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HOT ISSUES IN THE CARDIOMYOPATHIES

6606 | BEDSIDE
Prediction of thromboembolic (TE) risk in patients with hypertrophic cardiomyopathy (HCM Risk-CVA)

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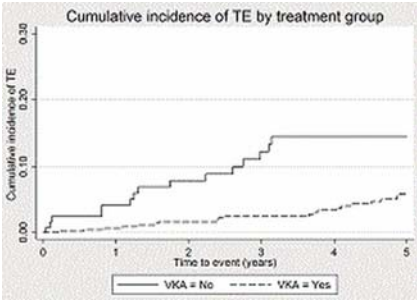
Aims: AF and TE are associated with reduced survival in HCM, but the absolute risk of TE in patients with and without AF is unclear. The primary aim of this study was to derive and validate a model for estimating the risk of TE in HCM. Exploratory analyses were performed to determine predictors of TE, the performance of the CHA2DS2-VASc score and outcome with vitamin K antagonists.
Methods: A retrospective, longitudinal cohort of seven institutions was used to develop multivariable Cox regression models fitted with preselected predictors. Bootstrapping was used for validation.
Results: Of 4821 HCM patients recruited between 1986 and 2008, 172 (3.6%) reached the primary endpoint of CVA, TIA or systemic peripheral embolus within 10 years. 27.5% of patients had a CHA2DS2-VASc score of 0 of whom 9.8% developed TE during follow up. Cox regression revealed an association between TE and age, AF, the interaction between age and AF, TE prior to first evaluation, NYHA class, LA diameter, vascular disease and maximal LV wall thickness. There was a curvilinear relation between LA size and TE risk. The model predicted TE with a C-index of 0.75 (95% CI: 0.70, 0.80) and the D-statistic was 1.30 (95% CI: 1.05, 1.56). VKA treatment was associated with a 54.8% (CI 31%-97%, p=0.037) RRR in HCM patients with AF.



Cumulative incidence of TE by treatment

Conclusions: The study shows that the risk of TE in HCM patients can be identified using a small number of simple clinical features. LA size, in particular, should be monitored closely and the assessment and treatment of conventional vascular risk factors should be routine practice in older patients. Exploratory analyses show for the first time evidence for a reduction of TE with VKA treatment. The CHA2DS2-VASc score performs poorly in HCM patients and should not be used to assess TE risk.

6607 | BEDSIDE
A systematic review and meta-analysis of long-term outcomes after septal reduction therapy in patients with hypertrophic cardiomyopathy

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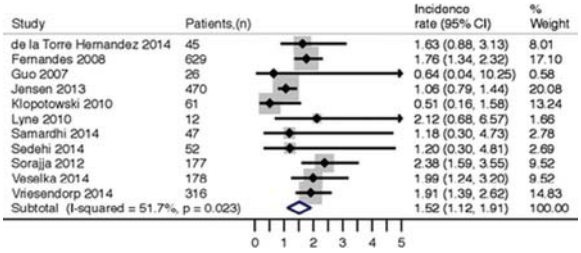
Background: Surgical myectomy and percutaneous alcohol septal ablation (ASA) are both accepted treatment options for medical therapy resistant obstructive hypertrophic cardiomyopathy (HCM). Questions remain however about the long-term outcomes, especially concerning the long-term risk of sudden cardiac death (SCD) after ASA.
Purpose: The aim of this meta-analysis is to compare long-term mortality and SCD rates after myectomy and ASA.
Methods: A systematic review was conducted for eligible studies with a follow-up of at least 3 years. Primary outcomes were all-cause mortality and (aborted) SCD. Sixteen myectomy cohorts (2791 patients, mean follow-up 7.4 years) and 11 ASA cohorts (2013 patients, mean follow-up 6.2 years) were included. Pooled estimates were calculated using a random effect meta-analysis.



Forest plot of all-cause mortality in ASA

Results: Long-term mortality was found to be similarly low after ASA (1.5% per year) as compared to myectomy (1.4% per year, P=0.60). The rate of (aborted) SCD, including appropriate implantable cardioverter defibrillator shocks, was 0.4% per year after ASA and 0.5% per year after myectomy (P=0.12). Permanent pacemaker implantation was performed following ASA in 10% of the patients, compared to 4% (P<0.001) after myectomy. Re-intervention was performed in 6% of the patients who underwent ASA, compared to 0.8% after myectomy (P=0.022).
Conclusion: Long term mortality and (aborted) SCD rates after ASA and myectomy are similarly low. Patients who undergo ASA have a 2.5 times higher risk of permanent pacemaker implantation and a 7.5 times higher risk of necessity for additional septal reduction therapy, as compared to those who undergo myectomy.

6608 | BEDSIDE
Randomised trial of combination cytokine and adult autologous bone marrow progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy - the regenerate-dcm randomized phase II

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Background: Non-ischaemic dilated cardiomyopathy (DCM) is a leading cause of heart failure and the most common indication for transplantation worldwide. It is associated with high levels of mortality and morbidity despite optimal medical care. Small numbers of open-labelled and pilot studies have separately assessed the benefit of bone marrow derived cells (BMC) or cytokine therapy in DCM with mixed results.
Purpose: The REGENERATE-DCM trial is the first phase II randomised, placebo-controlled trial that aims to assess if granulocyte colony stimulating factor (G-CSF) administration with or without adjunctive intracoronary delivery of autologous unfractionated BMC improves global left ventricular function in patients with DCM and significant cardiac dysfunction.
Methods: 60 patients with DCM and a documented LV ejection fraction (LVEF) at referral of ≤45%, NYHA classification ≥2 with no secondary cause for the cardiomyopathy were randomized equally into four groups (n=15 per group): peripheral placebo (saline), peripheral G-CSF, peripheral G-CSF & intracoronary serum and peripheral G-CSF & intracoronary BMC. All patients, except the peripheral placebo group, received 5-days of G-CSF. In the intracoronary groups this was followed by bone marrow harvest and processing on day six with intracoronary infusion of cells or serum on the same day. The primary endpoint was LVEF change from baseline to three months as determined by advanced cardiac imaging. Data analysers were masked to group assignment and the trial was fully blinded within treatment arms. This study is registered with ClinicalTrials.gov, NCT01302171 and EudraCT:2009–013112–12.
Results: At three months, peripheral G-CSF combined with intracoronary BMC therapy was associated with a 5·37% increase in LVEF (38·30±12·97 from 32·93±16·46 p=0·014), which was maintained to one year. This was associated with a decrease in NYHA classification at three months and one year, reduced NT-pro BNP, improved exercise capacity at one year and improved quality of life at three months and one year. The remaining treatment groups failed to show significant improvement in any of these endpoints at three months or one year. There was no difference in MACE between treatment groups.
Conclusion: This is the first randomized placebo-controlled trial with a novel combination of G-CSF and intracoronary cell therapy that demonstrates safety and an improvement in cardiac function. This functional difference was accompanied by an improvement in a panel of biochemical and symptom related outcomes supporting a potential clinical benefit of this therapy in patients with DCM.

6609 | BEDSIDE
Long-term prognosis according to different aetiologies in an adult population of patients with hypertrophic cardiomyopathy

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Background: Hypertrophic cardiomyopathy (HCM) is a generic term that encompasses a number of different diseases (or phenocopies). To date, there have been few studies examining the impact of aetiology on long term prognosis.
Purpose: To determine long-term outcomes in adult patients with various types of HCM.
Methods: A cohort of 1697 adult patients with HCM followed at two European referral centres were studied. Aetiological diagnosis was made on the basis of clinical examination, cardiac imaging and targeted genetic and biochemical testing. Main outcomes were: all-cause mortality or heart transplantation (HTx) and heart failure (HF) related-death. All-cause mortality included sudden cardiac death or equivalents, HF and stroke-related death and non-cardiovascular death.
Results: Prevalence of different aetiologies was as follows: sarcomeric HCM 1288 (76%); AL amyloidosis 115 (7%), hereditary TTR amyloidosis 86 (5%),

Anderson-Fabry disease 85 (5%), wild-type TTR amyloidosis 48 (3%), Noonan syndrome 15 (0.9%), mitochondrial disease 23 (1%), Friedreich's ataxia 11 (0.6%), glycogen storage disease 16 (0.9%), LEOPARD syndrome 7 (0.4%), FHL1 2 (0.1%) and CPT II deficiency 1 (0.1%). All-cause mortality/HTx was significantly higher in phenocopies compared to sarcomeric HCM (Figure 1a), as well as HF-related death ($p<0.001$). When considering specific aetiologies, all-cause mortality was significantly higher in cardiac amyloidosis (Figure 1b), as well as HF-related death ($p<0.001$).

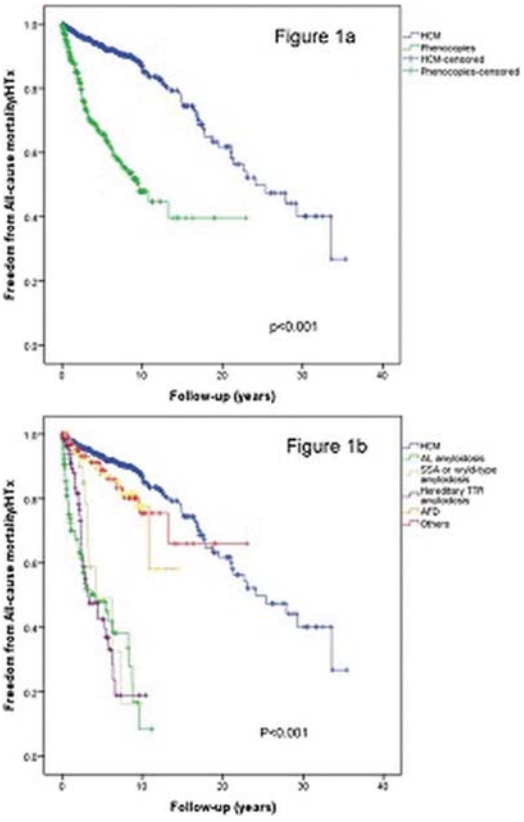

Figure 1. Survival curves

Conclusion: In an adult population of patients with HCM, long-term prognosis was more severe in phenocopies compared to sarcomere HCM and when comparing specific aetiologies, cardiac amyloidosis showed the worse outcomes.
Acknowledgement/Funding: Dr Rosmini was supported by Borse di Studio per la ricerca scientifica "SIC-SANOFI"

6610 | BEDSIDE
Comparison of two models estimating sudden cardiac death risk in hypertrophic cardiomyopathy. Impact on primary prevention practice

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Background: Hypertrophic cardiomyopathy (HCM) is associated with a risk of sudden cardiac death (SCD). Models have been developed to estimate SCD risk and guide preventive therapy by the implantation of cardioverter-defibrillator (ICD). "Old" model was published by the ACC/ESC joint guidelines in 2003, whereas "new" HCM Risk-SCD prediction model was recently published by the ESC. Previous guidelines identified 7 major risk factors for SCD and the presence of at least one was considered high risk and an indication for ICD. The HCM Risk-SCD calculator also identifies 7 predictors and using newly-developed formula provides probability of SCD in next 5 years. The SCD risk and management strategy, assessed according to those two models have never been compared. Aim: The aim of the study was to compare those two models in contemporary HCM population.
Methods: We included 90 consecutive HCM patients without previous cardiac arrest and/or ICD implanted (63% males; aged 54±13.7 years; mean ejection fraction of 59±19%). Each patient had SCD risk calculated, using two models, as a part of routine management and to guide therapy.
Results: Based on "old" model, patients have following scores: 0 points – 12 patients (13%), 1 point – 24 (27%), 2 points – 30 (33%), 3 points – 17 (19%), ≥4 points – 7 (8%). Whereas, according to HCM Risk-SCD calculator 75 (83%) patients had low risk (5-year SCD risk <4%), 10 (11%) had intermediate risk (5-year risk 4–6%), and only 5 (6%) patients had high risk (5-year risk >6%). Strictly followed 2003 guidelines only 12 patients have low SCD risk and 78 (87%) patients have intermediate-to-high risk and can be candidates for ICD therapy. On the other hand, based on new HCM Risk-SCD calculator great majority of patients 75 (83%) are considered low risk whereas only 15 (17%) have intermediate-to-high risk. Out of those 15 patients – in 10 ICD may be considered (recommendation for ICD – class IIb) and only in 5 patients ICD should be considered (class IIa).
Conclusions: Calculation of SCD risk using two-guidelines approved models provide completely different risk estimates. Furthermore, there is a dramatic change of practice and SCD primary prevention depending on the used model. According to "old" model up to 87% patients have indication for ICD, whereas based on new model only 17% are candidates for ICD. Those new implications should be taken into account in daily management of HCM patients.

6611 | BEDSIDE
Predictors of atrial fibrillation in hypertrophic cardiomyopathy (HCM Risk-AF)

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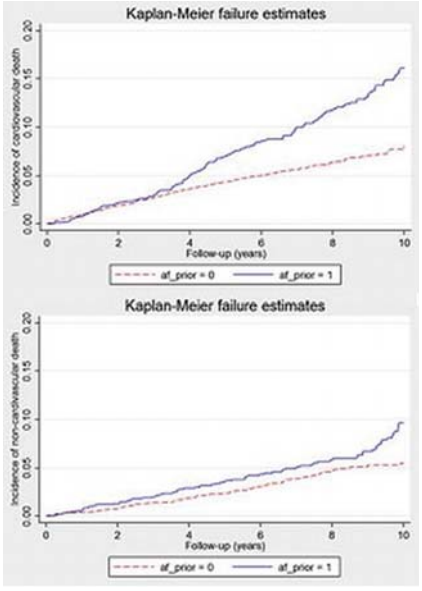
Aims: Atrial fibrillation (AF) is associated with increased morbidity and mortality in hypertrophic cardiomyopathy (HCM). The primary aim of this study was to investigate predictors of AF in a large multicentre cohort. Exploratory analyses were performed to investigate the effect of AF on mortality and the efficacy of antiarrhythmic therapy in the development of AF.
Methods: A retrospective, longitudinal cohort of seven institutions was used to develop multivariable Cox regression models fitted with preselected predictors.
Results: Of 4248 HCM patients recruited between 1986 and 2008, 740 (17.42%) patients reached the primary endpoint of AF within 10 years from first evaluation. Multivariable Cox regression revealed an association between AF and the following: female sex, LA diameter, NYHA class II, NYHA class III and IV, hypertension and vascular disease. The incidence of cardiovascular death was 4.92% in the sinus rhythm (SR) group and 10.86% in the AF group ($p<0.001$). The incidence of non-cardiovascular death was 3.15% in the SR group and 5.92% in the AF group ($p<0.001$) (Figure). An intention to treat analysis of β-adrenoreceptor blockers, calcium channel antagonists, disopyramide and amiodarone did not demonstrate a significant effect of these therapies on development of AF as a first diagnosis.



Mortality SR versus AF

Conclusions: This study confirms that AF is associated with a poor prognosis in HCM and that patients who are at risk of AF development can be identified using simple clinical parameters.

6612 | BEDSIDE
Utility of qualitative and quantitative evaluation of viral nucleic acids in cardiac biopsy and blood samples in patients with suspected myocarditis/ inflammatory cardiomyopathy

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Background: Diagnosis of myocarditis (MC)/ inflammatory cardiomyopathy (iDCM) is based on endomyocardial biopsy (EMB). The value of viral nucleic

acid (VNA) detected in peripheral blood (PB) and ventricle blood (VB) samples in patients with suspected MC/iDCM was not assessed so far.
Aim: To evaluate prevalence and utility of VNA in EMB specimens, PB and VB samples in patients with clinically suspected MC/iDCM.
Patients and methods: 65 patients (age 48±17 years) underwent evaluation of VNA by qPCR in EMB and blood samples collected during one catheterization. Quantitative evaluation of VNA was performed.
Results: VNA of parvovirus B19, enterovirus, adenovirus, human herpesvirus and cytomegalovirus were detected in EMB of 32 patients (49%). In VB or PB samples VNAs (except parvovirus B19) were diagnosed in 12 patients (18%) and in 19 patients (29%) respectively. VNA of the same virus as found in the EMB sample was present notably more often in VB than in PB (30% vs.6%, p=0.001). A significant concurrence was observed between the positive and negative results of VNA in EMB and VB (p=0.001). Quantitative evaluation of viral nucleic acids see below in table.

Quantitative evaluation of VNA

		VNA in EMB (n=32)	VNA in VB (n=12)	VNA in PB (n=19)
PVB19	N	18	0	0
	AVL±SD*	2.66±0.77	–	0 –
	range [copies per sample]	30–20,000	–	0 –
AdV	N	4	5	8
	AVL±SD*	1.97±0.53	1.85±0.23	2.24±0.29
	range [copies per sample]	30–500	40–190	40–440
EnV	N	4	6	8
	AVL±SD*	2.52±0.46	2.47±0.62	1.63±0.12
	range [copies per sample]	80–1000	70–1200	30–220
HHV-6	N	5	1	3
	AVL±SD*	2.51±1.9	3.9	2.46±1.02
	range [copies per sample]	30–800,000	8000	70–4300
CMV	N	1	0	0
	AVL±SD*	2.18	–	–

N, number of patients; AVL, average viral load. *[log10 of copies per sample].

Conclusion: For patients with suspected MC/iDCM, the presence of VNA both in EMB and VB samples could be relevant for the diagnosis of MC/iDCM. VB predicts the virus species in EMB specimens more effectively than PB. Evaluation of VNA in VB or PB samples seems not useful for diagnosis of parvovirus B19.

6613 | BEDSIDE
Morphological features in Noncompaction Cardiomyopathy - Data from the German NCCM Registry (ALKK)

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Objective: Isolated noncompaction cardiomyopathy (NCCM) is considered a primary genetic cardiomyopathy with a distinctive morphological feature. The clinical presentation varies from asymptomatic to life threatening events with heart failure symptoms, various arrhythmias and thromboembolic events. The data of the German NCCM registry regarding morphological parameters and severe clinical events were analysed.
Methods: By January 31th, 2015 the German NCCM registry had enrolled a total of 359 patients (pts) with NCCM (233 male, age 18 to 85 yrs, mean age 53.0 yrs) with a mean follow up period of 25 months. ECGs, echocardiographic and cardiac MR images were reviewed. The pts were followed for clinical events and symptoms. LV-EF and LV dilatation (LV dil) were measured and the incidence of severe heart failure symptoms (NYHA III/IV), maligne arrhythmias (VT/VF), atrial fibrillation (AF), embolic events and cardiac deaths were analysed in respect to the distribution of the affected segments of the left ventricle (LV), the ratio of the thickness of the compacted (c) and the noncompacted (nc) layer and the thickness of the compacted layer.
Results: All assessable apical LV segments showed LV noncompaction. 77% of the lateral, 44% of the posterior, 36% of the anterior and only 6% of the septal segments were involved. In the pts with reduced LV function significantly more lateral segments were affected (LV-EF <35% vs >35%; p=0.04) and significantly less septal segments (LV-EF <35% vs >35%; p=0.01). No correlation could be found between affected segments and LV dil or clinical events. In 54% of the pts the nc/c ratio was >2.3 (MR) or >2.0 (echo) to 3.0. In 46% of the pts the nc/c ratio was >3. The compacted layer was 5 mm or less in 71% of the pts, and up to 8 mm in 29%. There was no correlation between the wall thickness and the LV parameters or clinical events. There was a trend towards more embolic events in pts with a nc/c ratio >3, but no statistical correlation could be found to the other parameters.
Summary: In the pts of the German NCCM registry with an adequate image quality the LV apex was nearly always affected. In the cases with severely reduced LV function more lateral segments and less septal segments were involved compared to the pts with better LV function. No significant correlation could be found between the distribution of affected segments, the nc/c ratio, the thickness of the compacted layer and clinical events.
Acknowledgement/Funding: n.a.

6614 | BEDSIDE
Expression of stromal cell-derived factor 1 in endomyocardial biopsies of patients with suspected myocarditis predicts mortality

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Background: The identification of high-risk patients with suspected myocarditis is still an unmet need. Stromal cell-derived factor 1 (SDF-1) is an inflammatory chemokine expressed in the inflamed and failing myocardium. However, the role of SDF-1, in myocarditis is still unknown. We therefore explored whether endomyocardial expression of SDF-1 may serve as predictor of mortality in a cohort of patients undergoing endomyocardial biopsy (EMB) for suspected myocarditis.
Methods: We prospectively included 174 consecutive patients who underwent EMB between 3/2009 and 6/2011 as part of an evaluation for suspected myocarditis at our university heart center. The following risk factors were prospectively assessed: NYHA functional class, left ventricular ejection fraction (LVEF; using modified Simpson rule by echocardiography), brain natriuretic peptide (BNP), troponin I (TNI) and endomyocardial expression of SDF-1. EMB stained for SDF-1 were classified in a dichotomized way as “negative” (no/very low) or “positive” (moderate/high) expression by two co-investigators in a blinded manner from one to two sections for each staining. Patients presented in our outpatient clinics for follow-up visits scheduled at 6-months intervals. Study endpoint was all-cause mortality.
Results: SDF-1 expression was significantly enhanced in patients in whom a myocarditis was histologically confirmed (65.4% SDF-1 positive biopsies) as compared to patients with non-inflammatory cardiomyopathy (19.1% SDF-1 positive biopsies, p<0.001). During a mean follow-up of 27.5 months, 20 patients (11.5%) died. The 4-year mortality rate was 26.0% among the 92 SDF-1-positive patients vs. 9.5% among the 82 SDF-1-negative patients (p=0.001). On univariable analysis, elevated levels of BNP, TNI, a reduced LVEF and SDF-1 expression were significantly associated with mortality. In multivariable analysis, SDF-1 was the strongest independent predictor of mortality yielding a hazard ratio 6.1; 95% confidence interval 1.4–27.5; p=0.018. Subgroup analysis revealed SDF-1 as a predictor of mortality in both patients with inflammatory and with non-inflammatory cardiomyopathy.
Conclusions: Endomyocardial expression of SDF-1 is enhanced in patients with histologically proven myocarditis and is an independent predictor of mortality in patients with suspected myocarditis.
Acknowledgement/Funding: Deutsche Forschungsgemeinschaft (BO 3786/1-1 KFO 274 and SFB-TR19) and the fortüne research programme (2133-0 and 1895-0).

6615 | BEDSIDE
Parvovirus B19 nucleic acids copy number do not determine structural changes in cardiac tissue from patients with cardiac viral infection

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Background: Although the DNA of parvovirus B19 (B19V) is frequently detected in patients with dilated cardiomyopathy or myocarditis, whether the B19V causes disease is questionable, since even in health inviduals the virus persists in cardiac tissue.
Aim: Evaluation of the structural changes in cardiac tissue in patients with viral nucleic acid (VNA) of B19V in cardiac samples.
Patients and methods: 65 patients (age 48±17 years) underwent evaluation of

Abstract 6615 – Table 1. Structural changes

Number of VNA copies	Structural changes in microvessels		Contractil apparatus	Mitochondria	LVEF [%]	LVEDD [mm]
	Vessel lumen	Endothelium				
30	Closed/narrow	Partialy necrotic	Gradual and progresive loss, irregular aligned	Degenerative or loss triste, swollen	15	73
50	Open	Partially Necrotic	Gradual and progresive loss	Few swollen, numerous	30	57
120	Open	Unchanged	Very few strands of miofibrils	Cristes loss, swollen, numerous	15	73
500	Open/narrow	Partially necrotic	Regular distribution and gradual and progressive loss	Degenerative cristes, swollen, numerous	45	46
500	Open/closed	Partially necrotic	Regular distribution	Only few swollen	60	53
800	Narrow	Partially necrotic	Regular distribution	Degenerative or loss cristes, swollen	30	60
4000	Closed/narrow	Partially necrotic	Regular disrtibution or gradual and progressive loss	Few swollen, normal number, regular distribution	65	40
4000	Closed/narrow/ open	Partially necrotic	Regular distribution	Few swollen, normal number, regular dystribution	50	57

VNA by qPCR in endomyocardial biopsy (EMB) from left ventricle. Quantity evaluation of VNA was performed. EMB was studied for inflammation with histological and immunohistological criteria. Structural changes were evaluated in electron microscope.
Results: VNA of parvovirus B19, enterovirus, adenovirus, human herpesvirus and cytomegalovirus were detected in EMB of 31 patients (48%). VNA of parvovirus B19 was found in EMB of 18 patients (28% of all population and 58% of population with VNA in cardiac tissue). Number of VNA copies correlate with LVEF and LVEDD, but not with ultrastructure changes in cardiomyocytes, however number of VNA copies correlates with structural changes in local microvessels. For details, see table below.
Conclusion: Number of VNA copies is not related with structural changes in cardiomyocyte, but it is possible that it can influence structure of microvessels. Further analysis can help to understand meaning of B19V in cardiac tissue in patients with viral infection and make proper therapeutic decision.

INVASIVE IMAGING AND FUNCTIONAL ASSESSMENT FOR PLAQUE VULNERABILITY AND CLINICAL OUTCOMES

6616 | BEDSIDE
Using pressure wire to assess discrepancies between cardiac catheterization and echocardiography assessement of severe aortic stenosis, impact on clinical outcomes

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Background: Current guidelines discourage aortic stenosis (AS) evaluation by direct pressure measurement if echocardiography (echo) is adequate. Crossing the valve at catheterization (cath) is a class III recommendation due to potential stroke risk and the fact that echo derived Aortic Valve area (AVA) correlates highly with cath derived AVA. However several studies show sizable differences between echo and cath lab measurements.
Purpose: To determine whether using pressure wire for AS assessment may offer a safe and higher quality technique to assess the validity of echo results and evaluate the clinical impact of this assessment on surgical decision.
Methods: 112 patients with suspected AS by echo aged 61–94 underwent right and left heart cath by two operators with gradient assessed through simultaneous eft ventricular (St. Jude) pressure wire recording of left ventricular pressure and fluid filled pressure catheter recording of aortic pressure measured >5 cm above the valve. Cardiac output was calculated by thermodilution. Echos were from 5 different labs, interpreted by 18 different readers, and reviewed by 2 independent level III readers blinded to original reads and cath results to assess the quality of community-based readings.
Results: Independent readers considered 95 of the 112 echos to have good quality. There was no difference between these and poorer quality echos at predicting cath parameters. Independent reader interpretation did not significantly differ from the original interpretation. 32 patients had an EF <50%, 80 had an EF >50%. Cath Assessment of severity of AVA was discordant with echo by more than 0.2cm^2 in 50%, 0.3cm^2 in 32% and 0.5cm^2 in 12.5% of patients. Values changed to over or under the surgical threshold of AVA <1cm^2 in 32% of the patients (Pearson correlation of 0.47). Mean echo gradients had better correlation with cath gradients (72%, Pearson correlation of 0.80). Planned surgical valve replacement was avoided in 32 patients (28%). No clinical strokes or TIA were observed in the 30 days after cath.
Conclusion: Cath-echo correlation of AS severity is lower in contemporaneous practice than previously assumed. This can alter the decision for aortic valve replacement. Sole reliance on echo-derived assessment of AS may need to be reconsidered especially with the introduction newer safer techniques.

6617 | BEDSIDE
Randomized study comparing the impact of FFR measurement in patients with intermediate coronary stenoses allocated by angiography to conservative versus interventional treatment - SPECTRUM trial

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Introduction: Measurement of coronary fractional flow reserve (FFR) has been used in several studies of patients (pts) for whom an interventional therapeutic strategy (ITS) has been a priori determined by angiography (ANGIO). No systematic studies compared the impact of FFR in the opposite scenario, when ANGIO alone would dictate a conservative therapeutic strategy (CTS).
Purpose: Test the hypothesis that FFR will also significantly impact and lead to relevant change of the therapeutic strategy for clinically stable pts with intermediate coronary obstructions initially allocated to a CTS by ANGIO.
Methods: Bicentric prospective study of 178 consecutive pts (age = 60.0±9.5 yrs, female 44%) and 244 coronary intermediate stenosis (40–70% by visual estimate). Pts and lesions were allocated to follow a CTS of optimized medical treatment or to have an ITS. Following this ANGIO decision all stenoses in both groups were randomized 1:1 to maintenance of ANGIO decision, or FFR evaluation. A cut-off FFR <0.80 mandated intervention. The therapeutic strategy was changed in CTS when FFR <0.80 and in ITS when FFR ≥0.80.
Results: On the basis of ANGIO the allocation to CTS was markedly predominant (p<0.001): 121 pts, 155 lesions (64%) compared to 76 pts, 89 lesions (36%) to ITS. Randomization led to measurement of FFR in 65 pts (78 lesions) in group CTS and 38 pts (43 lesions) in group ITS. Measurement of FFR was successful in all protocol indicated lesions. The two subgroups evaluated with FFR were comparable regarding clinical and angiographic characteristics. In Group CTS, FFR <0.80 was observed in 19 lesions (24.4%) of 16 pts (24.6%) who received a coronary intervention. In Group ITS, FFR ≥0.80 occurred in 22 lesions (51.2%) of 20 pts (52.6%), for whom intervention was deferred. The change of therapeutic strategy dictated by FFR in both groups was highly significant (p<0.0001), but occurred more frequently in the Group ITS (p=0.03). Coronary interventions were performed without major events in both protocol mandated subgroups. At 12 months follow-up of 170 pts, the total number of MACE was 29 (17%): 1 cardiovascular death, 6 target lesion revascularizations and 22 acute coronary syndromes.
Conclusions: Although less frequently than in pts allocated to ITS, for the first time a randomized study shows that FFR changes the therapeutic strategy and warrants the performance of intervention in a substantial proportion of pts with intermediate coronary stenoses allocated to CTS by ANGIO. A full-scale trial is testing if therapeutic strategy change will translate into relevant clinical benefit over the long run.

6618 | BEDSIDE
Relationship between atherosclerotic plaque components on optical coherence tomography and chronic kidney disease in patients with coronary artery disease

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Purpose: Patients with chronic kidney disease (CKD) have increased risks of cardiovascular events. Progression of atherosclerosis has been reported to be influenced by the presence of CKD. However, the characteristics of atherosclerotic coronary plaques according to the stage of CKD have not been fully clarified. We sought to assess the relationship between the stage of CKD and coronary plaque morphologies by optical coherence tomography (OCT) examination.
Methods: We investigated 258 consecutive lesions in 258 consecutive patients with stable angina pectoris that underwent percutaneous coronary intervention with OCT examination. All lesions were divided into the three groups according to estimated glomerular filtration rate (eGFR); non-CKD group (eGFR ≥60 ml/min/1.73m^2, n=132), CKD group (15 ml/min/1.73m^2 ≤ eGFR <60 ml/min/1.73m^2, n=102), and end-stage kidney disease (ESKD) group (eGFR <15 ml/min/1.73m^2 and/or hemodialysis, n=24). Among the three groups, plaque morphologies at the narrowest culprit sites on OCT were evaluated.
Results: CKD group had a higher frequency of lipid-rich plaque (lipid arc >180 degrees) (62.8% vs. 44.7%, p=0.008), thin-cap fibroatheroma (lipid arc >180 degrees and cap thickness <70 μm) (25.5% vs. 13.6%, p=0.03) and longer lipid length (3.4±3.7 mm vs. 2.3±3.2 mm, p=0.03) than non-CKD group. There was no difference in the amount of calcification arc, thickness and length between CKD group and non-CKD group. ESKD group had a higher frequency of plaque rupture (33.3% vs. 14.7%, p=0.04), calcified plaque (calcification arc >90 degrees) (58.3% vs. 26.5%, p=0.007), and longer calcification length (5.7±5.9 mm vs. 2.8±5.3 mm, p=0.02) than CKD group. In hemodialysis patients, the duration of hemodialysis was not correlated with calcification arc, thickness or length.
Conclusions: In the present study, the prevalence of CKD was related with the growth of lipidic coronary plaques. Further, the advance of CKD was related with the occurrence of silent plaque rupture and plaque calcification. This study suggests that the progression of CKD might accelerate the atherosclerotic changes of coronary plaques, leading to the occurrence of cardiovascular events.

6619 | BEDSIDE
Impact of intravascular imaging guidance in high-risk percutaneous coronary intervention: propensity adjusted analysis

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Background: Use of intravascular imaging to guide intracoronary stenting has been purported to reduce the incidence of major adverse cardiovascular events (MACE). Despite expert recommendations, routine use in the US and Europe is under 10%.
Purpose: We sought to determine the impact of intravascular ultrasound or optical coherence tomography use in high-risk percutaneous coronary intervention (PCI) on ischaemic outcomes of death, target vessel revascularisation (TVR) and MACE. MACE was a composite of all-cause death, myocardial infarction (MI) and TVR at one year.
Methods: We analyzed patients in a high volume single-centre PCI registry between 1 January 2009 and 31 October 2013. Clinical characteristics and patient

outcomes were compared by use of intravascular imaging in high-risk PCI. High risk was defined as PCI of the left main, bifurcation lesions, thrombotic lesions or in-stent restenosis.

Results: A total of 6429 patients underwent PCI satisfying the study criteria, 749 (12.0%) with imaging and 5680 (88.0%) with angiographic guidance alone. The groups were similar for age (mean, 65.5±11.6 years) and female gender (31.0%). The imaging group had a higher prevalence of hypertension, hyperlipidemia, anaemia, but less chronic kidney disease, prior revascularisation or other vascular disease. They also had a greater prevalence of stable angina. Procedurally they had shorter, less complex, thrombotic or calcific lesions and less chronic total occlusions. They were more likely to have drug eluting stents, larger stents, post-dilation, and final TIMI 3 flow. Unadjusted rates of one-year death (1.87% vs 4.14%, p=0.0025), TVR (6.5% vs 9.5%, p=0.0089) and MACE (9.5% vs 14.9%, p<0.0001) were lower in the imaging group as compared to the angiography group. After adjusting for propensity scores, associations remained significant for lower death (HR 0.50, 95% CI 0.31–0.82, p=0.006), TVR (HR 0.79, 95% CI 0.62–1.00, p=0.048) and MACE (HR 0.73, 95% CI 0.58–0.92, p=0.008) with imaging guided PCI.

Conclusions: Among patients undergoing high-risk PCI, use of intravascular imaging was independently associated with a lower incidence of death, TVR and MACE at one year.

Acknowledgement/Funding: None

6620 | BEDSIDE
FFR risk continuum for target vessel failure: a FAME 2 trial subanalysis

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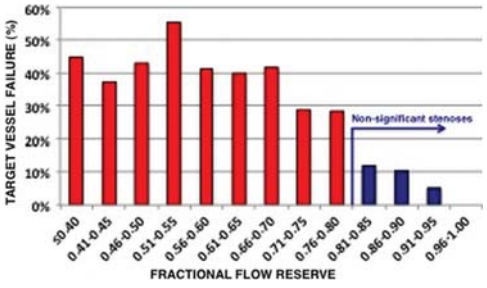
Purpose: In FAME 2 trial, 607 patients (pts) with stable coronary disease and in whom FFR was measured in all angiographically visible stenoses were put under medical therapy alone (MT). We investigated in these pts the relationship between the actual FFR values and target vessel failure at 2 years.

Methods: TVF was defined as the composite of cardiovascular death, myocardial infarction, and ischemia-driven target vessel revascularization (both urgent and non-urgent). The relationship between FFR and 2-year TVF was assessed as continuous function. Logistic and Cox proportional hazards regression models were used to calculate relative risks for each decrease of FFR by 0.05.

Results: TVF occurred in 272 (26.5%) out of 1029 lesions at a follow-up of 23.2±2.4 months. The TVF group presented more often with diameter stenosis (DS) ≥70% (p<0.01), as compared with non-TVF group. Mean FFR was significantly lower in TVF than in non-TVF group (0.66±0.14 vs. 0.77±0.14, p<0.001). FFR significantly correlated with TVF (OR: 0.81 [0.76–0.86], p<0.001). At the multivariate Cox regression analysis (adjusted for common cardiovascular risk factors), FFR was significantly associated with TVF at 2 years (HR [95% CI]: 0.84 [0.80–0.88]).



Conclusions: In pts with stable coronary disease, the actual value of FFR is an independent predictor of vessel-related clinical outcome. Each FFR increase by 0.05 was associated with a nearly 20% relative reduction in the risk of two-year TVF.

6621 | BEDSIDE
First clinical and intracoronary evaluation of indocyanine green for targeted intravascular near-infrared fluorescence imaging of high-risk atherosclerotic plaques

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Background: Novel, high-resolution, translatable imaging methods are needed to detect and understand high-risk atherosclerotic plaques over time. Indocyanine green (ICG), an FDA approved near-infrared fluorescence (NIRF) imaging agent, targets macrophages and lipids in experimental atherosclerotic plaques. It is unknown, however, whether ICG NIRF imaging targets human plaques.

Purpose: We hypothesized that ICG can be used for intravascular imaging of high-risk plaques features such as inflammation in human carotid atherosclerosis with a hybrid NIRF and optical coherence tomography (OCT) catheter imaging system. To extend our findings to coronary arteries, we also tested whether ICG targets coronary atheroma in swine using intravascular NIRF-OCT imaging.

Methods: Eight patients were enrolled in the BRIGHT-CEA trial (NCT01873716) and injected with ICG 99±25 minutes before clinically indicated endarterectomy. Three saline injected patients were selected as controls. All eight carotid plaques were excised and analyzed by NIRF-OCT, fluorescence reflectance imaging, fluorescence microscopy (FM), and histopathological analysis. Furthermore, intravascular NIRF-OFDI imaging was performed on three atherosclerotic coronary arteries of a diabetic, cholesterol-fed swine. After injecting ICG intravenously, we performed x-ray angiography, intravascular ultrasound (IVUS) and NIRF-OCT imaging to evaluate ICG coronary plaque uptake.

Results: No adverse events occurred up to 30 days after injection. We demonstrate that ICG accumulates in severely stenotic plaques in vivo of all of ICG injected patients and is detectable by NIRF-OCT. Plaques from control patients were uniformly negative. Intravascular NIRF-OCT identifies ICG uptake in all swine coronary atheroma in vivo. Mechanistically, we show the first evidence that ICG deposition depends on endothelial integrity, that ICG not only is found in macrophage-rich areas, but also regions of frank plaque rupture, intraplaque hemorrhage and vasa vasorum.

Conclusions: This study provides new insights into the mechanism of binding ICG binding in atheroma, targeting high-risk plaque features in clinical patients with severe atherosclerosis. Intravascular NIRF-OCT imaging offers a novel clinically translatable approach to image important pathobiology in carotid and coronary plaques.

6622 | BENCH
Mechanisms of stent thrombosis analyzed by optical coherence tomography: insights from the national PESTO French registry

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Background: Stent thrombosis (ST) remains a diagnosis and therapeutic challenge for interventional cardiologists. ST may be triggered by different phenomenon that require specific treatment. However, angiography alone is frequently limited to correctly identify these mechanisms.

Purpose: This work aimed to investigate the characteristics, mechanisms and relative incidences of ST among a large cohort of patients explored by optical coherence tomography (OCT).

Methods: The PESTO study was a prospective national registry involving 29 French catheterization labs. Patients with acute coronary syndromes (ACS) were prospectively screened for presence of definite ST and explored by OCT after culprit lesion deocclusion.

ST were classified as acute (AST), sub-acute (SAST), late (LST) and very late (VLST), according to the Academic Research Consortium criteria. Baseline clinical, biological and angiographic characteristics were collected for each subject. Three independent operators unaware of patients' characteristics reviewed OCT data to identify the ST etiologies.

Results: The final analysis involved n=120 subjects (age 61.6±1.1 y, 89% male) who presented as STEMI in 82% of the cases. VLST was the clinical presentation in 75%, LST in 6% and SAST+AST in 19% of the patients. Bare metal stents (BMS) were involved in 39%, drug-eluting stents (DES) in 59% and bioresorbable vascular scaffold (BVS) in 2% of the cases. The delay between initial PCI and ST was longer in the BMS compared to the DES patients (6.5±0.9 vs. 3.1±0.4 y, p<0.0001).

OCT identified an underlying morphological abnormality in 96.7% of the cases, including struts significant malapposition (34.2%), ruptured neoatherosclerotic lesion (22.5%), stent major underexpansion (10.8%), coronary evaginations (8.3%), isolated struts uncoverage (8.3%), neointimal hyperplasia with thrombus (4.3%) and edge related disease progression (7.5%).

Ruptured neoatherosclerotic lesions were more frequently observed in BMS than in DES (36.2 vs. 13.7%, p<0.01), whereas the incidence of coronary evaginations was higher in the DES group than in the BMS group (12.3 vs. 2.1%, p<0.05). L+VLST were mainly related to struts malapposition (30.9%) and neoatherosclerosis (27.8%), whereas main A+SAST etiologies were malapposition (47.8%) and stent underexpansion (26.1%).

Conclusions: In this study, ST mainly occurred ≥1 year after initial procedure. OCT identified an underlying mechanical cause in 96.1% of the cases. Although the underlying mechanisms were various, struts malapposition was the most frequently observed cause, either for acute/subacute and late/very late ST.

6623 | BEDSIDE
A novel optical coherence tomography system for detection of a lipid-rich plaque

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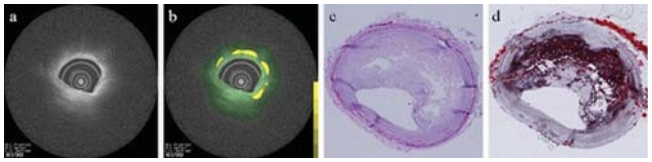
Background: A large lipid core within a coronary plaque is known as a risk for rupture. Intracoronary imaging devices are required to make a diagnosis of lipid-rich plaque accurately. Although commercially-available OCT systems use near-infrared light at 1,300 nm wavelength, lipid shows characteristic absorption in the short wavelength infra-red (SWIR) range. Therefore, we developed a novel, short wavelength infra-red (1,700 nm), spectroscopic and spectral-domain optical coherence tomography (SWIR-OCT).
Purpose: The aim of the present study is to validate the accuracy of SWIR-OCT for identification of lipid tissue within coronary plaques.
Methods: Twenty-five coronary arteries from 10 cadavers were examined. SWIR-OCT was performed at physiological pressure, and the images were acquired at 94 frames/s and digitally archived. SWIR-OCT generated gray-scale cross sectional images and color tissue maps of entire plaque by using an original lipid analysis algorithm. After SWIR-OCT imaging, the arteries were pressure-fixed, sliced by a cryostat and stained with H&E and Oil Red O, and then corresponding histology was collected in matched images. Regions of interest, selected from histology, were 110 lipidic and 29 non-lipidic regions.
Results: SWIR-OCT had high sensitivity (90%) and specificity (90%) for identifying lipid plaques in human coronary arteries. The positive predictive value and negative predictive value were 97% and 70%, respectively.



OCT images and sections of lipid plaque

Conclusion: SWIR-OCT accurately identified lipid tissue in coronary autopsy specimens. This new technique may hold promise for identifying histopathological feature of coronary plaques at risk for rupture.

6624 | BEDSIDE
Incidence, clinical presentation, and predictors of early-onset neoatherosclerosis after drug-eluting stent implantation

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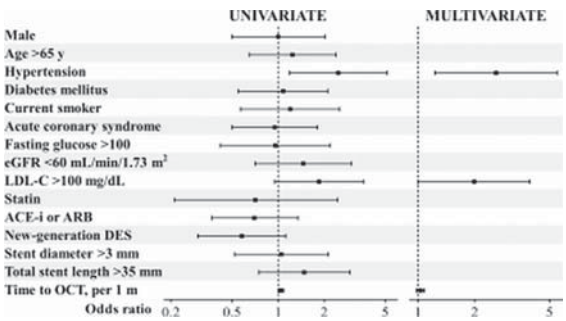
Background: Compared to bare-metal stent, neoatherosclerosis (NA) develops earlier and more frequently after drug-eluting stent (DES) implantation. Though NA has been recognized to be related to DES failure in process of time, the clinical implication of early-onset NA is not identified yet.
Purpose: This study purposed to evaluate the incidence, clinical presentation, and predictors of NA with early-onset within 30 months after DES implantation using optical coherence tomography (OCT).
Methods: Neointimal characteristics were evaluated in 529 patients (603 lesions) who underwent follow-up OCT $\leq$30 months after DES implantation (median 9.6 months), and displayed a mean neointimal thickness $>$100 μm. NA was defined as neointima with presence of lipid or calcification.
Results: Early-onset NA was observed in 41 lesions (6.8%). Patients with early-onset NA presented a higher incidence of clinical symptoms (15% vs. 55%, respectively; $p<0.001$) and had undergone a higher frequency of target-lesion revascularization (9% vs. 54%, respectively; $p<0.001$) compared to those without NA at the time of OCT follow-up. Independent predictors for early-onset NA were hypertension [odds ratio (OR) 2.60, 95% confidence interval (CI): 1.23–5.49; p=0.012] and low-density lipoprotein (LDL)-cholesterol $>$100 mg/dL at index procedure (OR 1.99, 95% CI: 1.00–3.93, p=0.049) in multivariate logistic regression analysis.



Predictors of neoatherosclerosis

Conclusions: Early-onset NA was detected in 6.8% of DES-treated lesions with neointimal thickness $>$100 μm at a median 9.6 months after DES implantation. Occurrence of early-onset NA was significantly associated with clinically symptomatic presentation. Independent predictors for early-onset NA were hypertension and high LDL-cholesterol level at index procedure.

6625 | BEDSIDE
Comparison between non-invasive coronary flow reserve, instantaneous wave-free ratio, and fractional flow reserve, to assess the functional significance of LAD stenosis of intermediate severity

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Assessment of the functional significance of left anterior descending coronary artery (LAD) stenosis of intermediate severity is challenging and often based on fractional flow reserve (FFR). The instantaneous wave-free ratio (iFR), a new vasodilator-free index of coronary stenosis severity, and non-invasive coronary flow reserve (CFR) by transthoracic Doppler echocardiography are also potentially useful. A direct comparison of FFR, iFR, and non-invasive CFR has never been performed. Therefore our objective was to test the usefulness of non-invasive CFR by comparison to invasive FFR and iFR in patients with LAD stenosis of angiographic intermediate severity and stable coronary artery disease.
Methods: Fifty eight stable consecutive patients (mean age, 68±10 years; 11 women, 19 diabetes; mean left ventricular ejection fraction, 59±10%) with angiographic proximal or mid LAD stenosis of intermediate severity (40–70% diameter stenosis on quantitative coronary angiography), no previous anterior myocardial infarction, were prospectively studied. They underwent iFR which was calculated as a trans-lesion pressure ratio during a specific period of baseline diastole, using fully automated algorithms, FFR with intracoronary bolus adenosine (150 μg), and CFR using intravenous adenosine (140 μg/kg/min over 2 min) in the distal part of the LAD, the same day. CFR was defined as hyperemic peak diastolic LAD flow velocity divided by baseline flow velocity, and FFR was defined as distal pressure divided by mean aortic pressure during maximal hyperemia.
Results: The mean values of iFR, FFR, and CFR were 0.88±0.07, 0.81±0.08, and 2.4±0.6 respectively. A significant correlation was found between CFR and FFR (r=0. 72, curvilinear relationship), FFR and IFR (r=0.63, linear relationship), and between CFR and IFR (r=0.44) (all, $p<0.01$). Using a ROC curve analysis, the best cut-off to detect a significant lesion based on FFR assessment (FFR $<$0.8, n=16) was iFR $\leq$0.86 with a sensitivity (Se) of 75%, specificity (Sp) of 81%, AUC 0.8±0.05; and CFR $\leq$2 with a Se of 82%, Sp of 85%, AUC 0.9±0.03, (all, $p<0.001$). Based on these cut-offs, discordant results between CFR and FFR were observed in 9 cases (accuracy 84%), between CFR and iFR in 14 cases (accuracy 76%), and between iFR and FFR in 11 cases (accuracy 81%).
Conclusion: In stable patients with LAD stenosis of intermediate severity, non-invasive CFR is a useful tool to detect a significant lesion based on FFR. Furthermore, CFR is better correlated to FFR than to iFR, and its accuracy seems as good as iFR in this setting.

CARDIOPULMONARY RESUSCITATION

6626 | BEDSIDE
Implementation of a medical emergency team leads to a reduction in cardiac arrest calls and enhanced patient care in the critically ill

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Background: The Modified Early Warning Score (MEWS) is a well-established guide used by hospital medical staff to help identify the acutely unwell patient. At our institution a dedicated Medical Emergency Team (MET) was introduced to attend when a patient's MEWS was 7 or above, to assess and optimize care before the development of peri-arrest or a cardiac arrest.
Purpose: To evaluate the MET impact on the quality of care in the critically ill hospital population.
Methods: A retrospective study of the resuscitation team database over 24 months. Introduced in December 2008, the MET – comprising of the on-call medical registrar, a HDU doctor and the critical care outreach team - would respond within 15 minutes once alerted when a patient's MEWS was 7 or above. Following each MET or cardiac arrest call, the team completed an audit form detailing the background, interventions and outcomes of each call. These forms were analyzed as were the long term outcomes of the patients.
Results: There were a total of 487 cardiac arrest calls over a 24 month period between 2007 & 2008 prior to the introduction of the MET. Between March 2012 and February 2014, 2204 MET calls were activated for 1484 patients. The median age was 77 (range: 67–86) years. 1887 calls (85.6%) resulted in the optimization of treatment: 188 patients (12.7%) were transferred to level 2 care (Coronary care unit/ High dependency Unit) and 69 (4.6%) were transferred to level 3 care (Intensive care unit). 133 patients (8.9%) were palliated in view of terminal illness. 317 patients were made not for resuscitation and of these 73 were discharged home alive. 624 patients (42.0%) who had MET calls were discharged from hospital alive. 117 (45.5%) patients whose care was escalated were discharged from hospital alive. Of the total activated MET calls 33 patients developed cardiac arrests. Overall cardiac arrest calls were reduced to 209 (P=$<$0.0001). 78 (37%) patients

in cardiac arrest group were successfully resuscitated and 10 (12.8%) of these patients had a MET call prior to arresting. 33 of the successfully resuscitated patients were discharged alive, and in this group, 4 (12.1%) patients had a MET call prior to arresting.
Conclusion: The MET has resulted in a 57.1% reduction in the number of cardiac arrest calls. It has augmented the management of critically unwell patients through; rapid assessment of patients; timely decision making on ward management; care escalation; and identifying patients for palliative management. Adoption of the MET approach in acute hospital care leads to enhanced patient care and efficient use of available clinical resources.

6627 | BEDSIDE
Bystander cardiopulmonary resuscitation associated with lower risk of nursing home admission and anoxic brain damage in out-of-hospital cardiac arrest survivors

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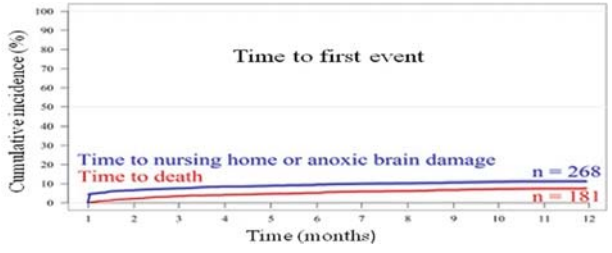
Introduction: Survival after out-of-hospital cardiac arrest (OHCA) has improved in recent years, but the degree of disability in survivors is not fully elucidated. Therefore, we examined admission to nursing homes and anoxic brain damage in survivors.
Methods: During 2001–2011 in Denmark, 2,469 of 32,883 OHCA patients survived 30 days. We excluded survivors <18 years of age (n=27), those living in a nursing home (n=51) and those who had anoxic brain damage (n=4) before arrest. We used cause-specific Cox regression to examine predictors of death and a composite end point of nursing home or anoxic brain damage within one year after OHCA.
Results: Of 2,387 30-day survivors (median age 62 years [IQR 18], 76.6% men), 1,938 (81.2%) did not experience any events during the first year after OHCA; 181 (7.6%) died and 268 (11.2%) were admitted to nursing homes or diagnosed with anoxic brain damage (see Figure). Age ≥75 years, Charlson 10-year comorbidity score >0, unwitnessed arrest, non-shockable rhythm and non-cardiac cause of arrest were significantly associated with death. Bystander cardiopulmonary resuscitation (CPR) was the only factor significantly associated with lower risk of nursing home admission or anoxic brain damage in multivariable modeling (HR 0.67 [95% CI: 0.51–0.89], p=0.005), adjusted for age, sex, comorbidity, year of arrest, witnessed status, rhythm and cause of arrest.



Conclusions: More than 80% of 30-day survivors were not admitted to nursing homes or diagnosed with anoxic brain damage nor died within the first year after OHCA. Bystander CPR was the only factor associated with lower risk of nursing home admission or anoxic brain damage, underscoring the importance of CPR not only for improved chance of survival but also for quality of life after OHCA.

6628 | BEDSIDE
Relationship between electrocardiographic changes and neurologic outcomes in patients treated with multidisciplinary therapy after out-of-hospital ventricular fibrillation cardiac arrest: SAVE-J Study

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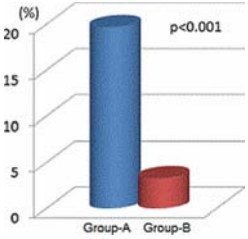
Background: Extracorporeal cardiopulmonary resuscitation (ECPR) have been reported to be effective in patients with out-of-hospital cardiac arrest (OHCA) associated with an initial rhythm of ventricular fibrillation (VF) refractory to standard advanced cardiac life support (ACLS). However, it remains unclear whether ECPR is effective for cardiac arrest (CA) patients with VF initially, but not when starting ECPR.
Methods: This multicenter prospective observational study was conducted in 46 hospitals. A total of 454 patients with OHCA aged 20–74 years had an initial rhythm of VF and arrived at the hospital within 45 minutes after the onset of CA. They did not respond to standard ACLS given for more than 15 minutes after hospital arrival and received combination therapy with ECPR, therapeutic hypothermia (TH) and intra-aortic balloon pump (ECPR group, n=260) or not (non-ECPR group, n=194). The ECPR group patients were divided into 2 groups according to rhythm changes by the time of starting ECPR, Group-A (sustained VF) and Group-B (changing from VF to non-shockable rhythm). A favorable outcomes defined as Cerebral Performance Category of 1–2 at 6 months after CA was compared.
Results: There were no significant differences among Group-A (n=127) and Group-B (n=123) in age, sex, and time from CA to ECPR start. The rate of favorable outcomes was significantly higher in Group-A than in Group-B (19.7% vs. 3.3%, p<0.001). Furthermore, the rate of favorable outcomes in patients with sustained VF improved about 5.5-fold by ECPR. In multivariate logistic-regression analysis, sustained VF during CPR was an independent risk factor associated with favorable outcomes as well as TH.



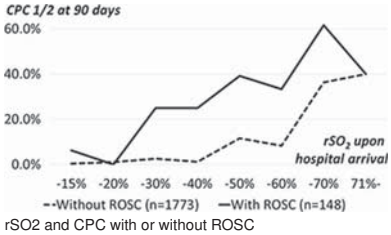
Comparison of favorable outcomes

Conclusions: Our results suggest that ECPR significantly improves neurologic outcomes in patients with sustained VF.

6629 | BEDSIDE
Characteristics of regional cerebral oxygen saturation levels in patients who experience out-of-hospital cardiac arrest with or without return of spontaneous circulation

K. Nishiyama[1], N. Ito[2], T. Orita[3], M. Abe[4], H. Yasuda[5], Y. Honma[6], H. Arimoto[7], M. Tokura[8], K. Hayashida[9], K. Nagao[10] on behalf of J-POP Registry Investigators. *[1]Kyoto University Graduate School of Medicine, Kyoto, Japan; [2]Kawasaki Saiwai Hospital, Kawasaki City, Japan; [3]Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan; [4]Kyoto Medical Center, Kyoto, Japan; [5]Musashino Red Cross Hospital, Musashino, Japan; [6]St Lukes International Hospital, Tokyo, Japan; [7]Osaka City General Hospital, Osaka, Japan; [8]Dokkyo Medical University Nikko Medical Center, Tochigi, Japan; [9]Keio University School of Medicine, Tokyo, Japan; [10]Nihon University, Tokyo, Japan*

Background: Regional brain oxygen saturation (rSO2) monitoring after out-of-hospital cardiac arrest (OHCA) is expected to be useful for estimating the quality of cardiopulmonary resuscitation for patients before the return of spontaneous circulation (ROSC). In addition, rSO2 may indicate the neurological prognosis upon hospital arrival for patients before or after ROSC.
Aim: The aim of our study was to evaluate the characteristics of rSO2 levels in OHCA patients with or without ROSC.
Methods: We enrolled 1,921 OHCA patients from the Japan - Prediction of Neurological Outcomes in Patients Post-cardiac Arrest Registry, and measured their rSO2 immediately upon arrival at the hospital using near-infrared spectroscopy via two independent forehead probes (right and left sides). We also assessed the percentage of patients with good neurological outcomes (defined as cerebral performance categories [CPC] 1 or 2) at 90 days post-cardiac arrest.
Results: After 90 days, 79 (4%) patients had good neurological outcomes and a lower median rSO2 level (15–20%). Compared to patients without ROSC, patients with ROSC upon arrival at the hospital had significantly high rSO2 levels (15% [15–17%] vs. 56% [39–65%], respectively; P<0.01) and significantly correlated right- and left-sided rSO2 levels (R=0.66 vs. 0.94, respectively). However, in both groups, the percentage of patients with a good 90-day neurological outcome increased significantly in proportion to the rSO2 levels upon arrival at the hospital (P<0.01, Figure).



rSO2 and CPC with or without ROSC

Conclusion: Our data indicate that measuring rSO2 levels after OHCA were effective for estimating and monitoring the quality of resuscitation and neurological prognosis upon hospital arrival.
Acknowledgement/Funding: JSPS KAKENHI (grant numbers 24390400 and 26462753)

6630 | BEDSIDE
Effectiveness of extracorporeal life support for patients with cardiogenic shock due to intractable arrhythmic storm

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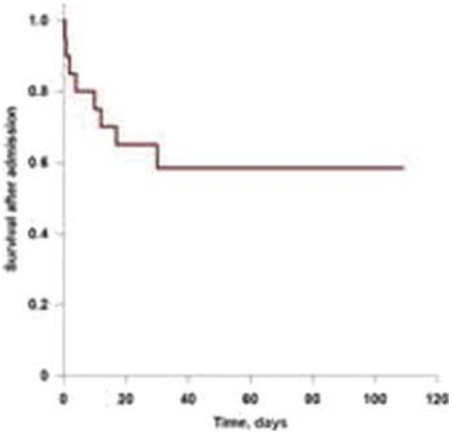
Background: Extracorporeal life support (ECLS) provides mechanical cardiopulmonary support and has been used for intractable heart failure as a bridge to heart transplantation or to recovery. Intractable arrhythmic storm is associated with high mortality.
Purpose: We aimed at analyzing the effectiveness of ECLS to treat refractory ventricular arrhythmias responsible for cardiogenic shock in patients non eligible for an urgent ablation.
Methods: Patients with intractable refractory ventricular arrhythmias and cardiogenic shock despite optimal medical therapy, and treated by ECLS implantation were retrospectively included. Patients' characteristics and outcome were analyzed.
Results: 20 patients (53±10 yo) were included. The underlying etiology to the refractory ventricular storm was ischemic cardiomyopathy (75%), short coupled Torsades de Pointes (10%), dilated cardiomyopathy (5%), myocarditis (5%) or unknown (5%). Mean LVEF was 33±17%. An average of 2.3±1.2 anti-arrhythmic drugs was tried before implantation. Arrhythmic storm stopped after a median time of 15 min after ECLS implantation. 8 patients (40%) eventually died, none of them because of a complication of ECLS implantation. The remaining 12 patients (60%) had ECLS withdrawn after a median time of 5.3 days, and were discharged after a median time of 29 days after admission (survival curve in the figure).



Survival after ECLS implantation

Conclusions: This is the largest database of patients temporary implanted with ECLS for refractory ventricular arrhythmia responsible for cardiogenic shock and non eligible for ablation. It provides efficient hemodynamic support to these critically ill patients, and survival rate after the implantation is 60%.

6631 | BEDSIDE
Outcome predictors in cardiopulmonary resuscitation facilitated by extracorporeal membrane oxygenation

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Background: Cardiac arrest remains a major cause of sudden death in developed countries. Extracorporeal cardiopulmonary resuscitation (ECPR) employs extracorporeal membrane oxygenation (ECMO) in patients without return of spontaneous circulation (ROSC) by conventional cardiopulmonary resuscitation (CPR). The aim of the current study was to assess short and long-term outcome in patients treated with ECPR in our tertiary center and to identify predictors of outcome.
Methods: We retrospectively collected data of all patients treated with ECPR at our institution from 2002 to 2013. Outcome was assessed according to patient records; good neurological outcome was defined as cerebral performance category 1 or 2. Data of quality of life was collected using EQ-5 questionnaire. Uni- and multivariate analysis was applied to identify predictors of outcome.
Results: One-hundred and seventeen patients were included into the study. Weaning from ECMO was successful in 61 (52%) patients. Thirty-day survival endpoint was achieved by 27 (23%) patients. Good neurological outcome was present in 17 (15%) patients. Multivariate analysis revealed serum lactate as the strongest predictor of outcome. The optimal lactate cut-off to discriminate outcome was revealed to be at 4.6 mmol/l (HR 3.55 (2.29–5.49), p log rank test <0.001).
Conclusions: ECPR represents a treatment option in patients without ROSC after conventional CPR rescuing 15% of patients with good neurological outcome.

6632 | BEDSIDE
Well-trained emergency life-saving technicians improve rates of return of spontaneous circulation and neurologic survival after out-of-hospital cardiac arrest

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Background: We found that dispatching emergency life-saving technicians (ELSTs) improved neurologic outcome of patients with cardiogenic out-of-hospital cardiac arrest (OHCA) witnessed by any ambulance service personnel, independent of advanced life support (ALS) provided by the ELSTs. In Japan, ELSTs are permitted to place peripheral intravenous (IV) catheters and supraglottic airway devices, and to use automated external defibrillator (AED). After advanced training ELSTs can be additionally qualified for endotracheal (ET) intubation and epinephrine (EPI) administration; we defined these individuals as well-trained ELSTs. We hypothesized that having well-trained ELSTs in attendance would improve rates of return of spontaneous circulation (ROSC) and neurologic survival after cardiogenic OHCA.
Methods: Data for all patients with witnessed cardiogenic OHCA from January 2008 to December 2012 were extracted from the Tokyo Utstein-style registry. Primary outcome measures were rates of ROSC before hospitalization and neurologic survival (Cerebral Performance Category [CPC] 1 or 2) 1 month later. A multiple logistic regression analysis was applied to assess the effects of well-trained ELST on resuscitation adjusted for factors known to potentially affect the outcomes.
Results: Out of 63,830 cases registered, we identified 780 adults with witnessed cardiogenic OHCA without physicians present. In all cases extracted, at least one ordinary or well-trained ELST was dispatched to every OHCA cases. The presence of well-trained ELSTs increased rates of ROSC and neurologic survival, with adjusted odds ratio (OR) of 2.557 (95% confidence interval [CI] 1.624–4.028) and 1.684 (95% CI 1.004–2.826), respectively.
Conclusion: The presence of well-trained ELSTs improved rates of ROSC and neurologic survival after cardiogenic OHCAs. Therefore, an increase in the number of ELSTs receiving advanced training may improve the resuscitation rate of OHCA patients in Japan.

6633 | BEDSIDE
Does the temperature influence on the moment of awakening in patients treated with therapeutic hypothermia after cardiac arrest?

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Introduction: Therapeutic hypothermia (TH) has shown to reduce brain damage after out-of-hospital cardiac arrest (OHCA). But the time to neurological recovery is not defined yet, and it may be altered by sedation and muscular relaxation. We sought to determine factors associated with a late post-arrest awakening.
Methods: We analysed a prospective database of OHCA patients treated with TH (32–34℃ during 24 hours), who regained conciousness after rewarming. We measured the time until awakening, defined as following commands.
Results: 123 of 256 OHCA patients treated with TH regained consciousness (84.5% male, mean age 60.1 years). Basal characteristics are shown in table 1. Mean temperature at admissionwas 35.3℃, target temperature was 32–33℃ (94.3%) or 34℃ (5.7%). Mean time to awakening was 4.8 days. We classified patients into four groups, separating the early awakers (<6 days, 3.2 days on average) from the late awakers (>6 days, 10.1 days on average). 39,8% of the patients awakened in <72 hours, 38.2% between day 3–6, 13.8% between day 7–9 and 8,1% after day 9. We found a higher proportion of late awakers among patients with a higher temperature at admission (p=0.049). A lower target temperature (32–33℃) was associated with a later awakening (4.87 vs. 2.8 days, p=0.02). 22.1% of the patients cooled to 32–33℃ were late awakers, one of them regained conciousness on day 33 after admission. No patientcooled to 34℃ awakened after day 6.
We found no significant association between other analysed factors and time to awakening.

Basal characteristics

	n=123 (100%)
Previous heart disease	45 (36.6%)
Witnessed arrest	116 (94.3%)
First rhythm VF	96 (78%)
First rhythm asystole	14 (11.4%)
First rhythm pulseless electrical activity	13 (10.6%)

Conclusions: Regarding OCHA patients treated with TH, withdrawal of life support after 5 days may be considered premature, regarding the high proportion of patients who awakened after 6 days. Although we didnd't find any predictors of late awakening, cooling to a lower target temperature may influence on a late neurological recovery.

6634 | BEDSIDE

In-hospital and mid-term outcome in resuscitated patients after out-of-hospital cardiac arrest complicating acute myocardial infarction (analysis from MIE ACS registry in Japan)

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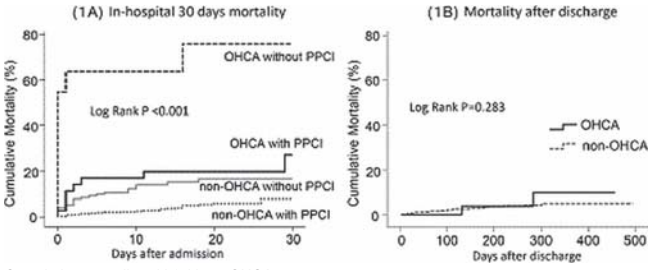
Background: The in-hospital outcome of resuscitated patients after out-of-hospital cardiac arrest (OHCA) complicating AMI remains poor. However, prognostic effect of early myocardial reperfusion and mid-term outcome have not been well evaluated.
Methods: From January 2013, we evaluated consecutive 1157 AMI patients (mean age 68±13 years, male 77%) from Mie ACS Registry, a prospective, multicenter registry. Mean follow-up duration was 269 days ranging 1 to 595. The clinical features, in-hospital and mid-term outcomes were compared between the patients with OHCA (OHCA group, n=48) and the patients without OHCA (non-OHCA group, n=1109).
Results: Among the OHCA group, the prevalence of VF/VT as first recorded rhythm was 58% and pre-hospital return of spontaneous contraction (ROSC) was obtained in 70%. Successful urgent primary PCI (PPCI) were underwent in 75% of OHCA and 87% of non-OHCA group (P=0.032). The in-hospital mortality rates were significantly higher in OHCA group than in non-OHCA group (34% vs. 5.4%, respectively, P<0.001). Moreover, among OHCA group, in-hospital mortality was much higher in the patients treated without PPCI than in the patients treated with PPCI (73% vs. 22%, respectively, P=0.002, Figure 1A). On the other hand, one-year mortality of OHCA patients who survived to hospital discharge were comparable to that of non-OHCA patients (4.2% vs. 9.1%, Log-rank P=0.283) (Figure 1B). The independent predictor of in-hospital survival among OHCA group were treatment with PPCI and pre-hospital ROSC (odds ratio (OR) 40.0, P=0.005 and OR 32.9, P=0.005, respectively).



Cumulative mortality with/without OHCA

Conclusion: Successful treatment with PPCI improved a chance of in-hospital survival for OHCA patients. Once survival to discharge, subsequent prognosis were relatively good regardless of with or without OHCA.

6635 | BEDSIDE

Pre-hospital cardiac arrest survivors sent for emergency angiography: who is more likely to experience an acute myocardial infarction?

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Background: Out-of-hospital cardiac arrest (OHCA) remains a major public health issue. Emergency coronary angiography (ECA) and percutaneous coronary intervention (PCI) might improve survival, especially when the cardiac arrest is caused by acute myocardial infarction (AMI). However, identifying patients with AMI after OHCA remains challenging.
Objectives: The aims of this study were to determine the clinical and ECG criteria in OHCA that may help to identify the patients with AMI and to determine the predictors of mortality.
Methods: Consecutive OHCA patients who underwent immediate coronary angiography at our center between 2009 and 2013 were included in this single-center registry.
Results: A total of 177 patients with complete datasets were included. Significant coronary artery disease (CAD) was found in 71% of the patients, and 43% presented AMI. The independent predictors of AMI were ST-elevation, including lead aVR (OR: 18.06; CI: 6.6–49.38), chest pain before cardiac arrest (OR: 4.05; CI: 1.55–10.54) and an initial shockable rhythm (OR: 2.99; CI: 1.34–6.45). An additive score that included these three predictors yielded a sensitivity and a specificity for detecting AMI of 93% and 63%, respectively. The survival rate was 33%. The independent predictors of death were age (OR: 1.09; CI 1.02–1.16), no-flow duration (OR: 1.21; CI: 1.02–1.43), low-flow duration (OR: 1.15; CI: 1.05–1.26) and a non-shockable rhythm (OR: 4.53; CI: 1.02–20.0).
Conclusions: These data suggest that fewer than half of patients with OHCA undergoing ECA present AMI. The identification of OHCA patients with AMI might be improved the use of a simple score using the post resuscitation ECG and simple clinical criteria.

PROGNOSIS

6636 | BEDSIDE

Nocturnal hypoxemic burden: time of hypoxemia represents a robust and independent predictor of death in chronic heart failure and reduced ejection fraction

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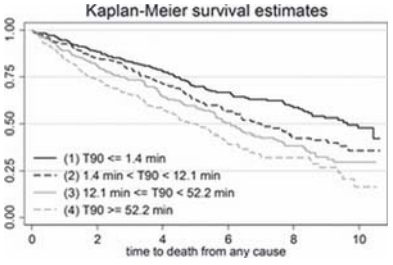
Background: Nocturnal oxygen desaturations, as seen in sleep-disordered breathing (SDB) may result in a progression of heart failure (HF).
Purpose: In a large cohort of chronic stable HF patients with reduced ejection fraction (HF-REF), we analyzed whether hypoxemic burden, defined as time patients spent with oxygen saturation below 90% (T90), predicts survival.
Methods: Cardiorespiratory polygraphy (PG) including pulse-oximetry was used to determine nocturnal oxygen saturation and T90 [min] in stable HF-REF (NYHA ≥II, LV-EF≤45%) patients treated according to present guidelines. Survival time (all-cause mortality) was analyzed in 963 HF-REF patients (65±11 years, 80.5% male, BMI 27±4, LV-EF 29.9±7.6%, median follow-up time 7.35 years (95% CI: 6.57- 7.81)). Quartiles of T90 were calculated and displayed as Kaplan-Meier survival estimates (figure).
Results: Death rates (per 100 person years) were 6.9 (95% CI: 5.7–8.4) in Q1, 9.4 (95% CI: 7.8–11.3) in Q2, 11.5 (95% CI 9.7–13.6) in Q3 and 14.9 (95% CI 12.6–17.6) in Q4, respectively. Using ROC analysis and the Youden criterion, a T90 of 22 min was identified to represent the best cut-point. In addition to known predictors of survival in HF-REF (e.g. age, ischemic etiology, NYHA class, LVEF etc), multivariate analysis revealed T90 as a robust predictor of all-cause mortality with a hazard ratio of 1.018 [95% CI: 1.008–1.029, p=0.001]: every minute up to 22 min a HF-REF patient has an oxygen saturation below 90%, his risk of death increases by 1.8%.



Conclusion: Nocturnal hypoxemic burden, defined as time of oxygen saturation below 90%, represents a strong, robust and independent prognostic parameter in HF-REF patients. Episodes of hypoxemia, like in sleep-disordered breathing, should be avoided and/or treated appropriately.

6637 | BEDSIDE

Prognostic impact of kidney disease in heart failure - A study of 47,716 heart failure patients in the Swedish heart failure registry

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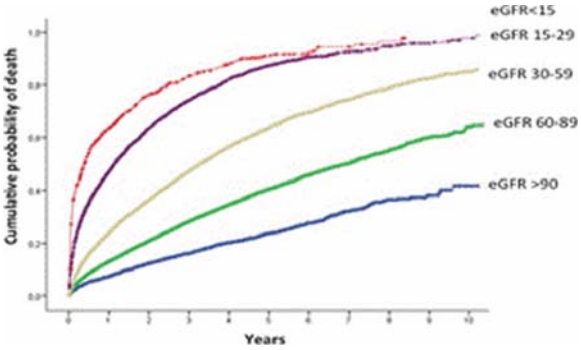
Background: Kidney dysfunction occurs in both acute and chronic heart failure (HF) and contributes to the severe outcome of HF. HF and kidney dysfunction constitute the cardiorenal syndrome. The long term prognostic impact of different degrees of kidney dysfunction in HF needs to be better addressed.
Purpose: The aim was to determine the prevalence of kidney dysfunction and to examine its association with baseline characteristics and the short and long term outcome in an unselected HF population.
Methods: We studied 47,716 patients in the Swedish Heart Failure Registry. Over 40 variables from the registry were included. Patients were divided into five degrees of renal function based on eGFR using CKD-EPI. Long term survival was assessed by Kaplan-Meier analyses and the association between kidney function and outcome by Cox proportional hazard regression.
Results: The median (IQR) age was 77 (67–84). A total of 24,225 (51%) patients had eGFR <60 ml/min/1.73 m^2 and 5,065 (11%) had eGFR <30. The 1-year mortality was 46% in those with eGFR <15–29 and 62% in eGFR <15. The cumulative probability of death at 5 years increased with lower eGFR (figure). The association between kidney dysfunction and outcome was still present after adjustment for variables related to kidney disease, heart failure and treatment with HR (95% CI) of 1.13 (1.03–1.24) in eGFR 30–59, 1.85 (1.67–2.07) in eGFR 15–29 and 2.96 (2.53–3.47) in eGFR <15. The association between kidney dysfunction and outcome showed a similar pattern regardless of age, presence of diabetes mellitus, anemia or NYHA class.



Kaplan-Meier, long term survival

Conclusion: Kidney dysfunction is strongly associated with short- and long-term outcome in patients with HF. These findings emphasize the importance of close follow- up and kidney preservation.

6638 | BEDSIDE
A Low baseline hsTnT value in acute heart failure identifies patients at very low risk for 180-day cardiovascular mortality: An analysis from the RELAX-AHF trial

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Background: Identification of acute heart failure (AHF) patients safe for discharge from the emergency department (ED) remains difficult. As myocardial injury identifies patients at higher risk, the absence of injury at baseline may identify low-risk patients.
Objective: To determine if a baseline hsTnT value ≤99th percentile upper reference limit (0.014 ug/L ("low hsTnT")) identifies patients at low risk for adverse events.
Methods: RELAX-AHF randomized AHF patients who were dyspneic, congested, with a SBP ≥125mmHg, moderate renal impairment, NT-proBNP ≥1600ng/L, and enrolled within 16 hours of presentation to serelaxin vs. placebo. Post-hoc analyses of patients (n=1076) with non-missing baseline troponin values (Roche Elecys assay) were performed using multiple regression models for continuous endpoints, and Cox-Proportional models for time-to-event endpoints including the troponin dichotomy, independent variables previously utilized in the main trial report, and other important clinical variables. Outcomes were pre-specified and consistent with previous RELAX-AHF analyses (Table).
Results: The 107 (9.9%) patients with a hsTnT value ≤0.014 ug/L were more likely to be female, have an EF >40%, lower uric acid, and NT-proBNP levels, and less severe renal impairment, and less diabetes, but no differences regarding history of ischemic heart disease. No cardiovascular (CV) deaths through day 180 were observed in the low hsTnT vs 79 CV deaths (7.3%) in higher hsTnT patients. By univariable analyses, a low hsTnT was associated with lower risk for all five primary outcomes (Table). However, after multivariable adjustment, only 180 day CV mortality remained significant (HR 0 (0, 0.736) p=0.0234).
Conclusion: No CV deaths through day 180 were observed in patients with a hsTnT ≤0.014ug/L. A low hsTnT at baseline may identify patients at very low risk for CV mortality.
Acknowledgement/Funding: RELAX AHF was sponsored by Corthera Inc, a Novartis affiliate company.

6639 | BEDSIDE
Absence of obesity paradox in ambulatory diabetic patients with heart failure

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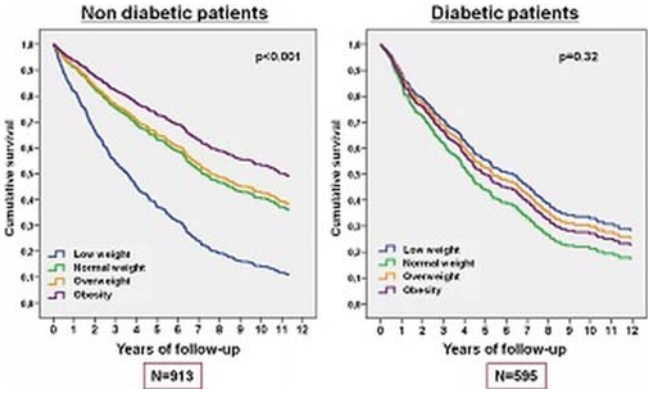
Introduction: Obesity is often paradoxically associated with survival in heart failure (HF). In HF patients of ischemic aetiology previous reports did not find such paradox; the effect of type-2 diabetes mellitus (T2D) is uncertain.
Purpose: To assess the relationship between body mass index (BMI) and long-term mortality in an ambulatory HF cohort relative to T2D presence or absence.
Patients and methods: Initial BMI and survival status after a mean follow-up of 6.1±2.1 years (up to 12 years) were available in 1508 ambulatory patients (73% men; mean age 68±2.1 years). T2D was present in 595 (39.4%) patients. Aetiology of HF was ischemic heart disease in 53% of patients. Mean LVEF was 33.5±17%. Patients were divided in 4 groups according to BMI (WHO 1999 classification): low weight (BMI <20.5 kg/m^2), normal weight (BMI 20.5 to <25.5 kg/m^2), overweight (BMI 25.5 to <30 kg/m^2) and obesity (BMI ≥30 kg/m^2).
Results: Mortality differed significantly across BMI strata in non-T2D patients but not in T2D patients (figure). Taking as reference normal weight patients, hazard ratios (HR) for low-weight, overweight and obesity were: 2.16 [1.54–3.04] p<0.001; 0.94 [0.75–1.18], p=0.60; and 0.66 [0.50–0.88], p=0.004; respectively for non-T2D patients; and 0.76 [0.37–1.56] p=0.46; 0.79 [0.60–1.02], p=0.07; and 0.80 [0.61–1.05], p=0.1, respectively for T2D patients. After adjustment for age, sex, HF aetiology, NYHA class, LVEF, and hypertension, BMI remained an independent predictor of survival in non-T2D (p<0.001) but not in T2D (p=0.76) patients.



Conclusion: The obesity paradox was only found in non-T2D HF patients after a long-term follow-up. BMI was not independently associated with survival in T2D HF patients.

6640 | BEDSIDE
Clinical implications of identifying co-morbid depression on heart failure prognosis in a community cohort

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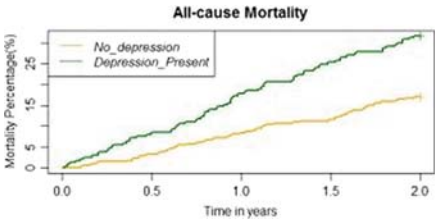
Background: Depression in Heart Failure (HF) patients is associated with poor outcomes; however, whether it is a prognostic marker above and beyond well known risk factors for HF prognosis is unknown.
Methods: HF patients in Minnesota, United States, completed a Patient Health Questionnaire (PHQ-9); those with a PHQ-9>4 were labelled as "depressed". Cox regression models were used to determine the risk of all-cause hospitalization and death over 2 years of follow-up, and negative binomial regression models estimated the rates of hospitalization for depressed vs. non-depressed patients. Results were adjusted for 10 commonly used prognostic factors (age, sex, systolic blood pressure, creatinine clearance, serum sodium and blood urea nitrogen, ejection fraction, raised brain natriuretic peptide, presence of diabetes and ischaemic etiology). Net Reclassification Improvement (NRI) was used to compare depression as a predictor against aforementioned factors.
Results: 604 patients (mean age 73 years, 56.3% males) were recruited to the study. Mortality after heart failure was worse for the depressed group (figure); the adjusted hazard ratio for death was 2.08 (95% CI 1.39–3.10.95) and for hospitalization was 1.48 (95% CI 1.18–1.84) for the depressed group. The rates of hospitalization for the depressed and non-depressed groups were 1.51 and 0.93 per person-year; while the adjusted rate ratio was 1.79 (95% CI 1.42–2.24 CI) for the depressed group. The NRI for depression as a predictor of death (risk categories: <10%, 10–40%, >40%) was 13.2% (p-value=0.01) and for hospital-

Abstract 6638 – Table 1. Effect sizes (95% CI) for outcomes

Outcome	Univariable model		Multivariable model	
	Effect	p-value	Effect	p-value
Days alive and out of hospital by day 60	3.671 (1.364, 5.978)	0.0018	1.876 (–0.443, 4.194)	0.1128
CV death or rehospitalization for HF or renal failure by day 60	0.463 (0.216, 0.991)	0.0472	0.758 (0.336, 1.712)	0.5053
Length of initial hospital stay (LOS)	–2.427 (–4.236, –0.619)	0.0085	–1.542 (–3.348, 0.265)	0.0944
Worsening Heart Failure (WHF) by day 5	0.259 (0.082, 0.821)	0.0217	0.303 (0.089, 1.034)	0.0566
CV death through day 180	0 (0, 0.422)	0.0025	0 (0, 0.736)	0.0234

ization (risk categories: <40%, 40–80%, >80%) was 9% (p-value=0.06), when compared to the commonly used prognostic model.



Conclusion: Identifying HF patients with depressive symptoms may have a potential role in HF risk prediction.

6641 | BEDSIDE
Long-term temporal patterns of serially measured circulating miR-22-3p and miR-378 are strong predictors of adverse clinical outcome in patients with chronic heart failure: results from the Bio-SHiFT

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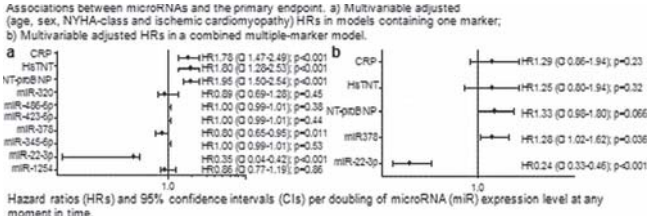
Background: Several studies have suggested circulating microRNAs (miRs) are associated with heart failure, but these studies were small, and limited to single miR measurements.
Purpose: We examined 7 earlier identified miRs and tested whether their temporal expression level predicts prognosis in a prospective cohort of chronic heart failure (CHF) patients.
Methods: In 2011–2013, 263 CHF patients were included. At inclusion and subsequently every 3 months, we measured 7 miRs. The primary endpoint (PE) comprised heart failure hospitalization, cardiovascular mortality, cardiac transplantation and LVAD-implantation. Associations between temporal miR patterns and the PE were investigated by joint modelling, which combines mixed models with Cox regression.
Results: Mean age was 68±12 years, 72% were men and 27% NYHA class III–IV. Mean follow-up was 1.0±0.5 years. We used 873 blood samples (median 3 (IQR 2–5) per patient). The PE was reached in 41 patients. Temporal patterns of miR22–3p and miR378 level were associated with the PE (figure). Instantaneous change in level (slope of temporal miR pattern) was also independently associated with the PE for these miRs (HR [95% CI] per doubling of slope for miR22–3p: 0.51 [0.22–0.90] and miR378: 0.48 [0.26–0.87]). A multiple-marker model containing the temporal patterns of miR22–3p, miR378, NT-proBNP, troponin T and CRP showed that miR22–3p and miR378 patterns were independently associated with the PE, whereas NT-proBNP, troponin T and CRP were not.



MicroRNAs and primary endpoint

Conclusion: Temporal expression levels of circulating miR22–3p and miR378 are strong and independent predictors of adverse prognosis in CHF. Our findings suggest that miRs reflect a different pathophysiologic process in CHF than natriuretic peptides or troponins and may aid in early therapeutic interventions.

6642 | BEDSIDE
Lower mortality but similar rates of heart failure readmission in young adults with heart failure: a nationwide Danish cohort study

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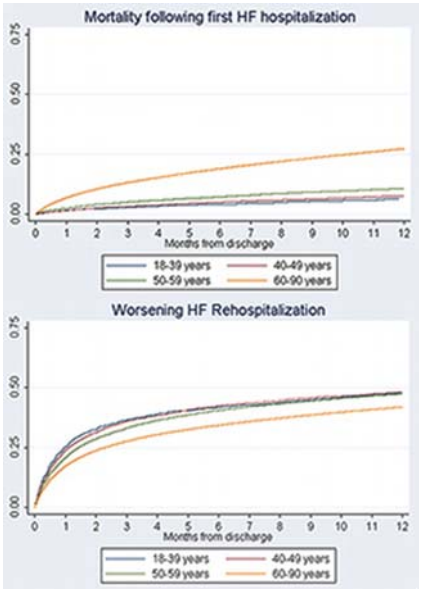
Background: Heart failure (HF) primarily affects older individuals and little is known about HF in unselected younger patients. To assess prognosis and burden of HF in young adults, we compared the risk of death and re-hospitalization after first HF hospitalization in Denmark according to age at diagnosis.

Methods: Patients with a first hospitalization for HF in 1997–2012 were grouped by age (18–39, 40–49, 50–59 and 60–90 years). In-hospital- and 30-days post-discharge rates of death, and rehospitalization for HF were assessed, and adjusted Cox regression models were applied to estimate 1-year risks of both outcomes as well as a composite of the two.
Results: Of 176,926 patients, 1916 (1.1%) were 18–39 years, 4512 (2.6%) 40–49 years, 13,839 (7.8%) 50–59 years, and 156,659 (88.5%) 60–90 years. In-hospital mortality ranged from 3.2% in the youngest group to 11.9% in the oldest. In patients discharged alive, 30-day mortality was 1.7%, 1.4%, 2.4%, and 6.0%, and 30-day rehospitalization for HF were 24.2%, 22.7%, 19.4%, and 14.6%, respectively. Compared to the youngest age group, 1-year risk of death were; 40–49 years, hazard ratio (HR) 1.38 (95% CI 1.08–1.75), 50–59 years, HR 1.75 (1.41–2.18), 60–90 years, HR 3.79 (3.07–4.68), whereas risk for HF rehospitalization was HR 0.93 (0.83–1.04), HR 0.94 (0.85–1.04), and HR 0.89 (0.81–0.98), respectively. Risk of the composite endpoint was HR 1.03 (0.92–1.15) in patients aged 40–49, HR 1.06 (0.96–1.17) in patients aged 50–59, and HR 1.15 (1.05–1.27) in the 60–90 years age group.



Conclusion: Young adults have lower mortality following first HF hospitalization but similarly high rates of re-hospitalization compared to older patients. Our findings emphasize the considerable disease burden associated with HF in young adults, despite the lower mortality.

6643 | BEDSIDE
Soluble ST2 is associated with outcome in patients with heart failure and anaemia: results from the RED-HF study

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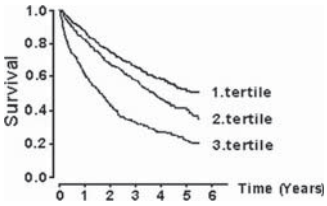
Background: The soluble ST2 receptor (sST2) is associated with outcome in patients with HF, but the value of repeated measurements of sST2 is not established.
Methods: We measured sST2 in plasma at baseline and after 6 months in 1582 patients enrolled in the Reduction of Events by Darbepoetin Alfa (RED-HF) trial. We explored the association between baseline tertiles of sST2 and the primary composite outcome of time to death from any cause or first hospital admission for worsening HF as well as time to all-cause death in multivariable Cox proportional hazard models. We also assessed the prognostic value of a change in sST2 levels with time.
Results: At baseline, the median sST2 plasma concentration was 38 (IQR 28–52) ng/ml. In univariate analyses, sST2 was a strong predictor of the primary outcome (hazard ratio [HR] for third tertile as opposed to first tertile: 2.67; p<0.001) (Figure) and all-cause death (HR 2.59; p<0.001). Its predictive value was attenuated, but remained significant for the primary endpoint (HR 1.46; p<0.001) and all cause death (HR 1.42; p<0.001) after adjusting for clinical variables, CRP, TnT, and NT-proBNP. There was no interaction between darbepoetin treatment and sST2 levels with regard to these endpoints. A stable sST2 level was associated with a significantly lower risk of reaching the primary endpoint and all-cause

death compared with an increase in ST2 levels ≥15% (HR 1.54 and 1.51, respectively) or a decrease in ST2 levels ≥15% (HR 1.44 and 1.31, respectively). These results remained significant after adjustment for clinical variables and CRP, TnT and NT-proBNP (all p-values <0.001).



Primary endpoint by tertiles of ST2

Conclusion: sST2 is a strong, independent predictor of outcome in patients with HF and anaemia. A stable level of sST2 seems to be associated with a favourable outcome.
Acknowledgement/Funding: The RED-HF study was funded by Amgen. The Presage ST2 assay was provided by Critical Diagnostics, San Diego, CA

6644 | BEDSIDE
Fibroblast growth factor 23 is an independent and specific predictor of mortality in patients with heart failure and reduced ejection fraction

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Background: As heart failure (HF) represents a common clinical condition associated with poor prognosis, strategies to improve risk prediction are of major importance in this critical patient group. Fibroblast growth factor 23 (FGF-23) is an endocrine regulator of phosphate and vitamin D homeostasis associated with an increased cardiovascular risk. We therefore aimed to assess the prognostic impact of FGF-23 on mortality in HF patients with a particular focus on differences between patients with reduced ejection fraction (HFrEF) and patients with preserved ejection fraction (HFpEF).
Methods: FGF-23 levels were measured in 980 HF (age: 63.8 [43.6–100.8] years, 66.8% male) patients enrolled in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study including 511 patients with HFrEF and 469 patients with HFpEF and a median follow-up time of 8.6 years. For external validation, FGF-23 was measured in a second cohort comprising 320 patients with advanced HFrEF. Diagnoses of HFpEF/HFrEF were based on current guidelines of the European Society of Cardiology. Cox regression models were used to assess the influence of FGF-23 on survival. The multivariate model was adjusted for age, sex, body mass index, NYHA classification, N-terminal pro B-type natriuretic peptide (NT-proBNP), left ventricular function, estimated glomerular filtration rate, coronary artery disease, hypertension, diabetes, atrial fibrillation, phosphate and 1,25-dihydroxyvitamin D3.
Results: In the LURIC cohort, FGF-23 independently predicted mortality with an adjusted (adj.) hazard ratio (HR) per one standard deviation (1-SD) increase of 1.30 (95% confidence interval [CI]: 1.14 - 1.48, P<0.001) in HFrEF patients, while no such association was found for patients with HFpEF (adj. HR per 1-SD: 1.12 [95% CI: 0.97 - 1.41], P=0.152; for interaction, P=0.043). Stratification into tertiles of FGF-23 showed a significant association with all-cause mortality with a crude HR of 2.26 (95% CI: 1.69 - 3.02; P<0.001) for the third tertile compared to the first tertile. External validation confirmed the significant association with mortality in HFrEF patients with an adj. HR per 1-SD of 1.23 (95% CI: 1.02 - 1.60, P=0.027). FGF-23 further demonstrated an increased discriminatory power to predict mortality in addition to NT-proBNP (C-statistic: 0.59 vs. 0.63, P=0.003) and an improvement in net reclassification index (39.6%, P<0.001).
Conclusion: Elevated levels of FGF-23 are independently associated with an increased risk of mortality in patients with HFrEF, but not in HFpEF, suggesting a different pathophysiologic role for both entities.

6645 | BEDSIDE
AHEAD score - long-term risc clasification in acute heart failure

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Background: Acute heart failure is a wide clinical syndrome and prognosis depends on large list of factors. So far there is no widely used long-term simple prognostic scoring system.
Objectives: To determine the role of co morbidities for the prognosis of patients hospitalized for acute heart failure using the AHEAD score system (A – atrial fibrillation, H – hemoglobin <130 g/l for male and 120 g/l for female (anemia), E - elderly (age >70 years), A - abnormal renal parameters (creatinine >130 mmol/l), D – diabetes mellitus).
Methods: For the statistical analysis data from 5 846 patients with primohospitalisation for acute heart failure (AHEAD registry; derivation cohort) were used to build AHEAD score. The Acute Heart Failure Database (AHEAD) Network registry comprises consecutive patients from ten centres with 24-h Catheter Laboratory services and centralised care for patients with acute coronary syndromes and from five regional centres. Each risk factor of the AHEAD score was count as 1 point. The model was validated externaly on international cohort of similar patients in the GREAT registry (n=6315).
Results: Mean age was 72±12 years, 61.6% of them were above 70 years, 43.4% were women. Atrial fibrillation was present in 30.7%, anemia in 38.2%, creatinine above 130 mmol/l (abnormal renal parameters) in 30.1% and diabetes mellitus in 44.0%. Mean AHEAD score was 2.1, the one year mortality for score 0 was 13.6%, for score 1 point 23.4%, for score 2 points 32.0%, for score 3 points 41.1%, for score 4 points 47.7% and for score 5 points 58.2% (p<0.001). The 90 month mortality for score 0 was 35.1%, for score 1 point 57.3%, for score 2 points 73.5%, for score 3 points 84.8%, for score 4 points 88.0% and for score 5 points 91.7% (p<0.001).
Conclusion: The AHEAD score system is a simple scoring system using co morbidities for estimating the short and long term prognosis in patients hospitalized for acute heart failure. Each comorbidity (age) increases the one year mortality by about 10%.

CARDIOVASCULAR PREVENTION: WHAT WORKS FOR WHOM?

6646 | BEDSIDE
Long-term effects of a cardiovascular prevention program in primary health care in Sweden

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Background: There are few studies of long-term effects from cardiovascular prevention programs. A cardiovascular prevention program, which combined an individual- and population based approach, started in 1988 in the primary health care in Sollentuna municipality, in Stockholm, Sweden.
Objective: To study first cardiovascular events (myocardial infarction, stroke, or cardiovascular death), during two decades after the implementation of a cardiovascular prevention program among those who participated (intervention group) compared with a matched population selected from the greater Stockholm area.
Methods: Individuals who underwent a health check-up and received advice on lifestyle to reduce cardiovascular risk in the prevention program during 1988–1993, aged ≥15 years and with no prior cardiovascular event (n=5 853, 35.7% men) were included in the study. They were compared with a population with no prior cardiovascular event and matched for age, gender, and education from the greater Stockholm area (n=35 118, 35.3% men). The enrollment time for the study populations was between 1988–08–08 and 1993–12–31. All subjects were followed until a cardiovascular event, death or 2012–12–31 whichever came first.
Results: The incidence of first cardiovascular event was lower in the intervention group (men 17.1%, women 9.2%) compared to the matched controls (men 18.0%, women 10.3%). The relative risk (95% confidence interval) was 0.90 (0.83–0.97), 0.92 (0.83–1.03) and 0.87 (0.78–0.98) in all subjects, in men and in women in the intervention group compared to the matched controls (referent 1.0).
Conclusion: This study indicates that a cardiovascular prevention program in primary health care focusing on identification of individuals at risk and lifestyle intervention, may have positive long-term effects on the incidence of cardiovascular events.
Acknowledgement/Funding: This study was supported by the Swedish Society of Medicine, and Heart and Lung Foundation in Sweden

6647 | BEDSIDE
Stairs instead of elevators at the workplace decreases PCSK9 levels in a healthy population

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Objective: Regular physical activity is recommended to lower low-density lipoprotein cholesterol (LDL-C) in a healthy population. Inhibition of proprotein convertase subtilisin/kexin-type 9 (PCSK9) was shown to reduce (LDL-C) levels, however the impact of physical exercise on PCSK9 levels remains unclear.

Approach and results: We used data from 67 healthy hospital employees who participated in a 6-month intervention promoting active use of stairs instead of elevators during 0–3 months, followed by 3 months without recommendation. We confirmed the degree of physical activity with estimated aerobic capacity (VO2 max) and measured serum PCSK9 levels at baseline, 3 month and 6 month. Using a multilevel regression model, we analysed changes of PCSK9 levels over time adjusting for age, gender, aerobic capacity, baseline LDL-C, LDL-C and body mass index (BMI) changes. At baseline, PCSK9 levels were associated with higher aerobic capacity (p value = 0.024). At 3 months, we observed a significant decrease of mean PCSK9 levels from 403.6 to 324.3 ng/ml (p value = 0.001), as well a significant decrease of mean LDL-C levels from 3.5 to 3.3 mmol/l (p value = 0.01). During this period, mean aerobic capacity (VO2 max) increased from 37.0 to 40.4 ml/kg per minute (p value <0.001). Physical activity was independently associated with a decrease in PCSK9 levels after adjustment for age, gender, baseline aerobic capacity, LDL-C values and BMI changes.
Conclusion: Daily physical activity at the work place is independently associated with a decrease of PCSK9 levels over time.

6648 | BEDSIDE
Comparative effectiveness of transitional care services in patients discharged from hospital with heart failure: a meta-analysis

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Background: Patients are at increased risk of death and readmissions following heart failure (HF) hospitalization. Services that support patients transitioning from hospital to home can improve clinical outcomes, but their comparative effectiveness is unclear.
Purpose: To compare the effectiveness of transitional care services (TCS) in decreasing all-cause mortality and readmissions following HF hospitalization.
Methods: We searched Pubmed, Embase, CINAHL, and Cochrane for articles published between 2000–2014. We included RCTs that recruited hospitalized patients with a primary diagnosis of HF, tested efficacy of a TCS intervention, provided >1 month of follow-up, and reported outcomes of all-cause mortality or readmissions. Two authors independently reviewed each study and extracted data.
Results: We included 45 RCTs with 9571 HF patients. Interventions included education alone, pharmacist, telemonitoring, telephone support, home visits, disease management clinics (DMCs) or case management. Overall, TCSs significantly decreased all-cause mortality (RR 0.83, 95% CI 0.77–0.88) and readmissions (RR 0.80, 95% CI 0.72–0.90). Among services that decreased all-cause mortality, DMCs (RR 0.65, 95% CI 0.53–0.81) were most effective, followed by telephone support (RR 0.78, 95% CI 0.61–0.99); home visits (RR 0.84, 95% CI 0.72–0.99); and case management (RR 0.85, 95% CI 0.77–0.94). Services that decreased all-cause readmissions include case management (RR 0.75, 95% CI 0.57–0.99), and DMCs (RR 0.79, 95% CI 0.68–0.92). The other interventions did not improve all-cause mortality or readmissions.

All-cause mortality & readmissions

Intervention	Mortality (RR, 95% CI))	Readmission (RR, 95% CI)
Education only	0.96 (0.30–4.74)	Nil
Pharmacist	0.83 (0.53–1.30)	0.90 (0.63–1.28)
Telemonitoring	0.89 (0.56–1.41)	0.76 (0.47–1.23)
Telephone	0.78 (0.61–0.99)*	0.95 (0.81–1.10)
Home visits	0.84 (0.72–0.99)*	0.64 (0.40–1.03)
Disease management clinics	0.65 (0.53–0.81)*	0.79 (0.68–0.92)*
Case-management	0.85 (0.77–0.94)*	0.75 (0.57–0.99)*

Conclusion: Telephone support, DMCs, home visits and case management decreased all-cause mortality or readmissions after HF hospitalization. These strategies should be considered following HF admission.

6649 | BEDSIDE
Effects of interactive patient support with a smartphone app on drug adherence and lifestyle changes in myocardial infarction patients

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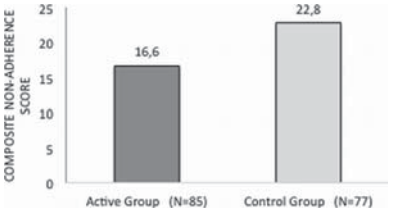
Background: Myocardial infarction (MI) patients seldom reach recommended targets for secondary prevention. Smartphone applications (apps) aimed at improving adherence and cardiovascular lifestyle in MI patients have not previously been evaluated in a randomised trial.
Methods: In this multicenter trial, 174 ticagrelor-treated MI patients were randomised to either an interactive motivational app (active group) or a simplified control app (control group) in addition to usual care. The primary end point pointwas a composite non-adherence score measuring patient-registered ticagrelor adherence, defined as number of non-adherence events (≥2 missed doses registered in 7-day cycles) and/or treatment gaps (≥4 consecutive missed doses). Secondary end pointspoints included change in cardiovascular risk factors, quality of life (EQ-5D), and patient satisfaction (System Usability Scale).
Results: The mean age of patients was 58 years; 81% were men, and 20% were current smokers. At 6 months, greater patient-registered drug adherence was achieved in the active group, compared with the control group (non-adherence score: 16.6 vs. 22.8 [p=0.025]). There was a positive trend for smoking cessation (80% vs. 45%; p=ns), improved quality of life (83 vs. 78; p=ns), increased physical activity (exercise, minutes/week: 79 vs. 67; p=ns) in the active, group compared with the control group. Patient satisfaction was higher in the active, group compared with the control group (87/100 vs. 78/100; p=0.001)



Composite non-adherence score

Conclusions: For MI patients, use of the smartphone app improved patient-registered drug adherence and showed positive trends in cardiovascular lifestyle changes and quality of life. The use of disease-specific interactive apps may be an appreciated, simple, and promising complement to standard secondary prevention.
Acknowledgement/Funding: The study was funded by AstraZeneca

6650 | BEDSIDE
Effect of a multi-dimensional secondary prevention program on cardiovascular events in patients hospitalized with acute coronary syndromes: a multicentric Swiss prospective trial

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Introduction: European guidelines recommend the implementation of national initiatives to improve secondary prevention after acute coronary syndromes (ACS). We designed an multidimensional program (ELIPS) early after ACS targeting patients, healthcare providers and the hospital organization to improve quality of care of patients after ACS. We report here its impact on clinical outcomes.
Methods: The ELIPS program was implemented in 4 Swiss academic hospitals from 2009 to 2012 (NCT01075867) with actions at three levels: (1) patient education using interactive tools (film, wall chart, informational cards, website,); (2) training of care-providers in motivational interviewing; (3) healthcare system intervention with codified transmission of patient discharge information. The evaluation was based on a before-after design (control-intervention groups). The primary efficacy outcome at one year was a composite of major adverse cardiovascular events (MACE) including all-cause death, myocardial infarction, coronary revascularization, stroke, hospitalization for unstable angina and lower limb ischaemia. The secondary outcome was limited to "hard" MACE (cardiac death, myocardial infarction and stroke).
Results: A total of 2465 patients were included, of whom 1197 in the control group (2009–2010) and 1268 in the ELIPS intervention group (2011–2012). The primary endpoint presented in 158 patients in the control group (13.2%) compared to 149 (11.8%) in the intervention group (age and sex adjusted Odds ratio [OR] 0.93, 95% confidence intervals [CI] 0.73–1.18, P=0.5). The secondary endpoint events presented in 6.6% patients in the control group compared to 5.4% in the intervention (OR 0.88, 95% CI 0.63–1.24, P=0.5). In stratified analyses, we found a significant reduction in patients younger than 65 years old (3.3% vs. 5.7%, OR 0.57, 95% CI 0.34–0.96, P=0.04).
Conclusions: The implementation of a multidimensional secondary prevention program early after an ACS was not associated with a significant reduction in cardiovascular events at one year. There was however a benefit in patients younger than 65 years old in whom there was a significant reduction of cardiac death, myocardial infarction and stroke events, suggesting the importance of intensive secondary prevention in this population.

6651 | BEDSIDE

Myocardial function and systemic anti-inflammatory drugs in patients with severe psoriasis: a prospective echocardiographic study

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Aims: Psoriasis is a chronic inflammatory disease and is associated with cardiovascular events, including myocardial infarction, stroke, heart failure, and cardiovascular death. Little is known about subclinical myocardial dysfunction and potential changes in myocardial function during anti-inflammatory treatment. We prospectively studied left ventricular function in patients with severe psoriasis who underwent systemic anti-inflammatory treatment between November 1 2013 and May 31 2014.
Methods: The study subjects underwent physical, laboratory, and comprehensive echocardiographic examination at baseline and after 3 months of treatment. Pearson correlation coefficients and Students t-test were applied to assess changes in diastolic function and global longitudinal strain (GLS).
Results: Twenty-two patients with severe psoriasis treated with systemic anti-psoriatic drugs with a mean follow-up of 88.2±21.3 days were included. The patients had a baseline psoriasis area and severity index (PASI) of 11.7±4.3 and normal left ventricular ejection fraction ([LVEF] 56.0±3.5%), diastolic dysfunction (E/e' 8.2±2.5), and GLS (– 16.9±2.1%). At follow-up an improvement of PASI (11.7±4.3 vs. 3.1±3.3, p<0.001), E/e' (8.2±2.5 vs. 6.9±2.0, p=<0.001), and GLS (–17.0±2.1 vs. –18.2±2.1%, p<0.001) were recorded. In addition, ΔPASI was non-significantly correlated with ΔGLS (r=0.35, p=0.11). Smoking status and concomitant medications use were unchanged at follow-up. No significant changes (baseline vs. follow-up) were demonstrated in, LVEF (56.0±3.5 vs. 56.5±3.2%, p=0.27), BMI (31.0±6.7 vs. 31.1±6.8 kg/m^2, p=0.68), MAP (102.4±9.0 vs. 102.8±10.5 mmHg, p=0.82), TC (4.7±0.9 vs. 4.7±0.8 mmol/L, p=0.92), LDL (2.6±0.75 vs. 2.6±2.2 mmol/L, p=0.44), HDL (1.2±0.26 vs. 1.3±0.4 mmol/L, p=0.49), eGFR (85.0±7.1 vs. 83.7±7.5 mmol/L, p=040), or HbA1c (40.5±11.5 vs. 40.6±9.8 mmol/mol, p=0.91). Improvements were also apparent when restricting the analyses to patients treated with tumour necrosis factor inhibitors, i.e. E/e' 8.1±2.7 vs. 6.7±1.9 (p=0.001), and GLS –16.8±2.1 vs. –18.3±2.2% (p<0.001).
Conclusion: This is the first study of changes in myocardial function during treatment with anti-inflammatory drugs in patients with severe psoriasis. Treatment with anti-inflammatory drugs was associated with amelioration of myocardial dysfunction. The results indicate an early beneficial effect of effective anti-psoriatic treatment on cardiac function in patients with severe psoriasis.

6652 | BEDSIDE

Change in CHD secondary prevention paradigm: improved medical blood pressure and hyperlipidaemia control, but increasing prevalence of obesity and diabetes inadequately controlled by lifestyle changes

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Background: The decline in cardiovascular mortality in Europe over the last three decades has resulted in particular from improved risk factor control and prevention interventions in addition to improved treatment.
Purpose: To ascertain the development of CHD secondary prevention in last 18 years.
Methods: EUROASPIRE I-IV cross sectional surveys were carried out in the Czech Republic in 1995/96, 1999/2000, 2006/2007, and 2012/13. Consecutive patients, men and women <70 years of age who had been hospitalized for acute coronary syndrome or revascularization procedures, were identified retrospectively. Data were collected through an interview with examinations at least six months after hospitalization according to EUROASPIRE Study protocols.
Results: In the period 1995/96–2013/14, systolic and diastolic blood pressure decreased significantly (by 9 and 5 mm Hg, respectively). A significant decrease was also seen in total and LDL-cholesterol (from 5.41 to 4.36 mmol/L and from 3.4 to 2.37 mmol/L, respectively). HDL-cholesterol a triglyceride levels did not change significantly. Fasting glycemia inreased significantly from EA II to the EA III survey. Prevalence of hypercholesterolemia and insufficiently controlled hypertension decreased from 87% to 39%, and from 64% to 40%, respectively. Prescription of aspirin, beta-blockers, ACEI and statins increased and most patients are treated by them now, though frequently not with sufficient doses. Prescription of statins increased from 7.3% to93.3%, and that of antidiabetics from 9.8% to 29.6%. The proportion of patients with revascularization procedure increased in the surveys from 49% to 95%. On the other hand, body mass index a waist circumference increased significantly (from 28.6 to 29.5 kg/m^2, and from 98.0 to 104.8 cm, respectively). Prevalence of obesity, central obesity and impaired glucose metabolism increased considerably - prevalence of diabetes from 23.4% to 47.7%. The prevalence of smoking did not change significantly.
Conclusion: There has been a change in CHD secondary prevention. While control of high blood pressure and hypercholesterolemia is improving, mainly due to extensive use of drug therapies, the prevalence of obesity and diabetes is increasing alarmingly, suggesting that implamentation of lifestyle changes is not sufficiently pursued. We need to improve physician-patient communication and patient motivation, not so much therapeutic procedures.
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6653 | BEDSIDE

Patterns of statin use and outcomes following myocardial infarction among Medicare beneficiaries

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Background: Current guidelines recommend high potency statins following a myocardial infarction (MI). However, few data are available on long-term adherence to this recommendation.
Objective: We estimated the percentage of patients who maintained high adherence to high potency statins, down-titrated to lower potency statins, or discontinued statins over 6 and 24 months after hospitalization for MI. Risk for death or recurrent MI associated with statin use patterns was also determined.
Methods: The study population included adults >65 years of age enrolled in Medicare, a government health insurance system for the elderly in the United States. We included Medicare beneficiaries hospitalized for MI in 2007–2010 with full fee-for-service insurance coverage, including pharmacy insurance from 6 months prior the admission through 6 months after discharge, whose first fill within 60 days following discharge was for a high potency statin (atorvastatin 40 or 80 mg, rosuvastatin 20 or 40 mg, simvastatin 80 mg). High adherence was defined by a proportion of days covered ≥80%. Down titration was defined by a high adherence to low/moderate potency statins following a fill for high potency statins. Discontinuation was defined by >60 days with no statin supply and no subsequent statin refills. We analyzed all-cause deaths and recurrent MIs from 6 months after discharge through December 2011 (median follow-up 1.7 years).
Results: Among 2,912 Medicare beneficiaries who filled high potency statins within 60 days following discharge for MI, 57% had high adherence to high potency statins, 8% down-titrated to a lower potency statin, and 18% discontinued statins at 6 months. By 24 months post-discharge for MI, 40% of beneficiaries had high adherence to high potency statins, 16% down-titrated to a lower potency statin, and 25% discontinued statins. The hazard ratios comparing Medicare beneficiaries who maintained high adherence to high potency statins versus a combined group of those who down-titrated or discontinued statins was 0.75 (95% CI: 0.62, 0.91) for mortality and 0.85 (95% CI: 0.66, 1.10) for recurrent MI.
Conclusion: Down-titration or discontinuation of high potency statins is common following hospitalization for MI. Maintaining high adherence to high potency statins is associated with lower risk for death.
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6654 | BEDSIDE

Health outcomes and platelet-aggregation inhibition after acute myocardial infarction in clinical practice. Findings from the PIPER Study

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The aim of the PIPER (Platelet-aggregation Inhibition: Persistence with treatment and cardiovascular Events in Real world) was performed to assess health outcomes after acute myocardial infarction (AMI) in relation to exposure to mono or dual platelet-aggregation inhibition in an un-selected Italian population under clinical practice setting.
A retrospective cohort analysis using administrative databases kept by 9 Local Health Units (LHU) geographically distributed was performed. All beneficiaries of these LHUs hospitalized and discharged with a primary diagnosis of AMI between January 1, 2010 and December 31, 2011 were included. Hospitalizations for AMI and all-cause mortality occurring during the 12 months follow-up period from discharge were considered. In the same follow-up period, exposure (defined as ≥2 prescriptions) to platelet-aggregation inhibition was calculated. Multivariable analyses were conducted to check for possible confounders using a proportional hazards Cox regression model: demographic characteristics, other guidelines-recommended post-AMI therapies, including beta-blockers, ACE inhibitors/ARB, statin, and antiplatelet therapy, previous hospitalizations for cardiovascular disorders, diabetes).
A total of 13,133 patients were included in the analysis (age 69.7±13.6 years old, 65.8% males, 9.6% previously hospitalized for cardiovascular disorders, and 20.6% with diabetes), of whom 3,130 (23.8%) were not treated with platelet-aggregation inhibition. Among those patients treated with platelet-aggregation inhibition, 2,494 (24.9%) received mono platelet-aggregation inhibition therapy. After controlling for possible confounders, exposure to platelet-aggregation inhibition (compare with no exposure) was associated with reduced all-cause mor-

tality (hazard ratio [HR] 0.26, 95% confidence interval [CI] 0.19–0.37) and recurrent AMI (HR 0.29, 95% CI 0.19–0.45). In addition, exposure to dual platelet-aggregation inhibition (compared with mono platelet-aggregation inhibition) was associated with reduced all-cause mortality (HR 0.50, 95% CI 0.31–0.81) and recurrent AMI (HR 0.75, 95% CI 0.56–0.99). Percutaneous coronary intervention (PCI) made at the hospitalization for AMI was found to be associated with reduced all-cause mortality (HR 0.66, 95% CI 0.56–0.78).
Exposure to platelet-aggregation inhibition therapy and, specifically, to dual platelet-aggregation inhibition therapy after AMI was independently associated with a reduction in all-cause mortality and recurrent AMI risk.
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6655 | BEDSIDE

Low oxygen concentration is an associated risk of contrast induced nephropathy in patients with impaired renal function after cardiovascular angiography

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Background: Renal ischemia and direct toxicity of contrast media are involved in the pathogenesis of CIN. We previously reported that sufficient oxygenation before contrast medium administration can mitigate kidney injury and reduce the incidence of CIN after cardiovascular angiography.
Purpose: We investigated which concentration of partial pressure of oxygen in arterial blood (PaO2) is suitable for preventing incidence of CIN.
Methods: We studied 200 consecutive patients with impaired renal function (eGFR$<$60mL/min/1.73m^2) undergoing elective cardiovascular angiography. Patients were selected and randomly assigned to either an oxygen preconditioning group (n=100) or a control group (n=100). Oxygen preconditioning was achieved by administering 2 L/min of pure oxygen 10 min before exposure to contrast medium. The primary endpoint was occurrence of CIN, defined as an increase in the serum creatinine levels of $\geq$25% or 0.5 mg/dL above the baseline level within 48hrs of exposure. We evaluated PaO2 levels before and the end of the procedure. We also evaluated the risk factors of CIN such as contrast volume, creatinie clearance, hemoglobin concentration, brain natrium peptide, hemoglobin A1c (HbA1c) and PaO2 by logistic analysis using continuous data.
Results: In the oxygen preconditioning group, PaO2 was significantly higher (127±24 vs. 88±12mmHg, P$<$0.001) and the incidence of CIN was lower (2% vs. 11%, Odds ratio:OR 0.10, P=0.01) compared to that of the control group. By univariate analysis, PaO2 and HbA1c were significantly associated with a high incidence of CIN (OR 0.97, P$<$0.05, OR 1.74, P$<$0.05, respectively). Multivariate analysis revealed that PaO2 and HbA1c was the significant predictor of CIN (OR 0.963, 95% CI 0.934 - 0.993, P$<$0.05, OR 1.8, 95% CI 1.123–2.893, P$<$0.05, respectively). The reduction in systemic PaO2 was statistically significant in the control group following the procedures (130±24mmHg to 127±26mmHg in the preconditioning group, P$<$0.05; 89±14mmHg to 84±15 mmHg in the control group, P$<$0.05). Comparison of area under the curve (AUC) values for various cut-off PaO2 with the incidence of CIN demonstrated that a cut-off PaO2 of 89.5mmHg is a significant predictor for CIN and area of ROC curve of 0.712 (95% CI 0.59–0.84, P=0.01). For incidence of CIN, a ROC-optimized absolute PaO2 89.5mmHg was identified, yielding produced a sensitivity of 73.9% and specificity of 58.3%.
Conclusions: Oxygen preconditioning reduced the incidence of CIN in patients with reduced eGFR. Patients with a low oxygen concentration should consider being treated before coronary angiography for prevention of CIN.