated with change in AHI between baseline and follow-up ($R = 0.81$, $p<0.001$). Change in LVEF was also correlated with the change in AHI. However, bivariate analysis revealed that the difference between AHI at baseline and AHI on ASV was an independent predictor of change in AHI.
Conclusions: More suppression of CSA by ASV may relate to greater improvement of CSA irrespective of change of cardiac function.

P4672 | BEDSIDE
Impact of myocardial sympathetic nervous activity on left ventricular hypertrophy and clinical outcome in heart failure patients with preserved ejection fraction

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Background: Iodine-123 metaiodobenzylguanidine (MIBG) is used to assess myocardial sympathetic nervous activity, and a decrease in myocardial MIBG uptake and an increase in spillover have been observed in heart failure patients with reduced ejection fraction (HFrEF). However, clinical significance of MIBG remains unclear in heart failure patients with preserved ejection fraction (HFpEF).
Methods: Consecutive 60 patients with HFpEF admitted to our hospital due to symptomatic heart failure were included in this study. Left ventricular ejection fraction in all patients were over 45%. MIBG scintigraphy was performed under the stable clinical condition just before discharge. Using an anterior planar image, we determined the heart to mediastinum activity ratio (H/M) in the early and the delayed phase. Washout rate (WR) of MIBG from the heart was calculated according to the standard formula. Left ventricular mass (LVM) was also calculated by echocardiographic parameters. We also investigated plasma brain natriuretic peptide (BNP), kidney function, anemia and discharge medications.
Results: LVM index was correlated with delayed H/M ($r=-0.44$, $p<0.001$) and WR ($r=0.55$, $p<0.0001$), although it was not associated with plasma BNP level on discharge. During a mean follow-up of 20 months, a cardiac event including cardiac death or decompensated heart failure requiring hospitalization occurred in 16 patients. Event-free survival curves indicated delayed H/M <2.0 (log-rank=10.59, p=0.001) and WR >30% (log-rank=9.38, p=0.0022) as prognostic factors. Multivariate analysis identified brain natriuretic polypeptide on discharge, anemia and delayed H/M as independent predictors of a cardiac event.
Conclusion: Myocardial sympathetic nervous activity is associated with LV hypertrophy and clinical outcome in patients with HFpEF.

P4673 | BENCH
Beneficial impact of vagal nerve stimulation on chronic heart failure depends on stimulus dose and frequency

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Background: Chronic heart failure (CHF) is the end stage of cardiovascular disease and refractory to medical treatment. Recent investigations indicated that vagal nerve stimulation (VNS) markedly improved left ventricular (LV) function and survival in CHF. However, optimal dosing of VNS remains unknown. In this investigation, we titrated the voltage and the frequency of VNS and examined its impact on clinical markers of heart failure in rat.
Methods: Two weeks after the ligation of the left main coronary artery, we randomized rats into vagal and sham stimulated groups. Using an implantable electrical stimulator, we stimulated the right vagal nerve for a month (0.2msec pulse, 10sec stimulation out of a minute). We defined the maximum stimulation voltage above which the stimulation induces adverse effects such as vomiting and cough. In protocol 1, we allocated the VNS rats, according to the stimulus dose (amplitude), into 3 groups, Max (3.48±2.5 volts, n=14), Half (2.02±1.46 volts, n=13) and Quarter (0.79±0.36 volts, n=14) with 20Hz of pulse frequency. In protocol 2, we assigned the VNS rats into two groups, 10Hz (1.02±0.39 volts, n=6) and 5Hz (1.18±0.64 volts, n=5) stimulation at the most effective amplitude derived from Protocol 1.
Results: In Protocol 1, Half most reduced biventricular weight (Sham: 3.7±0.09, Max: 3.3±0.11, Half: 3.2±0.13, Quarter 3.3±0.09 g/kg, $p<0.05$), lung weight (as a measure of pulmonary) (Sham: 10.1±0.37, Max: 9.0±0.61, Half: 6.7±0.75, Quarter: 9.0±0.73 g/kg, $p<0.05$) and LV end-diastolic pressure (Sham: 24.2±5.1, Max: 21.7±5.0, Half: 17.6±7.2, Quarter: 21.5±5.1 mmHg, $p<0.05$). LV ejection fraction was highest in Half (Sham: 28.4±9.6, Max: 34.7±9.0, Half: 37.9±6.8, Quarter: 33.6±11.0%, $p<0.05$). In protocol 2, compared with Half with 20Hz, 10 Hz VNS failed to reduce biventricular weight or lung weight nor to improve hemodynamic parameters.
Conclusion: The efficacy of VNS treatment on CHF is stimulus dose dependent. In addition, 20 Hz is needed to achieve the optimal VNS. The adjustment of VNS intensity and frequency enables us to maximize its beneficial impact on CHF patients.

EPIDEMIOLOGY AND REGISTRIES

P4675 | BEDSIDE
Clinical comparison between acute myocardial infarction, acute myocarditis and stress cardiomyopathy: a diagnostic challenge

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Introduction: The differential diagnosis of chest pain associated with elevation of myocardial necrosis biomarkers encompasses, among others, acute myocardial infarction (AMI), acute myocarditis (AM) and stress cardiomyopathy (SCM), which may be distinguished by some clinical particularities, not always obvious.
Objective: To identify the main clinical differences between AMI, AM and SCM.
Methods and results: Retrospective observational cohort study including patients admitted in a Coronary Unit for the period of 4 years, until June 2013, with the diagnosis of AMI (n=1836, 47% without ST elevation and 53% with ST elevation), AM (n=66) and SCM (n=39). The minimum follow-up realized was 6 months. In the next sentences we describe the results with statistic significance ($p<0.05$). Comparatively with AMI and SCM, AM was more frequent in male (92.4%) and younger patients (mean age 37 years), with lower prevalence of cardiovascular risk factors, which presented without heart failure (97.0%), absence of T wave inversion in ECG (91.7%) and were less medicated with beta-blockers (33.3%), ACE-I (39.4%) and diuretics (0%). These patients had better prognosis at short and long term (none died). Analytically, they expressed higher values of C-reactive protein (mean 49.2 mg/L). On the other hand, SCM was more frequent in women (74.4%) and was associated with higher heart rate (mean 93/min) and heart failure at admission (35.9%), large QRS in ECG (32.4%), left ventricle dysfunction (75.7% with ejection fraction ≤40%), high NT-proBNP (mean 8113 pg/mL), low peak troponin I (mean 4.5 ng/mL) and lower hemoglobin (mean 11.7 g/dL) during hospital stay. The patients with AMI had higher prevalence of diabetes (27.6%) and slow progression of r wave in ECG (64.0%). Peak troponin I value was the highest (mean 52.6 ng/mL). Intermediate values of heart failure at admission (21.7%), left ventricular dysfunction (32.4% with ejection fraction ≤40%) and NT-proBNP (mean 2936 pg/mL) were observed. The NT-proBNP/peak troponin I quotient was statistically different among the 3 groups, being higher in SCM (mean 4563), intermediate in AMI (mean 866) and lower in AM (mean 146). The same happened with QTc interval, which was superior in SCM (mean 466 ms), intermediate in AMI (mean 446 ms) and inferior in AM (416 ms).
Conclusion: Regarding the patient with chest pain and elevation of myocardial necrosis biomarkers, there are some clinical, analytical and echocardiographic parameters that may suggest the most probable diagnosis. These include gender, age, C-reactive protein level, NT-proBNP/peak troponin I quotient and QTc interval.

P4676 | BEDSIDE
The international takotsubo registry score

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Background: Takotsubo cardiomyopathy (TTC) also known as broken heart syndrome is clinically difficult to distinguish from acute coronary syndrome (ACS) in the acute setting.
Aim: The aim of the present study was to establish a scoring system based on clinical parameters that is easily applicable in the emergency department to identify TTC and to distinguish from ACS.
Methods and results: 218 consecutive patients with TTC and 436 consecutive ACS patients were included. Complete clinical profile, comorbidities and ECG parameters were assessed in order to develop the InterTAKScore by using the bestglm package10 in R (version 2.15.1) for model selection with Bayesian information criterion (BIC).
The diagnostic InterTAKScore (max. total Score = 100) integrates female gender (25 points), emotional (24 points) and physical triggers (13 points), absence of ST-segment depression (14 points), psychiatric (11 points) and neurologic disorders (9 points) and QTc time prolongation (5 points), differentiating TTC from ACS with high sensitivity (89%) and specificity (91%; AUC of 0.97, 95% CI, 0.96-0.98).
The median (IQR) of the TTC population was 61 (50-76) while the ACS population gained 18 (12-31) points. The validation showed similar results - TTC 59 (43-65) vs. ACS 24.5 (12-37).
Conclusion: The InterTAKScore is a novel scoring system to distinguish patients with TTC from those with ACS on presentation.

P4677 | SPOTLIGHT
The High prevalence of Primary Amyloidosis among Afro Caribbean Heart Disease

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Background: Primary amyloid (A) is a rare infiltrative disease in late adult life affecting the heart and other tissues diagnosed by tissue analysis of the affected organ. We reviewed our echocardiographic database of hypertensive Afro Caribbean (AC) patients seen with heart failure symptoms to define prevalence of this disease using accepted biopsy and/or MRI criteria.
Method: From ethnicity specific heart failure service records (from n=106 total subjects) we identified 86 AC subjects with a complete trans-thoracic (TT) echo dataset. A was defined by typical TT echo criteria and confirmed by positive RV septal tissue histology at biopsy and or typical features on late gadolinium MRI (reported independently). Cases positive for A (28) were compared to negative (58) controls (C) by multivariate regression (MVr).
Results: We found a high prevalence (33%) of A (n=29;18male;68±17yr;Y±Ykg) compared to C (n=58;39male;71±16yr;Y±Ykg) in this sample. Both demographic criteria (age;gender;body mass;blood pressure) and a range of standard TT echo measures of morphology (LVDDd LVDDs) or function (ePAP; Simpsons LVEF) were similar on MVr. Only septal (IVSs;A,1.86±0.77;C,1.45±0.39; IVSd A,1.7 (1.4-1.9cm);C,1.1 (1.0-1.4cm)p=0.033) and PW thickness (LVPWs A,1.89±0.69;C,1.44±0.61;LVPWd A 1.63±0.38;C,1.23±0.55 p=0.002) were significantly higher in A. LV internal diameters (d and s) were lower in A than C. Renal function was poorer in A cases (Urea A,13.5,7.9-21.3mM; C 8.5, 6.5-12.9mM p=0.02; Creat A,188,115-401; C,119, 98-155μM; p=0.004). Notably in our series neither atrial volume nor inter atrial septal wall thickness were recorded routinely despite their known sensitivity and specificity in the TT echo diagnosis of A.
Conclusion: We have recorded an unusually high retrospective prevalence of A in elderly AC heart disease patients with HF symptoms. Given the development of specific treatments for this condition all clinicians seeing AC patients with abnormal TT echo should consider biopsy and/or MRI in suspicious cases.

P4678 | BEDSIDE
Prevalence of atrial fibrillation in patients with heart failure according to age

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Purpose: Heart Failure is common in the western world, has multiple causes and confers significant morbidity and mortality. It is thought a significant proportion of Heart Failure patients also have Atrial Fibrillation although figures from a large population in the UK are lacking. We studied the prevalence of Atrial Fibrillation in patients with Heart Failure in the North West of England.
Methods: Anonymous data of adult patients aged ≥18 with Heart Failure and Atrial Fibrillation attending 7 hospitals between 2000 and 2013 was obtained and processed using the ACALM (Algorithm for Co-morbidity, Associations, Length of stay and Mortality) study protocol. ACALM uses the ICD-10 and OPCS-4 coding systems to identify patients. Analyses was performed in SPSS.
Results: Of 929465 adult patient population there were 31760 (3.4%) patients with Heart Failure. Mean age 73.6 years, Male 50.3%. Of these 10992 patients had Atrial Fibrillation (34.6%). The prevalence of Atrial Fibrillation in patients with Heart failure increases with age from 8.1% in the 30-39 year age group to 42.4% in the 80-89 years group.
Conclusion: Whilst a significant number of elderly patients with Heart Failure patients do have concurrent Atrial Fibrillation, the majority of patients do not. Our findings are important to appreciate whilst optimising Heart Failure management in elderly patients.

Table 1. Prevalence of atrial fibrillation in patients with heart failure according to age groups

	Heart failure patients (%)	Atrial fibrillation %	Mean age (years)
All age groups	31760 (100.0)	34.6	73.6
Age group 18–29 years	256 (0.8)	8.6	24.2
Age group 30–39 years	528 (1.7)	8.1	35.4
Age group 40–49 years	1158 (3.6)	12.8	45.2
Age group 50–59 years	2571 (8.1)	21.5	55.2
Age group 60–69 years	5423 (17.1)	29.0	65.0
Age group 70–79 years	9743 (30.7)	36.8	74.8
Age group 80–89 years	9503 (29.9)	42.4	84.0
Age group 90–99 years	2533 (8.0)	40.5	92.6
Age group ≥ 100 years	45 (0.1)	42.2	101.8

P4679 | BEDSIDE
Identification of climatic condition associated with the onset of acute heart failure syndrome: insights from acute heart failure Kyoto registry

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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 December 2013, 149 patients were admitted for AHF in our hospital. Among 275 days, we identified 107 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 (14.8±0.6℃ vs. 12.4±0.7℃, p=0.01) and average temperature (18.9±0.6℃ vs. 16.8±0.7℃, p=0.02) were significantly low, while maximum temperature (23.9±0.6℃ vs. 22.0±0.8℃, p=0.05) tended to be lower. On the previous days, maximum temperature (24.2±0.6℃ vs. 21.5±0.8℃, p=0.006), minimum temperature (14.8±0.6℃ vs. 12.5±0.7℃, p=0.01) and average temperature (19.0±0.6℃ vs. 16.6±0.7℃, p=0.009) were significantly low. Compared with the previous days, maximum temperature was increasing (-0.31±0.24℃ vs. 0.47±0.30℃, p=0.04), diurnal temperature range was extended (-0.33±0.27℃ vs. 0.53±0.33℃, p=0.04) and minimum humidity was decreasing (1.40±1.09% vs. -2.30±1.37%, p=0.03). There was no difference in mean atmospheric pressure on the AHF admission days, but mean atmospheric pressure from the previous days to 3 days ago tended to be high (1010.3±0.4 hPa vs. 1011.6±0.5 hPa, p=0.05). Interestingly, the maximum instantaneous wind speed was rising (-0.44±0.28 m/sec vs. 0.74±0.35 m/sec, p=0.009) 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 precipitation and sunshine duration. After adjustment for other factors, the difference from the previous day of the maximum instantaneous wind speed [odds ratio (OR), 1.08; 95% confidence interval (CI), 1.01-1.17], maximum temperature on the previous day [OR, 0.96; 95% CI, 0.93-0.99] and averaged maximum precipitation during previous 2 days [OR, 0.82; 95% CI, 0.66-0.98] were demonstrated as the independent risk factors for the onset of AHF syndrome. The difference from the previous day of minimum humidity [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.

P4680 | BENCH
Prevalence of heart failure in rural communities of Pakistan... the tip of the iceberg

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Background: Heart Failure (HF) is leading cause of death all over the world.

The data regarding HF in rural communities of Pakistan is lacking. Objective: To determine the prevalence of HF and its causes in a general rural population of Pakistan.
Methods: 2000 subjects of >30 years age, were selected by systematic stratified random sampling technique from 22 villages. Predesigned proforma describing demographics, coronary risk factors, WHO dyspnoea questionnaire and past history of HF/Heart Disease used for interview. Physical examination, fasting blood sample, 12 lead ECG were performed on all subjects and echocardiography carried out on clinically suspected cases. Overall prevalence was defined on the basis of current symptoms/signs pertaining to HF and past history of HF. Data was analyzed using SPSS version 16.
Results: Overall prevalence of HF was 24.4% with insignificant gender difference. Significantly higher prevalence observed with increasing age (p. value 0.001). Causes of HF were hypertension 39% coronary heart disease (CHD) 27%, diabetes 8.7%, valvular heart disease 2.5% and cardiomyopathy 0.8%. Hypertension, CHD, diabetes, smoking and illiteracy have strong association with HF. 21.6% patients has HF with reduced EF (LVEF <40%). 2.5% had LVEF 41-49% and 77% had preserved LVEF (EF>50%). 6.9% abnormal ECGs and 25.4% had past history of HF.
Conclusion: This study discovered a high prevalence of HF in rural communities of Pakistan. Hypertension and CHD were dominant causes. Implementations of preventive strategies can minimize the incidence of fatal syndrome of HF.

P4681 | BEDSIDE
Patient characteristics and outcomes in Japanese and British patients admitted with heart failure; the West Tokyo - Kingston-upon-Hull Collaboration

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Background: Although acute heart failure (AHF) is common in both Japan and the United Kingdom, the clinical characteristics and outcomes of patients in these two countries have never been directly compared.
Methods and results: We analyzed the in-hospital, and 180-day outcome of 197 patients from a single university hospital in the UK and 327 patients from Japan (multicenter registry from three hospitals) admitted with AHF between 2010 and 2013. The median (Interquartile range [IQR]) age of patients in the UK was 78 (70-84) years and 77 (68-83) years in Japan. 38% of the patients in the UK were women compared with 40% in Japan. A greater proportion of patients with left ventricular systolic dysfunction (LVEF<45%) was noted in the UK (64% vs. 48%). There were significant differences in serum creatinine and NT-proBNP upon presentation; both of which were higher in patients in the UK compared to Japan. In the UK, the median (IQR) NT-proBNP was 4957 (2291-10,897)ng/L and 2938 (1110-6437)ng/L in Japan. Length of stay was longer in Japan; median time 11 (7-18) days in the UK compared with 14 (10-22) days in Japan. In-hospital mortality rate was slightly higher in the UK (7.1% vs. 4.5%). Subsequent to discharge, mortality at 90- and 180-days was substantially higher in the UK (13.1% vs. 3% for 90-days mortality, 21.3% vs. 3.9% for 180-days mortality, P<0.001 for both comparisons). The UK mortality rates are consistent with those reported by the National Audit of England & Wales in more than 100,000 patients.
Conclusion: Important differences exist in patient demographics, renal dysfunction and plasma concentrations of NT-proBNP in Japanese compared to British patients but these did not explain the much better prognosis of Japanese patients. Further investigation is needed to identify whether ethnicity, case selection or care account for the observed differences in outcome.

P4682 | BEDSIDE
Analysis of length of stay in patients with acute heart failure using data from RICA registry

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Purpose: Length of stay (LOS) is a major driver of cost of care and a growing quality marker. The objective of this study was to determine factors influencing LOS in elderly heart failure patients.
Methods and results: RICA is a multicenter registry which isenrolling patients admitted to public and private Spanish hospitals. We included 3217 patients in this analysis with a mean LOS of 9.6 days (mean age 79 years, male 48%, mean ejection fraction 50% and 87% in NYHA II and III). We stratified LOS into <7 days and ≥7 days. Longer LOS was associated with a number of risk factors including more COPD, NYHA III, LVH, hospital acquired infections, higher creatinine and lower SBP, but paradoxically with lower age. Longer LOS was also associated with higher one year mortality.

Table 1. RICA baseline characteristics and length of stay

Variables	All	<7 days	≥7 days	P value
N	3217	1275	1942	
Age, years (SD)	78,8 (8,7)	80±8.8	78±8.6	<0.001
Mean length of stay, days (SD)	9,6 (8,2)	4.3±1.5	13±8.9	<0.001
COPD, n (%)	830 (25,9%)	282 (22%)	548 (28%)	<0.001
NYHA Class I, n (%)	284 (9,1%)	108 (8.8%)	176 (9.4%)	0.614
NYHA Class II, n (%)	1630 (52,5%)	692 (57%)	938 (50%)	<0.001
NYHA Class III, n (%)	1079 (34,8%)	383 (31%)	696 (37%)	0.001
NYHA Class IV, n (%)	112 (3,6%)	41 (3.3%)	71 (3.8%)	0.535
SBP (mmHg)	139,0 (28,1)	142±28	137±28	<0.001
Creatinine (mg/dl)	1,3 (1,7)	1.3±0.6	1.4±0.7	0.002
Left ventricular hypertrophy, n (%)	827 (26,9%)	293 (24%)	534 (29%)	0.003
Ejection fraction (%)	50,0 (15,8)	51±15	50±16	0.035
Mortality at year	476 (33%)	146 (27%)	330 (37%)	<0.001
Readmissions at one year	450 (28%)	170 (28%)	280 (28%)	0.989
Hospital acquired infection	180 (24%)	29 (17%)	151 (27%)	0.009

LOS: length of stay; SD: standar deviation.

Conclusions: Multiple factors influence LOS in elderly heart failure patients and understanding these can lead to strategies to reduce LOS and readmissions. More work is needed to develop simple screening tools to identify higher risk in elderly heart failure patients.

P4683 | BEDSIDE
Incidence of hospitalization for heart failure in atrial fibrillation patients with anemia: one-year follow-up of the Fushimi AF Registry

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Purpose: There is a well-documented relationship and a complex interaction between atrial fibrillation (AF) and heart failure (HF). Anemia interacts with clinical outcomes in patients with AF and HF. However a relationship between anemia and heart failure in AF patients is unknown.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku. At present, we have enrolled 3,821 patients from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013. We defined anemia as reduced hemoglobin level (<11g/dl). We previously reported the baseline clinical characteristics of AF patients with anemia, and here we report the one-year outcomes of those patients.
Results: Among 2,774 patients in the Registry whose hematological values were available, 471 patients (17.0%) had anemia. AF patients with anemia were older than those without anemia (79.2±10.3 vs. 73.1±10.3 years of age; p<0.01). They were more likely to have various co-morbidities: a history of stroke (27.2% vs. 20.7%; p<0.01), HF (42.0% vs. 25.5%; p<0.01), chronic kidney disease (CKD; 66.9% vs. 30.9%; p<0.01), and history of major bleeding (4.7% vs. 1.6%; p<0.01). Anemic AF patients showed greater CHADS2 score (2.54±1.36 vs. 2.01±1.31; p<0.01). Patients receiving the prescription of oral anticoagulants were less in anemic patients. During the one-year follow-up period, there was no significant difference in stroke (n=17 vs. 59) (3.6% vs. 2.6%; p=0.22), myocardial infarction (n=3 vs. 7) (0.6% vs. 0.3%; p=0.31), between anemic and non-anemic AF patients. In the anemic group, the incidence of hospitalization for HF (n=35 vs. 84) (7.4% vs. 3.7%; p<0.01) and major bleeding (n=15 vs. 29) (3.2% vs. 1.3%; p<0.01) were more. After the adjustment by age and gender in multiple logistic regression models, anemia was independently associated with the incidence of hospitalization for HF (adjusted odds ratio, 1.6; 95% confidence interval, 1.00 to 2.36; p=0.049). In patients with anemia, the presence of CKD did not affect the incidence of hospitalization for HF (8.5% in anemic AF patients with CKD vs. 5.1% in anemic AF patients without CKD; p=0.17) or that of major bleeding (4.1% vs. 1.3%; p=0.07).
Conclusion: In patients with AF, anemia was associated with higher incidence of hospitalization for HF and major bleeding, irrespective of the presence of CKD.

P4684 | BEDSIDE
The changes and prognostic value of pulse pressure and proportional pulse pressure in different systolic blood pressure range subgroups of severe systolic heart failure patients

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Background: Earlier studies showed that in severe systolic heart failure (HFrEF) low pulse pressure (PP) and proportional pulse pressure (PPP) are predictors of mortality.

Aim: To investigate the changes and prognostic value of PP and PPP in severe HFrEF pts (baseline /b/ left ventricular ejection fraction /LVEF/<35%; NYHA III-IV), on optimal therapy (OT).
Patients and methods: 396 consecutive hospitalized HFrEF pts (age: 61.4 ±16.8 years; male: 75.7%; ischemic: 48.0%; LVEF: 27.3±7.0%; NYHA: 3.5±0.5; eGFR: 66.1±23.8 ml/min/1.73m^2; systolic blood pressure /SBP/: 123.3±22.7 mmHg) followed at our heart failure outpatient clinic (HFOC) were included in the study. Every pt received optimal medical and device therapy. Pts were divided into 3 groups according to bSBP (Group 1: SBP <110 mmHg: 162pts; Group 2: SBP 110-130 mmHg: 117pts; Group 3: SBP >130 mmHg: 117pts). The mean follow-up was 55.0±33.0 months. SBP, PP, PPP as well as NYHA and LVEF were assessed before and after treatment optimization (TO). The prognostic effect of PP, PPP and their change during TO on survival of pts were analysed with univariate and multivariate Cox-regression in the 3 predefined subgroups.
Results: After TO in the total cohort (TC) SBP decreased by 4.0±23.5mmHg ($p<0.05$), NYHA decreased to 1.7±0.7 ($p<0.05$), while LVEF improved to 36.4±10.3% ($p<0.05$). In Group 1 SBP, PP, PPP increased significantly (+9.0±19.0mmHg; +9.6±15.5mmHg and +0.08±0.07, all $p<0.05$), in Group 2 a small but significant early decrease of SBP (-2.7±14.8mmHg, $p<0.05$) with an early increase of PP and PPP (+4.9±15.4mmHg and +0.08±0.06) was observed, while in Group 3 beside a slight, non-significant increase of PPP (+0.02±0.08), SBP and PP decreased significantly (-25.1±22.4mmHg and -8.1±16.6mmHg, $p<0.05$). In Group 2 and 3 univariate Cox analysis demonstrated prognostic value of age, ischemic etiology, eGFR, LVEF, NYHA on survival ($p<0.05$). In these subgroups multivariate Cox regression showed that age, LVEF and NYHA remained independent prognostic factors of survival. In Group 1 univariate and multivariate Cox analysis demonstrated, that beside age, ischaemic etiology and eGFR, changes in PP and PPP during TO were also predictors of survival ($p<0.05$).
Conclusion: In severe HFrEF pts on OT with low bSBP the increase of PP and PPP is associated with beneficial prognosis. In our study changes in these parameters do not have significant prognostic value in pts with higher baseline systolic blood pressure.

P4685 | BEDSIDE
The relationship between left atrial enlargement and incidence of heart failure in patients with non-valvular atrial fibrillation: From the Fushimi AF registry

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Purpose: Atrial fibrillation (AF) patients are increasing significantly (reportedly 0.6% of total population in Japan), and have an increased risk of heart failure. Although age, history of heart failure, hypertension, diabetes mellitus (DM), anemia, and chronic kidney disease (CKD) were reported to be the predictor of hospitalization for heart failure, the impact of left atrial enlargement on the incidence of heart failure in AF patients has not been well evaluated.
Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Kyoto, Japan. At present, we have enrolled 3,821 patients (1.4% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013. Left atrial enlargement (LAE) was diagnosed if the left atrial diameter measured by transthoracic echocardiography was >45 mm. We compared the baseline clinical backgrounds and incidences of clinical events during one-year follow-up period between those with LAE and those without it (non-LAE). We excluded the patients with mitral stenosis and severe mitral regurgitation in this analysis.
Results: Patients with LAE accounted for 39.7% of all the patients. LAE group was older (LAE 75.0±.10.1 vs. non-LAE 73.3±10.9 years; $p<0.01$). Distribution of AF types (paroxysmal, persistent, and permanent) was 26.1%, 7.4%, and 66.5% in LAE group, 64.1%, 7.6%, and 28.3% in non-LAE group respectively. History of heart failure, hypertension and CKD were more in LAE group (36.7% vs. 22.7%; $p<0.01$, 64.8% vs. 59.5%; p=0.01, 42.4% vs. 34.2%; $p<0.01$, respectively). DM and anemia were comparable between the two groups. LAE group showed higher incidence of hospitalization for heart failure during one-year follow-up, compared with non-LAE group (6.7% vs. 3.1%; $p<0.01$). This was also the case in patients with paroxysmal AF (5.8% vs. 2.6%; p=0.02), as well as those with permanent AF (7.2% vs. 3.8%; p=0.03). After adjusting the confounders such as age, history of heart failure, hypertension, DM, anemia, and CKD, LAE had statistically significant association with the incidence of hospitalization for heart failure during one-year follow-up (adjusted odds ratio: 1.66; p=0.02).
Conclusion: The Fushimi AF registry represents the clinical profile of real-world AF patients. AF patients with LAE showed higher incidence of hospitalization for heart failure during one-year follow-up. LAE may help us identify AF patients who are at high risk for developing heart failure.

P4686 | BEDSIDE
Clinical characteristics of patients hospitalized for heart failure in China: observations from the first 3740 cases in china national heart failure registry (CN-HF)

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Purpose: China is facing the great challenge of the epidemic of heart failure because of the aging of the population and the rapid increase in the prevalence of the major risk factors for cardiovascular diseases. In 2013, we launched the Nationwide Inpatient Heart Failure Registry (CN-HF).The goal is to study clinical characteristics, management and outcomes of patients with heart failure, thereby promoting better quality of heart failure care in China.
Methods: The sample of hospitals in the CN-HF was stratified on geographic region (Middle, North and South) and hospital Grade (University hospital and Community hospital) to better represent heart failure population. Enrolled patients will be followed annually. Participating hospitals is responsible to validate HF diagnosis during discharge. Data about medical history, management, and outcomes are collected through review of medical records and entered into a database via secure web browser technology.
Results: In calendar year 2013, data on 3740 patients have been received from 34 participating hospitals. Of enrollees with available analyzable data, the median age was 73.0 (interquartile range (IQR): 63-80), and 59% were men. 70% were newly diagnosed. The most common comorbid conditions were hypertension (61.4%), coronary artery disease (44.0%), diabetes (24.3%) and valvular heart disease (17.9%). Among above patients, 48% had more than one comorbid conditions. The median left ventricular ejection fraction (LVEF) was 56% (IQR: 41-64), while median of NT-proBNP was 1415.5 ng/L (IQR: 393.0-3728). The median hospital length of stay was 10 days (IQR: 7-14). In-hospital mortality rate was 1.06%. Prescriptions of guideline-recommended medications at discharge were as follows: angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor II blocker (ARB), 78.3%; beta-blocker (BB), 64.1%; and aldosterone antagonist (AA),69.0%.
Conclusions: Through nationwide registry of "real-world" clinical characteristics, management and outcomes from patients hospitalized due to heart failure in China, CN-HF registry demonstrated a substantial gap in heart failure care in China between daily clinical practice and available guideline recommendation.

BIOMARKERS UPDATE – II

P4688 | BEDSIDE
Independent influence of triiodothyronine and testosterone on the severity of heart failure in men

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Purpose: Heart failure (HF) is a multifaceted disorder affecting hormonal body system, particularly low triiodothyronine (T3) and total testosterone (TT). In addition, creatine clearance (CC) and haemoglobin (HGB) levels are well known contributors to HF severity. The objective of this study was to assess the independent influence of T3 and TT serum levels and left ventricular ejection fraction (LVEF) on the severity of HF in men.
Methods: This prospective study included consecutive male patients with HF, hospitalized at the Division of Cardiology, Department of Internal Medicine of our hospital. Statistical analysis was performed by means of T–test and linear regression in univariate analysis and multiple logistic regression in multivariate analysis. The P value of less than 0.05 was considered statistically significant.
Results: The study enrolled 121 male patients mean age 73.9±8.5. There were 36.7% diabetics, 57.9% with arterial hypertension, 68.6% non-smokers, 13.2% former smokers and 18.2% current smokers and 58.3% of those with atrial fibrillation. Patients had median (interquartile range) values of T3 1.3 nmol/L (0.9–1.6), NT-proBNP 555.9 pmol/L (211.9–1410.5), TT 9.9 nmol/L (5.8-12.8), LVEF 50% (37.5-57), CC 52.5 mg/dL (41.3-63.6) and HGB 133 g/L (121-147). In a univariate analysis TT ($r=-0.371$; $p<0.001$), T3 ($r=-0.421$; $p<0.001$), LVEF ($r=-0.247$; p=0.006), CC ($r=-0.532$; $p<0.001$) and HGB ($r=-0.290$; p=0.001) significantly correlated with serum values of NT-proBNP while all other clinical variables showed no association. In a multivariate analysis, after adjustment for age, lower values of TT ($\beta=-0.185$; p=0.016), T3 ($\beta=-0.226$; p=0.004), CC ($\beta=-0.399$; $p<0.001$) and LVEF ($\beta=-0.167$; p=0.025) were independent predictors of higher values of NT-proBNP. In contrast HGB and diabetes mellitus showed no association with NT-proBNP.
Conclusion: The results revealed that the complex interdependence of the hormonal body system is a significant aspect of the HF condition and suggest further investigation regarding hormonal disbalance in this disorder.

P4689 | BENCH
In sepsis supplemental tetrahydrobiopterin decreases ROS release, but failed to prevent septic cardiomyopathy

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Sepsis is a serious and common problem in intensive care units, and its incidence and sepsis-related deaths are increasing steadily, especially when patients develop a septic cardiomyopathy. Although nitric oxide has been implicated in the pathogenesis of septic shock, understanding of the underlying mechanism of septic cardiomyopathy remains incomplete. It is well known that an uncoupled endothelial nitric oxide synthase (eNOS), caused by low tetrahydrobiopterin (BH4) bioavailability, results in increased production of superoxide and consecutive deterioration of myocardial function. Here, we investigate in a mouse model whether BH4 may prevent myocardial dysfunction in an endotoxin-induced sepsis.
We induced sepsis by intraperitoneal injection of endotoxin (lipopolysaccharide) after BH4 pretreatment for 8 weeks in both wild-type (WT) and eNOS-knockout (eNOS–/–) mice, while comparing with control groups (n=7 each) with normal feed. Hemodynamic parameters were obtained via Millar tip catheter. As expected, in serum we found significantly increased nitrate levels in septic WT compared to non-septic WT (3.65±0.25 vs. 1.35±0.029nmol/l, $p<0.001$) as well as in septic eNOS–/– mice (2.19±0.17nmol/l, $p<0.05$). In aorta of septic eNOS–/– the radical oxygen species (ROS) release was unchanged after treatment with BH4 (19.98x105±6.2x105 vs. 20.55x105±3.88x105RLU/mg, p=0.1) but decreased compared to untreated WT (19.98x105±6.2x105 vs. 25.10x105±6.67x105RLU/mg, p=0.08), yet not significantly. When combined with BH4 treatment, the ROS release in sepsis was significantly decreased in WT compared to untreated WT (4.31x105±1.89x105 vs. 25.10x105±6.67x105RLU/mg, $p<0.05$). Despite this positive effect of BH4, hemodynamic parameters, in particular left ventricular develop pressure (LVDP), left ventricular enddiastolic pressure (LVEDP) and cardiac output (CO), did not improve under BH4 in septic WT (LVDP 70.3±1.8 vs. 84.44±5.9mmHg; LVEDP 7.2±0.2 vs. 8.27±0.65mmHg; CO 10.1±1.1 vs. 12.44±1.0ml/min).
This data shows that supplemental BH4 in sepsis decreases ROS release but suggests that ROS from uncoupled eNOS are probably not responsible for the development of septic cardiomyopathy. In conclusion, BH4 does not seem to provide protection against myocardial dysfunction after endotoxin-induced sepsis in mice.

P4690 | BEDSIDE
Galectin-3 is an independent predictor of abnormal functional capacity and ventilatory response to exercise in patients with nonischaemic dilated cardiomyopathy

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Purpose: Cardiopulmonary exercise test (CPET) has a prominent value in assessing clinical severity in chronic heart failure (HF) patients. Galectin-3, a lectin protein, has also a prognostic role in HF. We aimed to evaluate the relationships between galectin-3 plasma level and reduced exercise capacity in a cohort of patients with nonischaemic dilated cardiomyopathy (NIDCM).
Methods: Sixty-five consecutive patients diagnosed with NIDCM by World Health Organization criteria (71% males, 57±13 years, NYHA class I-II: 86%, NT-proBNP plasma level: 413 ng/L (IQR: 149-1276), left ventricular ejection fraction, LVEF: 34±10%, E/E'medium: 12±5), on guideline recommended medical treatment, undergoing a comprehensive clinical assessment, including CPET and galectin-3 assay, were evaluated (exclusion criteria: neoplasms, systemic inflammatory diseases, autoimmune disorders and severe renal failure, clinical conditions affecting galectin-3 plasma level).
Results: Median galectin-3 value was 14.4 ng/mL (IQR 11.9-19.0). On Weber classification, at CPET, 36 patients (55%) presented with mild reduction in exercise capacity (maximal oxygen consumption -peak VO2- ≥16 mL/kg/min, stage A-B), and 29 (45%) with moderate-severe inability (peak VO2 <16 mL/kg/min, stage C-D); moreover, 18 patients (28%) showed a value of minute ventilation/carbon dioxide production (VE/VCO2 slope) ≥34. Patients in stage C-D showed higher galectin-3 (13.3±4.1 vs 19.4±6.4 ng/mL, $p<0.001$) and NT-proBNP circulating levels (1105 [354-2218] vs 232 [80-520] ng/L, p=0.001). At regression analysis galectin-3 ($p<0.001$) and NT-proBNP (p=0.001), but not parameters of LV dysfunction at echocardiography, were correlated to peak VO2. The subset with VE/VCO2 slope ≥34 was characterized by a more severe LV dysfunction (LVEF 29±8 vs 36±9%, p=0.005; E/E' medium 15±6 vs 11±4, p=0.007), and higher galectin-3 (20.7±7.2 vs 14.3±4.4 ng/mL, p=0.002) and NT-proBNP levels (1462 [495-2066] vs 285 [94-618] ng/L, p=0.001). Among univariate predictors of VE/VCO2 slope (NYHA class -p=0.002, LVEF -p=0.002, E/E'medium -p=0.030, NT-proBNP - $p<0.001$, galectin-3 -$p<0.001$), only galectin-3 emerged as independent predictor at multivariate analysis (p=0.012).
Conclusions: Galectin-3 plasma level predicts lower peak VO2 and higher VE/VCO2 slope at CPET, irrespectively of LV dysfunction in NIDCM patients, supporting its clinical value in assessing the severity of the disease, and contributing to individual risk stratification.

P4691 | BEDSIDE
The effect of enhanced external counter pulsation therapy on myeloperoxidase in lowering cardiovascular events for patients with chronic heart failure

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Purpose: Inflammation has a pivotal role in the progression and symptomatology of Chronic Heart Failure (CHF). Many studies have shown that myeloperoxidase (MPO) as a marker of inflammation increased in patients with CHF. Furthermore, the high level of MPO was predictive of cardiovascular events and it was related with progression and severity of disease in CHF patients. The management of heart failure is not only consisting of pharmacological treatment but also non-invasive treatment. Enhanced external counterpulsation (EECP) is a non-invasive therapy for patients who are resistant to pharmacological treatment or failed with invasive procedures.
Methods: The design of the study was a prospective randomized interventional study. Consecutive sampling was performed and the study was done among patients with CHF who visited Outpatient Cardiology Unit at Multicenter who fulfilled inclusion criteria. The study was conducted between Januari 2012 and December 2013. There were 133 subjects who had EECP treatment and 133 subjects without EECP treatment (non-EECP). Both groups were observed periodically for 6 months to evaluate major adverse cardiovascular events (MACE).
Results: There were 266 patients included in the study. One hundred thirty three patients in each group, consist of 69.7% male with median age 59.2 + 8.3 years in EECP group and 72.6% male with median age 60.3 + 9.0 years in non-EECP group. Myeloperoxidase levels in the initial study and after 6 months of follow up decreased significantly in EECP group ($p<0.001$) compared with non-EECP group (p=0.110). After 6 months of follow up, the observation of MACE showed significant difference between two groups. Major cardiovascular events were reported in 29 patients (21.8%) of EECP group and 65 patients (48.8%) of non-EECP group.
Conclusion: The present study showed that in patients with CHF, EECP therapy there were reduced MPO level, and decreased cardiovascular events.

P4692 | BENCH
Early IL-1 beta antibody gevokizumab treatment reduces myocardial ischemia/reperfusion injury in Goto Kakizaki rats

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Aims: Enhanced cardiac interleukin-1 beta (IL1-β) contributes to myocardial ischemia/reperfusion (I/R) injury leading to the development of chronic left ventricular (LV) dysfunction. We have shown that the IL-1β modulating antibody gevokizumab (Gevo) limits chronic left ventricular (LV) remodeling induced by LV ischemia/reperfusion in Goto-Kakizaki diabetic rats, but whether limitation of infarct size could contribute to these long-term beneficial effects of Gevo is unknown.
Methods: Gevokizumab (Gevo; 10 mg/kg IP) was administered 1 hour following reperfusion, after 20 min of transient ischemia induced by LV artery occlusion. LV remodeling and function were assessed by echocardiography and LV catheterization (Millar) 2 days post I/R. Necrotic tissue (TTC) and scar formation (collagen by Sirius Red staining) were determined 2 and 7 days post I/R, respectively.
Results: Gevo reduced infarct size (16.6±1.8 and 7.6±1.9% of LV in I/R and I/R +Gevo, respectively; $p<0.05$) 2 days post I/R associated with a reduction of scar surface (300±18 and 238±20 μm^2 of LV in I/R and I/R +Gevo, respectively; $p<0.05$) 7 days after I/R. Gevo limited the LV expansion and increased LV FS already 2 days after I/R, which associated with improved systolic and diastolic function (Table).
Conclusions: In a clinically relevant model of myocardial I/R, the IL-1β antibody gevokizumab started 1 hour after myocardial reperfusion exerts immediate cardiac protection which probably contributes to the long term beneficial effects of Gevo.

Abstract P4692 – Table 1

Groups	LVDD (mm)	LVSD (mm)	LVFS (%)	CO (ml/min)	LVESP (mm Hg)	LVESPVR (mmHg/RVU)	LVEDP (mm Hg)	LVEDPVR (mmHg/RVU)
GK I/R (n=8)	7.2±0.1	5.0±0.2	31±2	116±3	94±7	12.5±1.0	2.06±0.31	2.15±0.21
GK I/R + early Gevo (n=10)	6.6±0.2*	4.2±0.1*	37±2*	125±4	99±5	16.4±1*	1.27±0.15*	1.44±0.17*

LVDD, LV diastolic diameter; LVSD, LV systolic diameter; LVFS, LV fractional shortening; CO, cardiac output; LVESP and LVEDP, LV end-systolic and end-diastolic pressures; LVESPVR and LVEDPVR, LV end-systolic and end-diastolic pressure volume relations. *$p<0.05$ vs GK I/R.

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Echo and natriuretic peptide guided therapy prevents renal dysfunction in patients with chronic heart failure due to systolic dysfunction

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Background: The concept of echo and natriuretic peptide (NP) guided therapy is appealing since currently there is no objective guide to optimal dosing of loop diuretic therapy in patients with chronic heart failure (CHF).
Aim: To assess whether echo and NP guided therapy may be useful to properly use loop diuretic drugs in patients with CHF due to left ventricular systolic dysfunction (LSD).
Materials and methods: In group of 377 patients with CHF (EF% 0.32), loop diuretic dosing was titrated according to the presence of echo Doppler signs of elevated left ventricular filling pressure, evidence of increased extravascular lung water and NP serum levels, while in another group, 241 patients with EF% 0.34, the dose of diuretics was based on clinical judgment. Serial NP and echo Doppler assessments were performed at the time of the scheduled follow-up visits. The simplified Modification of Diet in Renal Disease (MDRD) equation was used to estimate the glomerular filtration rate (eGFR).
Results: The median follow-up duration was 1,054 days and was comparable in the two groups. During the observation period, the dose of loop diuretics increased by 25% in the group in which the drug regimen was guided according to echo and NP criteria, while it increased by 67% in the clinically assessed patients ($p<0.0001$). No significant differences in survival were apparent between the two groups at 36 months (89% vs 86%). An increase of $\geq$0.3 mg/dL in serum creatinine was reported in 12% of the echo and NP guided group and in 22% of the clinical assessed group (p=0.0026). Newly diagnosed renal dysfunction (eGFR $<$60 ml/1.73 m^2) occurred in 9% of patients followed-up by echo and NP criteria and in 15% of those followed-up clinically (p=0.017).
Conclusion: This study shows that echo and NP guide therapy is useful to prevent renal dysfunction in patients with CHF due to LSD.

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Cardiac troponin concentrations in aged nursing home residents: independent contribution of heart failure and renal dysfunction

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Purpose: Highly sensitive cardiac troponins (hs-cTn) are the preferred biomarkers to detect cardiac injury. However, hs-cTn concentrations are also known to be elevated in patients with renal dysfunction, complicating their interpretation. Therefore, we investigated hs-cTn concentrations on their relative association with cardiac and renal function in nursing home residents with advanced age.
Methods: A cohort of 495 nursing home residents, aged $\geq$65 years, were measured using the hs-cTnT and a new hs-cTnI assay. Renal function was assessed by the estimated glomerular filtration rate (eGFR), established from serum creatinine and cystatin C. Also, the presence of heart failure in the residents was evaluated using echocardiography.
Results: In these older adults aged 82$\pm$7 years, hs-cTnT concentrations (21 (15-31) ng/L; median (interquartile range, IQR)) were markedly higher than hs-cTnI concentrations (7 (4-12) ng/L). Consequently, 77% of the residents had hs-cTnT concentrations above the 99th percentile cut-off (14 ng/L), while only 8% were above the cut-off for hs-cTnI (26.2 ng/L). In the residents diagnosed with heart failure (34%), significantly higher median (IQR) hs-cTnT (27 (19-44) ng/L) and hs-cTnI (11 (7-20) ng/L) concentrations were measured in comparison to those without heart failure (hs-cTnT: 19 (13-25) ng/L; hs-cTnI: 5 (4-9) ng/L; both $p<0.001$). Moreover, we found a strong association of eGFR with hs-cTnT (st.β =-0.410) and hs-cTnI concentrations (st.β=-0.259) (both $p<0.001$). Interestingly, the association between eGFR and both hs-cTn concentrations remained highly significant (hs-cTnT: st.β =-0.340; hs-cTnI: st.β =-0.175; both $p<0.001$), irrespective of the presence of heart failure.
Conclusions: Elevated hs-cTnT concentrations were observed in the majority of aged nursing home residents. Moreover, we identified heart failure and renal dysfunction as two most important and independent reasons for hs-cTnT and hs-cTnI elevations.

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Lower activity value of antithorombin reflects worsening of heart failure in infants with ventricular septal defect

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Background: Antithorombin (AT), which is produced in liver, is activated on vascular endothelial cells. Heart failure prompts endothelial damage. However, there are no reports about relation between activity value of AT (AT-activity) and heart failure. Infants with ventricular septal defect (VSD) develop heart failure, if they need surgical intervention. We predicted lower AT-activity was provoked in VSD infants with serious heart failure. We attempted identify cardiac function and clinical presentation in VSD infants with lower AT-acivity.
Methods: Between 2004 and 2013, 106 symptomatic infants with VSD were studied. Cardiac catheterization was performed with surgical intervention in view. Venous blood samples for analysis of AT-activity were obtained before surgery. We defined lower AT-activity as AT-activity levels in the lower quartile of 106 infants ($\leqq$86%). First, cardiac performances influencing lower AT-activity were determined. Second, we compared clinical feathers between VSD infants with lower AT-activity and those without lower AT-activity.
Results: After multiple logistic regression analysis lower AT-activity was independently associated with odds ratio of 9.3 (p=0.002) for high ratio of pulmonic flow to systemic flow ($\geqq$4.4), 5.8 (p=0.002) for low stroke volume ($\leqq$60ml/m^2), 5.7 (p=0.004) for high end-diastolic pressure of right ventricle ($\geqq$8mmHg), and 3.6 for high right-left ventricular pressure ratio on end-systole ($\geqq$0.86). Explanatory coefficient was 0.45. In VSD infants with lower AT-activity, the levels of total protein, albumin, and fibrinogen were significantly decreased. The levels of gamma-glutamyl transpeptidase and creatinine were significantly increased. Clinically, VSD infants with lower AT-activity had more histories of hospital care (40% vs. 15%, p=0.0073) and smaller standard deviation of body weight (-2.6SD vs. -1.9SD, p=0.0044). The percentage of patients operated early (within 5 week after catheterization) was significantly higher in infants with lower AT-activity (73% vs. 43%, p=0.013).
Conclusion: Our study showed lower AT-activity in VSD infants was independently associated with increased right ventricular pressure on end-diastole or end-diastole, increased pulmonary flow and decreased stroke volume. All these factors indicate heart failure is getting worse in VSD infants. Laboratory data suggested VSD infants with lower AT-activity potentially had trouble with liver and kidney. Furthermore, patients with lower AT-activity had more serious heart failure clinically. We could use lower AT-activity as the method of picking out the exacerbation of heart failure in VSD infants.

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Red cell distribution width predicts length of stay in patients with acutely decompensated heart failure

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Purpose: Red cell distribution width (RDW) is known as the measure of variability in size of erhythrocytes, and the higher values were previously shown to designate poor prognosis in heart failure (HF). On the other hand, length of hospital stay is a crucial and costly part of management of patients with acutely decompensated HF (ADHF). We aimed to search for the potential association of RDW with length of stay (LOS).
Methods: 230 consecutive ADHF patients, admitted and hospitalized in single tertiary care HF center, were considered for the analysis. Length of hospital stay (LOS) and other data at admission were evaluated.
Results: There were 230 consecutive patients (149 males, 81 females), admitted with ADHF to a single tertiary care HF center. Mean age was 70.7$\pm$11.2 years. There were 182 patients with ischemic HF, and 48 patients with nonischemic HF. Mean LVEF was 31$\pm$11%, and there were 189 patients with HFREF and 41 patients with HFPEF. Mean hemoglobin was 12.9$\pm$2 gr/dl. Mean LOS was 7.6$\pm$4.9 days ranging from 2-27 days. LOS was correlated with BUN (r=0.142, p=0.030), RDW (r=0.232, p=0.001), and was not correlated with LVEF, and other laboratory parameters. LOS was slightly longer in females compared to males (8.3$\pm$5.6 vs 7.2$\pm$4.3 days, p=0.096). Patients with permanent AF had slightly longer LOS than those without (8.3$\pm$5.2 vs. 7.3$\pm$4.7 days, p=0.139). Since median LOS was 6 days, patients were classified into two as those with LOS$\leq$6 days and those with LOS$\geq$7 days. RDW at admission was higher in those with LOS$\geq$7 days (16.72$\pm$2.85 vs. 15.58$\pm$2.15, p=0.001). Triglyceride level was lower in those with LOS$\geq$7 days (86$\pm$39 vs 104$\pm$68 mg/dl, p=0.024). Presence of hypertension, diabetes mellitus, ischemic HF were not associated with longer LOS ($\geq$7 days). Those with previous AMI had slightly longer LOS than those without (54.6% vs 44.1%, p=0.113, out of 226 patients).
Stepwise regression analysis was built up including BUN, RDW, gender, presence of permanent AF and previous history of AMI, and it was shown that RDW was the only parameter that independently predicted LOS in hospitalized patients with ADHF (ExpB=1.212, p=0.001, 95% CI: 1.078-1.362).
Conclusion: It seems in a cohort of hospitalized ADHF patients, RDW at admission predicts LOS independently.

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NT-proBNP as a predictor of outcome in patients with septic shock: a suitable cut-off

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Aim: To determine the role of NT-proBNP in regard to outcome of septic patients and to evaluate how levels of Nt-ProBNP can reflect the hemodynamic evolution of sepsis.

Methods: Forty patients (55% males, median age 64 years, 25-75 percentiles 49-72) with severe sepsis were retrospectively evaluated. Patients were treated with gold standard therapy for sepsis (either std therapy or std therapy plus polymyxin B (PMX) fiber hemoperfusion). NT-BNP levels, E.A. (endotoxin activity) concentration, SOFA score and SAPS II score, C.I. (cardiac index), MAP (mean arterial pressure) and PAP (pulmonary arterial pressure) were evaluated at admission and after 72 hours. Overall survival was evaluated after 28 days from admission.

Results: At 4-week follow-up, 22 patients died (55%). Survival was not associated with age, gender, baseline E.A. and treatment, while it was associated with NT-proBNP at baseline and at time 72. NT-proBNP $>$1000 pg/ml at 72 hours was the strongest independent determinant of survival. The area under curve (AUC) of NT-proBNP at admission was 0.73 (CI 0.56-0.901), whereas after 72 h it was 0.99 (CI 0.91-1).

At time 72 h, AUC of SOFA score was 0.94 (CI 0.88-1.01; $p<0.01$); AUC of SAPS II score was 1 (CI 1-1 $p<0.01$); AUC curve of E.A. was 0.73 (CI 0.57-0.89 $p<0.01$). Levels of NT-proBNP $>$1000 pg/ml at 72 h are highly predictive of adverse outcome, irrespectively of different therapeutic strategies (sensitivity = 95.5% specificity =94.4%). NT-proBNP at 72 h correlated with CI, MAP and PAP (p values <0.01, <0.01, 0.03, respectively).

Conclusions: Elevated NT-proBNP levels ($>$1000 pg/ml), combined with clinical score, could be a powerful midterm predictor of mortality in patients with septic shock. NTproBNP assessed at 72 hours from admission reflects the hemodynamic evolution of sepsis.